OptumRx SP

Prior Authorization Guideline

GL-15425 Adcetris (brentuximab vedotin)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/7/2016

Technician Note :

P&T Approval Date: 11/15/2011; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Adcetris (brentuximab vedotin)

Indications

Classical Hodgkin Lymphoma (HL)

Indicated for treatment of patients with classical HL after failure of autologous hematopoietic stem cell transplantation (auto-HSCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates.

Classical Hodgkin Lymphoma (HL) Post-auto-HSCT Consolidation

Indicated for the treatment of patients with classical HL at high risk of relapse or progression as post-auto-HSCT consolidation. **Systemic Anaplastic Large Cell Lymphoma (sALCL)** Indicated for the treatment of patients with sALCL after failure of at least one prior multi-agent chemotherapy regimen.

2 . Criteria

Product Name: Adcetris

Diagnosis	Hodgkin Lymphoma (HL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Hodgkin lymphoma (HL) [1, 2]

AND

2 One of the following: [1,2]

- Failure of autologous hematopoietic stem cell transplant (auto-HSCT)
- Failure of at least two prior multi-agent chemotherapy regimens
- As post-auto-HSCT consolidation therapy for patients at high risk of relapse or progression

AND

3 Prescribed by or in consultation with an oncologist/hematologist

Product Name: Adcetris

Diagnosis	Hodgkin Lymphoma (HL)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Adcetris therapy.

AND

2 One of the following:

2.1 Patient does not show evidence of peripheral neuropathy [A]

OR

2.2 Both of the following: [B]

2.2.1 Patient has symptoms of new or worsening peripheral neuropathy

AND

2.2.2 Adcetris dose has been adjusted (eg, held dose, lowered dose)

Product Name: Adcetris

Diagnosis	Systemic Anaplastic Large Cell Lymphoma (sALCL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of systemic anaplastic large cell lymphoma (sALCL) [1, 2]

AND

2 Failure of at least one prior multi-agent chemotherapy regimen [1, 2]

AND

3 Prescribed by or in consultation with an oncologist/hematologist

Product Name: Adcetris

Diagnosis	Systemic Anaplastic Large Cell Lymphoma (sALCL)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Adcetris therapy.

AND

2 One of the following:

2.1 Patient does not show evidence of peripheral neuropathy [A]

OR

2.2 Both of the following: [B]

2.2.1 Patient has symptoms of new or worsening peripheral neuropathy

AND

2.2.2 Adcetris dose has been adjusted (eg, held dose, lowered dose)

3 . Endnotes

A. Adcetris treatment causes a peripheral neuropathy that is predominantly sensory. Cases of peripheral motor neuropathy have also been reported. Adcetris-induced peripheral neuropathy is cumulative [1]

B. For new or worsening Grade 2 or 3 neuropathy, dosing should be held until neuropathy improves to Grade 1 or baseline and then restarted at 1.2 mg/kg. For Grade 4 peripheral neuropathy, Adcetris should be discontinued. [1]

4 . References

1. Adcetris Prescribing Information. Seattle Genetics, August 2015.
2. National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium. http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed October 26, 2015.

Prior Authorization Guideline

GL-16900 Afinitor, Afinitor Disperz (everolimus)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/24/2016

Technician Note :

P&T Approval Date: 8/18/2009; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Afinitor (everolimus)

Indications

Advanced Neuroendocrine Tumors of Pancreatic Origin (PNET)

Indicated for the treatment of progressive PNET in patients with unresectable, locally advanced or metastatic disease. Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.

Advanced Renal Cell Carcinoma (RCC)

Indicated for the treatment of patients with advanced RCC after failure of treatment with sunitinib or sorafenib.

Renal Angiomyolipoma with Tuberous Sclerosis Complex (TSC)

Indicated for the treatment of adult patients with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery. The effectiveness of Afinitor in treatment of renal angiomyolipoma is based on an analysis of durable objective responses in patients treated for a median of 8.3 months. Further follow-up of patients is required to determine long-term outcomes.

Subependymal Giant Cell Astrocytoma (SEGA)

Indicated for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected in pediatric and adult patients with tuberous sclerosis complex (TSC). The effectiveness of Afinitor is based on demonstration of durable objective response, as evidenced by reduction in SEGA tumor volume. Improvement in disease-related symptoms and overall survival in patients with SEGA and TSC has not been demonstrated.

Advanced Hormone Receptor-Positive, HER2-Negative Breast Cancer (Advanced HR + BC)

Indicated for the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ BC) in combination with exemestane, after failure of treatment with letrozole or anastrozole.

Neuroendocrine tumors of gastrointestinal or lung origin

Indicated for the treatment of adults with progressive, well-differentiated, non-functional neuroendocrine tumors (NET) of gastrointestinal (GI) or lung origin that are unresectable, locally advanced or metastatic. AFINITOR is not indicated for the treatment of patients with functional carcinoid tumors.

Drug Name: Afinitor Disperz (everolimus)

<u>Indications</u>

Subependymal Giant Cell Astrocytoma (SEGA)

Indicated for the treatment of subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected in pediatric and adult patients with tuberous sclerosis complex (TSC). The effectiveness of Afinitor Disperz is based on demonstration of durable objective response, as evidenced by reduction in SEGA tumor

volume. Improvement in disease-related symptoms and overall survival in patients with SEGA and TSC has not been demonstrated.

2 . Criteria

Product Name: Afinitor

Diagnosis	Advanced Neuroendocrine Tumors of Pancreatic Origin (PNET)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of progressive neuroendocrine tumors of pancreatic origin

AND

2 Disease is one of the following:

- Unresectable, locally advanced
- Metastatic

AND

3 Prescribed by or in consultation with an oncologist

Diagnosis	Advanced Neuroendocrine Tumors of Pancreatic Origin (PNET)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor

Diagnosis	Advanced Renal Cell Carcinoma
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced/metastatic renal cell carcinoma

AND

2 History of failure with one of the following:

- Sutent (sunitinib)
- Nexavar (sorafenib)

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Afinitor

Diagnosis	Advanced Renal Cell Carcinoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor

Diagnosis	Renal Angiomyolipoma with Tuberous Sclerosis Complex (TSC)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery

AND

2 Prescribed by or in consultation with a nephrologist

Product Name: Afinitor

Diagnosis	Renal Angiomyolipoma with Tuberous Sclerosis Complex (TSC)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor, Afinitor Disperz

Diagnosis	Subependymal Giant Cell Astrocytoma
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis (TS)

AND

2 Patient is not a candidate for curative surgical resection

AND

3 Prescribed by or in consultation with an oncologist.

Product Name: Afinitor, Afinitor Disperz

Diagnosis	Subependymal Giant Cell Astrocytoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor

Diagnosis	Breast cancer
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of hormone receptor positive, HER-2 negative advanced breast cancer

AND

2 History of failure, contraindication, or intolerance to one of the following:

- Femara (letrozole)
- Arimidex (anastrozole)

AND

3 Used in combination with Aromasin (exemestane)

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Afinitor

Diagnosis	Breast cancer
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on therapy

Product Name: Afinitor

Diagnosis	Neuroendocrine tumors of gastrointestinal or lung origin
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of progressive, well-differentiated, non-functional neuroendocrine tumors of gastrointestinal or lung origin

AND

2 One of the following:

- Unresectable, locally advanced disease
- Metastatic disease

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Afinitor

Diagnosis	Neuroendocrine tumors of gastrointestinal or lung origin
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on therapy

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

These products are subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . References

1. Afinitor and Afinitor Disprerz Prescribing Information. Novartis Oncology, February 2016.

Prior Authorization Guideline

GL-17401 Aldurazyme (laronidase)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 6/1/2016

Technician Note :

P&T Approval Date: 2/2/2004; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Aldurazyme (laronidase)

Indications

Mucopolysaccharidosis I (MPS I)

Indicated for patients with Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I) and for patients with the Scheie form who have moderate to severe symptoms. The risks and benefits of treating mildly affected patients with the Scheie form have not been established. Has been shown to improve pulmonary function and walking capacity. Aldurazyme has not been evaluated for effects of the central nervous system manifestations of the disorder.

2 . Criteria

Product Name: Aldurazyme

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Diagnosis of Hurler and Hurler-Scheie forms of Mucopolysaccharidosis I (MPS I)

OR

1.2 Diagnosis of Scheie form of Mucopolysaccharidosis I (MPS I) in patients with moderate to severe symptoms

3 . References

1. Aldurazyme Prescribing Information, Genzyme Corporation, April 2013.

Prior Authorization Guideline

GL-17450 Alfa Interferons

Formulary OptumRx SP

Formulary Note

Approval Date 5/20/2015

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 3/17/2000; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Intron A (interferon alfa-2b)

Indications

Hairy Cell Leukemia

Indicated for the treatment of patients 18 years of age or older with hairy cell leukemia.

Malignant Melanoma

Indicated as adjuvant to surgical treatment in patients 18 years of age or older with malignant melanoma who are free of disease but at high risk for systemic recurrence, within 56 days of

surgery.

Follicular Lymphoma

Indicated for the initial treatment of clinically aggressive follicular Non-Hodgkin's Lymphoma in conjunction with anthracycline-containing combination chemotherapy in patients 18 years of age or older. Efficacy of Intron A therapy in patients with low-grade, lowtumor burden follicular Non-Hodgkin's Lymphoma has not been demonstrated.

Condylomata Acuminata

Indicated for intralesional treatment of selected patients 18 years of age or older with condylomata acuminata involving external surfaces of the genital and perianal areas. The use of this product in adolescents has not been studied.

AIDS-Related Kaposi's Sarcoma

Indicated for the treatment of selected patients 18 years of age or older with AIDS-Related Kaposi's Sarcoma. The likelihood of response to INTRON A therapy is greater in patients who are without systemic symptoms, who have limited lymphadenopathy and who have a relatively intact immune system as indicated by total CD4 count.

Chronic Hepatitis C

Indicated for the treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease who have a history of blood or blood-product exposure and/or are HCV antibody positive. Studies in these patients demonstrated that INTRON A therapy can produce clinically meaningful effects on this disease, manifested by normalization of serum alanine aminotransferase (ALT) and reduction in liver necrosis and degeneration. A liver biopsy should be performed to establish the diagnosis of chronic hepatitis. Patients should be tested for the presence of antibody to HCV. Patients with other causes of chronic hepatitis, including autoimmune hepatitis, should be excluded. Prior to initiation of INTRON A therapy, the physician should establish that the patient has compensated liver disease. The following patient entrance criteria for compensated liver disease were used in the clinical studies and should be considered before INTRON A treatment of patients with chronic hepatitis C: - No history of hepatic encephalopathy, variceal bleeding, ascites, or other clinical signs of decompensation - Bilirubin less than or equal to 2 mg/dL - Albumin stable and within normal limits - Prothrombin time less than 3 seconds prolonged - WBC greater than or equal to 3000/mm3 - Platelets greater than or equal to 70,000/m3 Serum creatinine should be normal or near normal. Prior to initiation of Intron A therapy, CBC and platelet counts should be evaluated in order to establish baselines for monitoring potential toxicity. These tests should be repeated at Weeks 1 and 2 following initiation of Intron A therapy, and monthly thereafter. Serum ALT should be evaluated at approximately 3-month intervals to assess response to treatment. Patients with preexisting thyroid abnormalities may be treated if thyroidstimulating hormone (TSH) levels can be maintained in the normal range by medication. TSH levels must be within normal limits upon

initiation of INTRON A treatment and TSH testing should be repeated at 3 and 6 months. Intron A in combination with Rebetol is indicated for the treatment of chronic hepatitis C in patients 3 years of age and older with compensated liver disease previously untreated with alpha interferon therapy and in patients 18 years of age and older who have relapsed following alpha interferon therapy. See Rebetol prescribing information for additional information.

Chronic Hepatitis B

Indicated for the treatment of chronic hepatitis B in patients 1 year of age or older with compensated liver disease. Patients who have been serum HBsAg positive for at least 6 months and have evidence of HBV replication (serum HBeAg positive) with elevated serum ALT are candidates for treatment. Studies in these patients demonstrated that Intron A therapy can produce virologic remission of this disease (loss of serum HBeAg), and normalization of serum aminotransferases. Intron A therapy resulted in the loss of serum HBsAg in some responding patients. Prior to initiation of Intron A therapy, it is recommended that a liver biopsy be performed to establish the presence of chronic hepatitis and the extent of liver damage. The physician should establish that the patient has compensated liver disease. The following patient entrance criteria for compensated liver disease were used in the clinical studies and should be considered before Intron A treatment of patients with chronic hepatitis B: • No history of hepatic encephalopathy, variceal bleeding, ascites, or other signs of clinical decompensation • Bilirubin normal • Albumin stable and within normal limits • Prothrombin Time - adults < 3 seconds prolonged, pediatrics less than or equal to 2 seconds prolonged • WBC greater than or equal to 4000/mm^3 • Platelets - adults greater than or equal to 100,000/mm^3, pediatrics greater than or equal to 150,000/mm^3. Patients with causes of chronic hepatitis other than chronic hepatitis B or chronic hepatitis C should not be treated with Intron A Interferon alfa-2b, recombinant for Injection. CBC and platelet counts should be evaluated prior to initiation of Intron A therapy in order to establish baselines for monitoring potential toxicity. These tests should be repeated at treatment Weeks 1, 2, 4, 8, 12, and 16. Liver function tests, including serum ALT, albumin, and bilirubin, should be evaluated at treatment Weeks 1, 2, 4, 8, 12, and 16. HBeAg, HBsAg, and ALT should be evaluated at the end of therapy, as well as 3- and 6-months post-therapy, since patients may become virologic responders during the 6-month period following the end of treatment. In clinical studies in adults, 39% (15/38) of responding patients lost HBeAg 1 to 6 months following the end of Intron A therapy. Of responding patients who lost HBsAg, 58% (7/12) did so 1 to 6 months post-treatment. A transient increase in ALT greater than or equal to 2 x baseline value (flare) can occur during Intron A therapy for chronic hepatitis B. In clinical trials in adults and pediatrics, this flare generally occurred 8 to 12 weeks after initiation of therapy and was more frequent in Intron A responders (adults 63%, 24/38; pediatrics 59%, 10/17) than in non-responders (adults 27%, 13/48; pediatrics 35%, 19/55). However, in adults and pediatrics, elevations in bilirubin 3 mg/dL (2 times ULN) occurred infrequently (adults 2%, 2/86; pediatrics 3%, 2/72) during therapy. When ALT flare occurs, in general, Intron A therapy should be continued unless signs and symptoms of liver failure are observed. During ALT flare, clinical symptomatology and liver function tests including ALT, prothrombin time, alkaline phosphatase, albumin, and bilirubin, should be monitored at approximately 2-week intervals.

Drug Name: Pegasys (peginterferon alfa-2a)

Indications

Chronic Hepatitis C

As part of a combination regimen with other hepatitis C virus (HCV) antiviral drugs, is indicated for the treatment of adults with chronic hepatitis C (CHC) with compensated liver disease. For information about the safe and effective use of other HCV antiviral drugs to be used in combination with Pegasys, refer to their prescribing information. Pegasys in combination with ribavirin is indicated for treatment of pediatric patients 5 years of age and older with CHC and compensated liver disease. Pegasys monotherapy is only indicated for the treatment of patients with CHC with compensated liver disease if there are contraindications or significant intolerance to other HCV antiviral drugs. Limitations of use: - Pegasys alone or in combination with ribavirin without additional HCV antiviral drugs is not recommended for treatment of patients with CHC who previously failed therapy with an interferon-alfa. - Pegasys is not recommended for treatment of patients with CHC who have had solid organ transplantation.

Chronic Hepatitis B

Indicated for the treatment of adult patients with HBeAg-positive and HBeAg-negative chronic hepatitis B infection who have compensated liver disease and evidence of viral replication and liver inflammation.

Drug Name: PegIntron (peginterferon alfa-2b)

Indications

Chronic Hepatitis C

As part of a combination regimen, is indicated for the treatment of Chronic Hepatitis C (CHC) in patients with compensated liver disease. - PegIntron in combination with ribavirin and an approved Hepatitis C Virus (HCV) NS3/4A protease inhibitor is indicated in adult patients with HCV genotype 1 infection (see labeling of the specific HCV NS3/4A protease inhibitor for further information). - PegIntron in combination with ribavirin is indicated in patients with genotypes other than 1, pediatric patients (3-17 years of age), or in patients with genotype 1 infection where use of an HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications or other clinical factors. PegIntron monotherapy should only be used in the treatment of CHC in patients with compensated liver disease if there are contraindications to or significant intolerance of ribavirin and is indicated for use only in previously untreated adult patients. Combination therapy provides substantially better response rates than monotherapy.

2 . Criteria

Product Name: Intron A or Pegasys

Diagnosis	Chronic Hepatitis B
Approval Length	48 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic hepatitis B infection

AND

2 Patients without decompensated liver disease†

Notes	†Defined as Child-Pugh Class B or C

Product Name: Intron A

Diagnosis	Chronic Hepatitis C
Approval Length	48 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic hepatitis C

AND

2 Patients without decompensated liver disease†

AND

3 For patients who have not previously been treated with interferon

AND

4 One of the following:

- Used in combination with ribavirin
- Contraindication or intolerance to ribavirin

Notes	†Defined as Child-Pugh Class B or C

Product Name: Pegasys or PegIntron

Diagnosis	Chronic Hepatitis C
Approval Length	28 Week
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization
Approval Criteria	

1 Diagnosis of chronic hepatitis C infection

AND

2 Patient without decompensated liver disease†

AND

3 One of the following:

3.1 Used in combination with one of the following:

- Victrelis (boceprevir)
- Olysio (simeprevir)
- Sovaldi (sofosbuvir)
- Ribavirin

OR

3.2 Contraindication or intolerance to all other HCV agents (e.g., Victrelis (boceprevir), Olysio, (simeprevir), Sovaldi (sofosbuvir), ribavirin)

Notes	†Defined as Child-Pugh Class B or C

Product Name: Pegasys or PegIntron

Diagnosis	Chronic Hepatitis C
Approval Length	20 Week
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has an undetectable HCV RNA at week 24

AND

2 Additional treatment weeks of peginterferon are required to complete treatment regimen

AND

3 Patient has not exceeded 48 weeks of therapy with peginterferon

Product Name: Intron A

Diagnosis	Condylomata acuminata
Approval Length	6 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of condylomata acuminata (genital or perianal)

Product Name: Intron A

Diagnosis	Diagnoses other than hepatitis and condylomata acuminata
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Diagnosis of hairy cell leukemia

OR

1.2 Diagnosis of AIDS-related Kaposi's sarcoma

OR

1.3 All of the following:

1.3.1 Diagnosis of metastatic renal cell carcinoma

AND

1.3.2 Used in combination with Avastin (bevacizumab)

AND

1.3.3 Prescribed by or in consultation with an oncologist

OR

1.4 Diagnosis of malignant melanoma

OR

1.5 Diagnosis of Stage III or IV follicular Non-Hodgkin's Lymphoma

OR

1.6 As maintenance therapy for the treatment of multiple myeloma (non-FDA approved indication)

3 . References

1. Pegasys Prescribing Information. Genentech, March 2015.
2. PegIntron Prescribing Information. Merck, January 2015.
3. Intron Prescribing Information. Merck, October 2014.
4. Avastin Prescribing Information. Genentech, November, 2011.

Prior Authorization Guideline

GL-30196 Alpha-1 Proteinase Inhibitors

Formulary OptumRx SP

Formulary Note

Approval Date 7/1/2016

Revision Date 7/1/2016

Technician Note :

P&T Approval: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Aralast NP (alpha-1-proteinase inhibitor [human])

Indications

Alpha-1 proteinase inhibitor deficiency (also known as alpha-1-antitrypsin (AAT) deficiency) Indicated for chronic augmentation therapy in patients having congenital deficiency of alpha-1-proteinase inhibitor (PI) with clinically evident emphysema. Clinical and biochemical studies have demonstrated that with such therapy, Aralast is effective in maintaining target serum alpha-1-PI trough levels and increasing alpha-1-PI levels in epithelial lining fluid (ELF). Aralast NP pharmacokinetics are comparable with the pharmacokinetics of Aralast after singledose administration in 25 subjects with congenital deficiency of alpha-1-PI. Clinical data

demonstrating the long-term effects of chronic augmentation or replacement therapy of individuals with Aralast NP or Aralast are not available. The effect of augmentation therapy with Aralast NP on pulmonary exacerbations and on the progression of emphysema in alpha-1-antitrypsin deficiency has not been demonstrated in randomized, controlled clinical trials. Aralast NP is not indicated as therapy for lung disease patients in whom congenital alpha-1-PI deficiency has not been established.

Drug Name: Glassia (alpha-1-proteinase inhibitor [human])

Indications

Alpha-1 proteinase inhibitor deficiency (also known as alpha-1-antitrypsin (AAT) deficiency) Indicated for chronic augmentation and maintenance therapy in individuals with emphysema due to congenital deficiency of alpha-1-proteinase inhibitor (Alpha-1-PI), also known as alpha-1-antitrypsin (AAT) deficiency. The effect of augmentation therapy with Glassia or any Alpha1-PI product on pulmonary exacerbations and on the progression of emphysema in Alpha1-PI deficiency has not been demonstrated in randomized, controlled clinical trials. Clinical data demonstrating the long-term effects of chronic augmentation and maintenance therapy of individuals with Glassia are not available. Glassia is not indicated as therapy for lung disease in patients in whom severe Alpha1-PI deficiency has not been established.

Drug Name: Prolastin-C (alpha-1-proteinase inhibitor [human])

Indications

Alpha-1 proteinase inhibitor deficiency (also known as alpha-1-antitrypsin (AAT) deficiency) Indicated for chronic augmentation and maintenance therapy in adults with emphysema due to deficiency of alpha1-proteinase inhibitor (Alpha-1-PI, alpha1-antitrypsin deficiency). The effect of augmentation therapy with any Alpha-1-PI product on pulmonary exacerbations and on the progression of emphysema in alpha1-antitrypsin deficiency has not been demonstrated in adequately powered, randomized, controlled, clinical trials. Prolastin-C is not indicated as therapy for lung disease in patients in whom severe Alpha-1-PI deficiency has not been established.

Drug Name: Zemaira (alpha-1-proteinase inhibitor [human])

Indications

Alpha-1 proteinase inhibitor deficiency (also known as alpha-1-antitrypsin (AAT) deficiency) Indicated for chronic augmentation and maintenance therapy in individuals with alpha-1-proteinase inhibitor (A1-PI) deficiency and clinical evidence of emphysema. Zemaira

increases antigenic and functional (ANEC) serum levels and lung epithelial lining fluid levels of A1-PI. Clinical data demonstrating the long-term effects of chronic augmentation therapy of individuals with Zemaira are not available. The effect of augmentation therapy with Zemaira or any A1-PI product on pulmonary exacerbations and on the progression of emphysema in A1-PI deficiency has not been demonstrated in randomized, controlled clinical trials. Zemaira is not indicated as therapy for lung disease patients in whom severe A1-PI deficiency has not been established.

2 . Criteria

Product Name: Aralast NP, Glassia, Prolastin-C, or Zemaira

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of alpha-1 antitrypsin (AAT) deficiency

and

2 Diagnosis of emphysema [A]

and

3 One of the following:

3.1 Patient has a high risk phenotype: Pi*ZZ, Pi*Z(null) or Pi*(null)(null) protein phenotypes (homozygous) [10]

OR

3.2 Patient has serum alpha-1 antitrypsin concentrations of less than 11 Âµmol/L (80 mg/dL) [B, 12]

and

4 One of the following:

4.1 The FEV1 level is between 30% and 65% of predicted

OR

4.2 Patient has experienced a rapid decline in lung function (i.e., reduction of FEV1 more than 120 mL/year) that warrants treatment

and

5 Patient is NOT a current smoker

3 . Definitions

Definition	Description
AAT deficiency	A chronic, hereditary, usually fatal, autosomal recessive

	disorder in which a low concentration of A1-PI (or AAT) is associated with slow progressive, severe panacinar emphysema that most often manifests itself in the third to fourth decades of life. [1-3, 8] However, an unknown percentage of patients with severe A1-PI deficiency apparently never develop clinically evident emphysema during their lifetime. The most direct approach to therapy for A1-PI deficiency in patients with emphysema has been to partially replace the missing protease inhibitor by intravenous infusion and, thus, attempt to ameliorate the imbalance in the anti-neutrophil elastase protection of the lower respiratory tract.

4 . Endnotes

A. Currently, augmentation therapy is not recommended for patients without emphysema. [4] Some individuals with ATT deficiency will not go on to develop panacinar emphysema, only those with evidence of such disease should be considered for augmentation therapy.
B. Population studies suggest a minimum plasma threshold of 11 Î¼mol/L (corresponding to 80 mg/dL in some assays and ~57 mg/dL by nephelometry), below which there is insufficient AAT to protect the lung, leading to a risk of developing emphysema. [12]

5 . References

1. Aralast NP Prescribing Information. Baxter Healthcare Corporation. April 2010.
2. Prolastin Prescribing Information. Talecris Biotherapeutics, Inc. June 2013.
3. Zemaira Prescribing Information. CSL Behring LLC. May 2013.
4. American Thoracic Society/European Respiratory Society Statement: Standards for diagnosis and management of individuals with alpha-1 antitrypsin deficiency. Am J Resp Care Med 2003; 168:818-900.
5. Seersholm N, Wencker M, Banik N, et al. Does Î±-1 antitrypsin augmentation therapy slow the annual decline in FEV(logbase1) in patients with severe hereditary Î±-1 antitrypsin deficiency? Eur Respir J 1997;10:2260-2263.
6. Wencker M, Banik N, Buhl R, Seidel R, Konietzko N. Long-term treatment of Î±-1 antitrypsin deficiency-related pulmonary emphysema with human Î±-1 antitrypsin. Eur Resp J 1998;11:428-433.
7. Alpha-1-antitrypsin Deficiency Registry Study Group. Survival and FEV1 decline in individuals with severe deficiency of Î±-1 antitrypsin. Am J Respir Crit Care Med 1998;158:49-59.
8. Prolastin-C Prescribing Information. Grifols Therapeutics, Inc. June 2012.
9. Glassia Prescribing Information. Kamada Ltd., June 2012.

10. Marciniuk DD, Hernandez P, Balter M, et al. Alpha-1 antitrypsin deficiency targeted testing and augmentation therapy: A Canadian Thoracic Society clinical practice guideline. Canadian Respiratory Journal 2012;19(2):109-116.
11. Alpha-1 Proteinase Inhibitor [ACG: A-0468 (AC)]. MCGâ„¢ Ambulatory Care17th edition. 2013 MCG Health, LLC. http://www.careguidelines.com/ Accessed. March 2, 2014.
12. Rovner MS, Stoller JK. Treatment of of alpha-1 antitrypsin deficiency. UpToDate. Accessed February 19, 2014.

Prior Authorization Guideline

GL-30902 Ampyra (dalfampridine)

Formulary OptumRx SP

Formulary Note

Approval Date 8/24/2016

Revision Date 8/24/2016

Technician Note :

P&T Approval Date: 4/6/2010; P&T Revision Date: 8/18/2016 **Effective 9/15/2016**

1 . Indications

Drug Name: Ampyra (dalfampridine)

Indications

Improvement in walking in patients with multiple sclerosis Indicated as a treatment to improve walking in patients with multiple sclerosis (MS). This was demonstrated by an increase in walking speed.

2 . Criteria

Product Name: Ampyra

Approval Length	6 months [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple sclerosis [A]

AND

2 Physician confirmation that patient has difficulty walking (e.g., timed 25-foot walk test) [B]

AND

3 One of the following:

- Patient has an expanded disability status scale (EDSS) score less than or equal to 7
- Patient is not restricted to using a wheelchair (if EDSS is not measured)

AND

4 Prescribed by or in consultation with a neurologist

Product Name: Ampyra

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Physician confirmation that the patientâ€™s walking improved with Ampyra therapy

AND

2 One of the following:

- Patient has an expanded disability status scale (EDSS) score less than or equal to 7
- Patient is not restricted to using a wheelchair (if EDSS is not measured)

3 . Endnotes

A. Patients with clinically definite MS of any type were included in the pivotal trials for Ampyra. [2, 3]
B. Inclusion criteria in the Ampyra pivotal trials included patients who were able to walk (with or without an assistive device) 25 feet in 8-45 seconds and 8-60 seconds in the two studies, respectively. [2, 3]
C. Response to treatment with Ampyra was assessed over a 14-week double-blind treatment period. Patients who were dalfampridine non-responders (i.e., patients who did not demonstrate a faster walking speed for at least three out of the four visits during the treatment period compared to the maximum speed for any of the first five off-drug

non-treatment period visits based on the average of two trials of the timed 25-foot walking test conducted at each visit) did not demonstrate statistically significant improvements in walking speed compared to placebo in three out of the four study visits during the 14-week treatment period. [2]

4 . References

1. Ampyra Prescribing Information. Acorda Therapeutics, Inc., April 2015.
2. Goodman AD, Brown TR, Krupp LB, et al. Sustained-release oral fampridine in multiple sclerosis: a randomised, double-blind, controlled trial. Lancet 2009;373:732-738.
3. Goodman AD, Brown TR, Cohen JA, et al. Dose comparison trial of sustained-release fampridine in multiple sclerosis. Neurology. 2008;1134-1141.

Prior Authorization Guideline

GL-32006 Anti-Programmed Death Receptor-1 (PD-1) Antibodies

Formulary OptumRx SP

Formulary Note

Approval Date 10/3/2016

Revision Date 10/3/2016

Technician Note :

P&T Approval Date: 10/14/2014; P&T Revision Date: 9/28/16 **Effective 10/15/2016**

1 . Indications

Drug Name: Keytruda (pembrolizumab)

Indications

Melanoma, Unresectable or Metastatic Indicated for the treatment of patients with unresectable or metastatic melanoma.

Non-Small Cell Lung Cancer (NSCLC), Metastatic Indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1 as determined by an FDA-approved test with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on

FDA-approved therapy for these aberrations prior to receiving Keytruda. *This indication is approved under accelerated approval based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.*

Head and Neck Squamous Cell Carcinoma (HNSCC), Recurrent or Metastatic Indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy.

Drug Name: Opdivo (nivolumab)

Indications

Melanoma, Unresectable or Metastatic Indicated as a single agent for the treatment of patients with BRAF V600 wild-type or BRAF V600 mutation-positive unresectable or metastatic melanoma; indicated in combination with ipilimumab for the treatment of patients with unresectable or metastatic melanoma. *Indications as a single agent for BRAF V600 mutation-positive unresectable or metastatic melanoma, and in combination with ipilimumab for unresectable or metastatic melanoma were approved under accelerated approval based on progression-free survival. Continued approval for these indications may be contingent upon verification and description of clinical benefit in the confirmatory trials.*

Non-Small Cell Lung Cancer (NSCLC), Metastatic Indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo.

Renal Cell Carcinoma, Advanced Indicated for the treatment of patients with advanced renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.

Classical Hodgkin Lymphoma Indicated for the treatment of patients with classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous hematopoietic stem cell transplantation (HSCT) and post-transplantation brentuximab vedotin. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

2 . Criteria

Product Name: Keytruda or Opdivo

Diagnosis	Melanoma
Approval Length	12 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of melanoma [1, 2, 3]

AND

2 One of the following: [1, 2, 3]

- Disease is unresectable
- Disease is metastatic

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Keytruda or Opdivo

Diagnosis	Melanoma
Approval Length	12 Months
Therapy Stage	Reauthorization

Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on the requested therapy

Product Name: Keytruda

Diagnosis	Non-Small Cell Lung Cancer (NSCLC)
Approval Length	12 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of non-small cell lung cancer [1, 4]

AND

2 Disease is metastatic [1, 4]

AND

3 Tumors express PD-L1 as determined by an FDA-approved test [1]

AND

4 History of failure, contraindication, or intolerance to platinum-based chemotherapy (eg, cisplatin, carboplatin)

AND

5 Prescribed by or in consultation with an oncologist

Product Name: Keytruda

Diagnosis	Non-Small Cell Lung Cancer (NSCLC)
Approval Length	12 Months
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Keytruda therapy

Product Name: Opdivo

Diagnosis	Non-Small Cell Lung Cancer (NSCLC)
Approval Length	12 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of non-small cell lung cancer [2]

AND

2 Disease is metastatic [2]

AND

3 History of failure, contraindication, or intolerance to platinum-based chemotherapy (eg, cisplatin, carboplatin) [2]

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Opdivo

Diagnosis	Non-Small Cell Lung Cancer (NSCLC)
Approval Length	12 Months
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Opdivo therapy

Product Name: Opdivo

Diagnosis	Renal Cell Carcinoma
Approval Length	12 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of renal cell carcinoma [2, 5]

AND

2 Disease is advanced [2, 5]

AND

3 History of failure, contraindication, or intolerance to anti-angiogenic therapy (eg, Sutent, Nexavar) [2]

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Opdivo

Diagnosis	Renal Cell Carcinoma
Approval Length	12 Months

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Opdivo therapy

Product Name: Opdivo

Diagnosis	Classical Hodgkin Lymphoma (cHL)
Approval Length	12 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of classical Hodgkin lymphoma

AND

2 Patient has had relapse or progression after autologous hematopoietic stem cell transplantation and post-transplantation Adcetris (brentuximab vedotin) therapy

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Opdivo

Diagnosis	Classical Hodgkin Lymphoma (cHL)
Approval Length	12 Months
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Opdivo therapy

Product Name: Keytruda

Diagnosis	Head and Neck Squamous Cell Carcinoma (HNSCC), Recurrent or Metastatic
Approval Length	12 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of head and neck squamous cell carcinoma

AND

2 One of the following:

- Disease is recurrent
- Disease is metastatic

AND

3 History of failure, contraindication, or intolerance to platinum-based chemotherapy (eg, cisplatin, carboplatin)

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Keytruda

Diagnosis	Head and Neck Squamous Cell Carcinoma (HNSCC), Recurrent or Metastatic
Approval Length	12 Months
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Keytruda therapy

3 . References

1. Keytruda Prescribing Information. Merck & Co, Inc., August 2016.
2. Opdivo Prescribing Information. Bristol-Myers Squibb Co., May 2016.
3. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Melanoma, V2.2016. NCCN Web site. http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf. Accessed February 5, 2016.
4. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer, V4.2016. NCCN Web site. http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 5, 2016.
5. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer, V2.2016. NCCN Web site. http://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed February 5, 2016.

Prior Authorization Guideline

GL-16285 Apokyn (apomorphine HCl injection)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 3/25/2016

Technician Note :

P&T Approval Date: 10/2/2004; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Apokyn (apomorphine HCl injection)

Indications

Parkinson's Disease

Indicated for the acute, intermittent treatment of hypomobility, "off" episodes ("end-of-dose wearing off" and unpredictable "on/off" episodes) associated with advanced Parkinson's disease. Apokyn has been studied as an adjunct to other medications.

2 . Criteria

Product Name: Apokyn

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced Parkinson's disease

AND

2 Patient is experiencing acute intermittent hypomobility (defined as "off" episodes characterized by muscle stiffness, slow movements, or difficulty starting movements)

AND

3 Patient is receiving Apokyn in combination with other medications for the treatment of Parkinson's disease (e.g., carbidopa/levodopa, pramipexole, ropinirole, benztropine, etc.)

AND

4 Patient is not using Apokyn with any 5-HT3 antagonist (e.g., ondansetron, granisetron, dolasetron, palonosetron, alosetron)

Product Name: Apokyn

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Apokyn therapy

AND

2 Patient is not using Apokyn with any 5-HT3 antagonist (e.g., ondansetron, granisetron, dolasetron, palonosetron, alosetron)

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . References

1. Apokyn Prescribing Information. Louisville, KY: US WorldMeds, LLC. February 2012.
2. Dewey RB, Jr., Hutton JT, LeWitt PA, Factor SA. A randomized, double-blind, placebo-controlled trial of subcutaneously injected apomorphine for parkinsonian off-state events. Arch Neurol 2001;58:1385-1392.
3. Pahwa R, Factor SA, Lyons KE, et al.. Practice parameter: treatment for Parkinson's disease with motor fluctuations and dyskinesia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006;66:983-995.
4. National Institute of Health and Clinical Excellence of England (NICE). Parkinson's disease: diagnosis and management in primary and secondary care, Full guideline. 06/2006. Available at: http://www.nice.org.uk/nicemedia/live/10984/30087/30087.pdf. Accessed May 27, 2014.

Prior Authorization Guideline

GL-16973 Arcalyst (rilonacept injection)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/20/2016

Technician Note :

P&T Approval Date: 8/19/2008; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Arcalyst (rilonacept injection)

Indications

Cryopyrin-Associated Periodic Syndromes (CAPS)

Indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older.

2 . Criteria

Product Name: Arcalyst

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is 12 years of age or older

AND

2 Diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) and/or Muckle-Wells Syndrome (MWS)

AND

3 Prescribed by or in consultation with an immunologist, allergist, dermatologist, rheumatologist, neurologist or other medical specialist

AND

4 The medication will not be used in combination with another biologic

Product Name: Arcalyst

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has experienced disease stability or improvement in clinical symptoms while on therapy as evidenced by one of the following:

- Improvement in rash, fever, joint pain, headache, or conjunctivitis
- Decreased number of disease flare days
- Normalization of inflammatory markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], serum amyloid A [SAA])

3 . Definitions

Definition	Description
CIAS1 gene:	Also known as cold-induced auto-inflammatory syndrome 1, is a gene responsible for the regulation of IL-1 production. Mutation(s) in this gene leads to CAPS. [4]
Chronic Infantile Neurologic Cutaneous and Articular Syndrome:	Also known as neonatal-Onset Multisystem Inflammation, is the most severe form of the CAPS. It is characterized by nearly continuous symptoms of inflammation presenting first during the neonatal period or early infancy with migratory and nonpruritic urticaria-like rash and fever. Other features of this disease include chronic aseptic meningitis, sensorineural

	hearing loss and ocular changes (conjunctivitis, optic nerve atrophy), and disabling arthropathy caused by overgrowth of the patella and epiphyses of the long bones. Approximately 20% of patients with this disease die before reaching adulthood. [4, 5]
Cryopyrin-Associated Periodic Syndromes (CAPS):	A group of rare, autosomal dominantly inherited auto-inflammatory conditions comprising of Familial-Cold Auto-inflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS), Neonatal-Onset Multisystem Inflammatory Disease (NOMID) or also known as Chronic Infantile Neurologic Cutaneous Articular Syndrome (CINCA), which are caused by the CIAS1 gene mutation and characterized by recurrent symptoms (urticaria-like skin lesions, fever chills, arthralgia, profuse sweating, sensorineural hearing/vision loss, and increased inflammation markers the blood). Approximately 300 people in the United States are affected by CAPS. [4, 5, 6]
Familial Cold Autoinflammatory Syndrome:	The mildest form of CAPS, is characterized by cold-induced, daylong episodes of fever associated with rash, arthralgia, headaches and less frequently conjunctivitis, but without other signs of CNS inflammation. Symptoms usually begin during the first 6 months of life and are predominantly triggered by cold exposure. Duration of episodes usually is less than 24 hours. [4, 5]
Muckle-Wells Syndrome:	A subtype of CAPS, which is characterized by episodic attacks of inflammation associated with a generalized urticaria-like rash, fever, malise, arthralgia, and progressive hearing loss. Duration of symptoms usually lasts from 24-48 hours. [4, 5]

4 . Endnotes

A. CAPS refer to rare genetic syndromes generally caused by mutations in the NLRP-3 [Nucleotide-binding domain, leucine rich family (NLR), pyrin domain containing 3] gene (also known as Cold-Induced Auto-inflammatory Syndrome-1 [CIAS1]). CAPS disorders are inherited in an autosomal dominant pattern with male and female offspring equally affected. Features common to all disorders include fever, urticaria-like rash, arthralgia,

myalgia, fatigue, and conjunctivitis. In most cases, inflammation in CAPS is associated with mutations in the NLRP-3 gene which encodes the protein cryopyrin, an important component of the inflammasome. Mutations in NLRP-3 result in an overactive inflammasome resulting in excessive release of activated IL-1? that drives inflammation. [1]

B. In clinical studies, Arcalyst has not been administered concomitantly with tumor necrosis factor (TNF) inhibitors. An increased incidence of serious infections has been associated with administration of an IL-1 blocker in combination with TNF inhibitors. Taking Arcalyst with TNF inhibitors is not recommended because this may increase the risk of serious infections. Treatment with Arcalyst should be discontinued if a patient develops a serious infection. Patients should be counseled not to take any IL-1 blocking drug, including Arcalyst, if they are also taking a drug that blocks TNF such as etanercept, infliximab, or adalimumab. Use of Arcalyst with other IL-1 blocking agents, such as anakinra, is not recommended. [1]

5 . References

1. Arcalyst (rilonacept) for Subcutaneous Injection Prescribing Information. Regeneron Pharmaceuticals, September, 2014.
2. Hoffman HM et al. Durability of response to rilonacept (IL-1 Trap) in a phase 3 study of patients with cryopyrin-associated periodic syndromes (CAPS): familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome. Journal of Allergy and Clinical Immunology. 2008; 121(2):S175.
3. Data on File. Regeneron Pharmaceuticals, Inc. Tarrytown, NY. February 2008.
4. Aksentijevich I, et al. The clinical continuum of cryopyrinopathies: novel CIAS1 mutations in North American Patients and a new cryopyrin model. Arthritis and Rheumatism. 2007; 56(4):1273-1285.
5. McDermott M, Aksentijevich I, The auto-inflammatory syndromes. Current Opinion in Allergy and Clinical Immunology. 2002; 2:511-516.

Prior Authorization Guideline

GL-31996 Arzerra (ofatumumab)

Formulary OptumRx SP

Formulary Note

Approval Date 10/3/2016

Revision Date 10/3/2016

Technician Note :

P&T Approval Date: 2/16/2010; P&T Revision Date: 9/28/2016 **Effective 11/1/2016**

1 . Indications

Drug Name: Arzerra (ofatumumab)

Indications

Relapsed and Refractory Chronic Lymphocytic Leukemia (CLL) Indicated for the treatment of patients with CLL refractory to fludarabine and alemtuzumab.

Previously Untreated Chronic Lymphocytic Leukemia (CLL) Indicated, in combination with chlorambucil, for the treatment of previously untreated patients with CLL for whom fludarabine based therapy is considered inappropriate.

2 . Criteria

Product Name: Arzerra

Diagnosis	Refractory Chronic Lymphocytic Leukemia
Approval Length	6 months [D]
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic lymphocytic leukemia (CLL)

AND

2 Relapsed or refractory to at least two prior CLL regimens that contain one or more of the following: [2, 7, A, B]

- Campath (alemtuzumab)
- Cytoxan (cyclophosphamide)
- Fludara (fludarabine)
- Leukeran (chlorambucil)
- Leustatin (cladribine)
- Nipent (pentostatin)
- Rituxan (rituximab)
- Treanda (bendamustine)
- Gazyva (obinutuzumab)

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Arzerra

Diagnosis	Previously Untreated Chronic Lymphocytic Leukemia
Approval Length	12 months [C]
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic lymphocytic leukemia (CLL)

AND

2 Patient is previously untreated for CLL

AND

3 Patient is not an appropriate candidate for fludarabine-based therapy

AND

4 Used in combination with chlorambucil

AND

5 Prescribed by or in consultation with a hematologist/oncologist

3 . Endnotes

A. Relapse is defined as a patient who has responded to treatment, but after a period of 6 or more months, demonstrates evidence of disease progression. [6]
B. Refractory disease is defined as treatment failure (stable disease, progressive disease, or nonresponse) or disease progression within 6 months to the last antileukemic therapy. [6]
C. For previously untreated CLL, the recommended dosage and schedule is 300 mg on Day 1 followed 1 week later by 1,000 mg on Day 8 (Cycle 1) followed by 1,000 mg on Day 1 of subsequent 28-day cycles for a minimum of 3 cycles until best response or a maximum of 12 cycles. [1]
D. For refractory CLL, the recommended dosage and schedule is 12 doses administered as follows: 300 mg initial dose (Dose 1), followed 1 week later by 2,000 mg weekly for 7 doses (Doses 2 through 8), followed 4 weeks later by 2,000 mg every 4 weeks for 4 doses (Doses 9 through 12). [1]

4 . References

1. Arzerra Prescribing Information. GlaxoSmithKline, August 2016.
2. National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology - V.2.2014 Non-Hodgkin's Lymphomas. Available at: www.nccn.org. Accessed June 6, 2014.
3. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium. Available at: www.nccn.org. Accessed June 6, 2014.
4. Wierda W, Kipps T, Mayer J, on behalf of the 406 Study Investigators. Ofatumumab, a novel CD20 monoclonal antibody, is active in patients with fludarabine- and alemtuzumab-refractory or bulky fludarabine-refractory chronic lymphocytic leukemia irrespective of prior rituximab [abstract]. Clin Lymphoma Myeloma. 2009;9(6):E36. Abstract 502.
5. Cheson BD, Bennett JM, Grever Cheson BD, Bennett JM, Grever M, et al. National Cancer Institute-sponsored Working Group guidelines for chronic lymphocytic leukemia: revised guidelines for diagnosis and treatment. Blood. 1996;87:4990-4997.

6. Hallek M, Cheson BD, Catovsky D, et al. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute Working Group 1996 guidelines. Blood. 2008;111:5446-5456.
7. Per clinical consult with hematology/oncology specialist. February 5, 2010.

Prior Authorization Guideline

GL-15465 Benlysta (belimumab)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/7/2016

Technician Note :

P&T Approval Date: 7/12/2011; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Benlysta (belimumab)

Indications

Systemic Lupus Erythematosus (SLE)

Indicated for the treatment of adult patients with active, autoantibody-positive, SLE who are receiving standard therapy. Limitations of Use: The efficacy of Benlysta has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system (CNS) lupus. Benlysta has not been studied in combination with other biologics or IV cyclophosphamide. Use of Benlysta is not recommended in these situations.

2 . Criteria

Product Name: Benlysta

Approval Length	6 months [2, A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active systemic lupus erythematosus

AND

2 Autoantibody positive (ie, anti-nuclear antibody [ANA] titer greater than or equal to 1:80 or anti-dsDNA level greater than or equal to 30 IU/mL) [1-4]

AND

3 Currently receiving at least one standard of care treatment for active systemic lupus erythematosus (eg, antimalarials [eg, Plaquenil (hydroxychloroquine)], corticosteroids [eg, prednisone], or immunosuppressants [eg, methotrexate, Imuran (azathioprine), CellCept (mycophenolate mofetil)]) [1-4,6-7]

AND

4 Prescribed by or in consultation with a rheumatologist

Product Name: Benlysta

Approval Length	6 months [2, A]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Documentation of positive clinical response to Benlysta therapy	

3 . Endnotes

A. SLE is a disease that fluctuates. The undulating course of typical lupus patients requires frequent reassessment. A 6-month authorization period is reasonable. [2]

4 . References

1. Benlysta Prescribing Information. Human Genome Sciences,Inc.; March 2012.
2. Per clinical consult with rheumatologist, April 29, 2011.
3. American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus Guidelines. Guidelines for referral and management of systemic lupus erythematosus. Arthritis Rheum. 1999 Sep;42(9):1785-96.

Prior Authorization Guideline

GL-17429 Blincyto (blinatumomab)

Formulary OptumRx SP

Formulary Note

Approval Date 2/18/2015

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 2/18/2015 P&T Revision Date; 2/25/2016; ** Effective 7/1/2016 **

1 . Indications

Drug Name: Blincyto (blinatumomab)

Indications

Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)

Indicated for the treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL. This indication is approved under accelerated approval. Continued approval for this indication may be contingent upon verification of clinical benefit in subsequent trials

2 . Criteria

Product Name: Blincyto

Approval Length	12 Weeks [1, A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia/acute lymphoblastic lymphoma [1, B]

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Blincyto

Approval Length	18 Weeks [1, A]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Blincyto therapy

3 . Endnotes

A. A single cycle of treatment of Blincyto consists of 4 weeks of continuous intravenous infusion, followed by a 2-week treatment-free interval. A treatment course consists of up to 2 cycles of Blincyto for induction, followed by 3 additional cycles for consolidation treatment (up to a total of 5 cycles). [1]
B. The World Health Organization (WHO) 2008 classification lists acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma as the same entity, distinguished only by the primary location of the disease. Patients with lymphoblastic lymphoma generally benefit from treatment with ALL-like regimens. [3]

4 . References

1. Blincyto Prescribing Information. Amgen, Inc., December 2014.
2. Topp MS, Gökbuget N, Stein AS, et al. Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia: a multicentre, single-arm, phase 2 study. Lancet Oncol. 2015;16:57-66.
3. NCCN Clinical Practice Guidelines in Oncology: Acute lymphoblastic leukemia (Version 2.2014). National Comprehensive Cancer Network Web site. http://www.nccn.org/. Accessed January 6, 2015.

Prior Authorization Guideline

GL-16903 Bosulif (bosutinib)

Formulary OptumRx SP

Formulary Note

Approval Date 11/13/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 11/13/2012; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Bosulif (bosutinib)

Indications

Resistant or intolerant Chronic Myelogenous/Myeloid Leukemia

Indicated for the treatment of adult patients with chronic, accelerated, or blast phase Philadelphia chromosome-positive (Ph+) chronic myelogenous leukemia (CML) with resistance or intolerance to prior therapy.

2 . Criteria

Product Name: Bosulif

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Philadelphia chromosome-positive chronic myelogenous/myeloid leukemia (Ph+ CML)

AND

2 History of failure, contraindication, or intolerance to one of the following:

- Gleevec (imatinib)*
- Tasigna (nilotinib)*
- Sprycel (dasatinib)*

AND

3 Patient does not have the T315I or V299L mutation

AND

4 Prescribed by or in consultation with a hematologist/oncologist	
Notes	*These products may require prior authorization.

Product Name: Bosulif

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Patient does not show evidence of progressive disease while on Bosulif therapy	

3 . References

1. Bosulif Prescribing Information. Pfizer. November 2014.

Prior Authorization Guideline

GL-16550 Botox (onabotulinumtoxinA)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/25/2016

Technician Note :

P&T Approval Date: 3/17/2000; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Botox (onabotulinumtoxin A)

Indications

Detrusor overactivity associated with a neurologic condition

Indicated for the treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (eg, spinal cord injury, multiple sclerosis) in adults who have an inadequate response to or are intolerant of an anticholinergic medication.

Cervical dystonia (spasmodic torticollis)

Indicated for the treatment of cervical dystonia in adults to decrease the severity of abnormal head position and neck pain associated with cervical dystonia.

Primary axillary hyperhidrosis

Indicated for the treatment of severe primary axillary hyperhidrosis that is inadequately managed with topical agents.

Blepharospasm and strabismus

Indicated for the treatment of strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders (involving muscles of the face) in patients 12 years of age and above.

Upper limb spasticity

Indicated for the treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), finger flexors (flexor digitorum profundus and flexor digitorum sublimis), and thumb flexors (adductor pollicis and flexor pollicis longus). Safety and effectiveness have not been established for the treatment of other upper limb muscle groups or for the treatment of lower limb spasticity. Treatment with Botox is not intended to substitute for usual standard of care rehabilitation regimens.

Chronic migraine

Indicated for the prophylaxis of headaches in adult patients with chronic migraine (greater than or equal to 15 days per month with headache lasting 4 hours a day or longer). Safety and effectiveness have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) in seven placebo-controlled studies.

Overactive Bladder

Indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication.

Lower limb spasticity

Indicated for the treatment of lower limb spasticity in adult patients to decrease the severity of increased muscle tone in ankle and toe flexors (gastrocnemius, soleus, tibialis posterior, flexor hallucis longus, and flexor digitorum longus).

Off Label Uses

Focal hand dystonia [2, 3]

Used in the treatment of focal hand dystonia, including writer's cramp and musician's cramp.

Chronic low back pain [2, 3]

Used in the treatment of chronic low back pain. [36, 37]

Other uses [2, 3]

Used in the treatment of achalasia, chronic anal fissures, dynamic muscle contracture in pediatric cerebral palsy patients, sialorrhea, hand tremor, and oromandibular dystonia.

2 . Criteria

Product Name: Botox

Diagnosis	Neuromuscular and Autonomic Disorders
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of one of the following:

- Blepharospasm associated with dystonia (e.g., benign essential blepharospasm)
- Cervical dystonia (also known as spasmodic torticollis)
- Upper or lower limb spasticity
- Strabismus
- VII cranial nerve disorders (hemifacial spasms)

Product Name: Botox

Diagnosis	Neuromuscular and Autonomic Disorders

Approval Length	3 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Confirmed improvement in symptoms with initial Botox treatment

AND

2 At least 3 months have or will have elapsed since the last treatment with Botox

Product Name: Botox

Diagnosis	Hyperhidrosis, axillary
Approval Length	1 Time
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of primary axillary hyperhidrosis [G]

AND

2 One of the following:

2.1 Score of 3 or 4 on the Hyperhidrosis Disease Severity Scale (HDSS) [A, 1, 7]

OR

2.2 Skin maceration with secondary infection [8]

AND

3 History of failure, contraindication, or intolerance to topical prescription strength drying agents [e.g., Drysol, Hypercare, Xerac AC (aluminum chloride hexahydrate)]

Product Name: Botox

Diagnosis	Hyperhidrosis, axillary
Approval Length	1 Time
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 At least a 2-point improvement in HDSS [1, 7]

AND

2 At least 3 months have or will have elapsed since the last series of injections [1, 7]

Product Name: Botox

Diagnosis	Migraine headache, chronic
Approval Length	3 Month [B]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic migraines, defined by both of the following: [1, 31-34, I]

- Greater than or equal to 15 migraine headache days per month
- Headache lasts 4 hours a day or longer

AND

2 Prescribed by or in consultation with one of the following specialists:

- Neurologist
- Pain specialist

AND

3 History of failure after a trial of at least two months, contraindication, or intolerance to two of the following prophylactic therapies: [36, 40-41, H , K]

- Antidepressants [i.e., Elavil (amitriptyline), Effexor (venlafaxine)]
- Antiepileptics [i.e., Depakote/Depakote ER (divalproex sodium), Topamax (topiramate)]
- Beta-blockers [i.e., atenolol, Inderal (propranolol), nadolol, timolol, Toprol XL (metoprolol)]

Product Name: Botox

Diagnosis	Migraine headache, chronic
Approval Length	3 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Reduction of one of the following: [41]

- Headache frequency
- Headache intensity

AND

2 Submission of chart notes documenting one of the following:

- Decreased utilization of pain medications (e.g., narcotic analgesics, NSAIDs) or triptans
- Reduction in the number of emergency room visits

Product Name: Botox

Diagnosis	Urinary incontinence associated with a neurologic condition OR Overactive bladder with symptoms
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following conditions: [1, 3, E, F]

- Urinary incontinence that is associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis)
- Overactive bladder with symptoms (e.g., urge urinary incontinence, urgency, and frequency)

AND

2 Prescribed by or in consultation with a urologist

AND

3 History of failure, contraindication, or intolerance to at least one oral anticholinergic (antispasmodic or antimuscarinic) agent [e.g., Bentyl (dicyclomine), Donnatal (atropine/ scopolamine/ hyoscyamine/ phenobarbital), Levsin/Levsinex (hyoscyamine), Ditropan (oxybutynin), Enablex (darifenacin), or VESIcare (solifenacin)]

AND

4 Patient is routinely performing clean intermittent self-catheterization (CIC) or is willing/able to perform CIC if he/she has post-void residual (PVR) urine volume greater than 200 mL

Product Name: Botox

Diagnosis	Urinary incontinence associated with a neurologic condition OR Overactive bladder with symptoms
Approval Length	3 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Confirmed improvement in symptoms with initial Botox treatment

AND

2 At least 3 months have or will have elapsed since the last treatment with Botox

Product Name: Botox

Diagnosis	Chronic anal fissure (Off-Label)
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic anal fissure [11, 12]

AND

2 At least 2 months of one of the following symptoms:

- Nocturnal pain and bleeding
- Postdefecation pain

AND

3 History of failure, contraindication, or intolerance to one of the following conventional therapies:

- Topical nitrates
- Topical calcium channel blockers (CCBs) (e.g., diltiazem, nifedipine)

Product Name: Botox

Diagnosis	Chronic anal fissure (Off-Label)
Approval Length	3 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

- Incomplete healing of fissure
- Recurrence of fissure

AND

2 Improved symptoms with prior treatment with Botox

AND

3 At least 3 months have or will have elapsed since the last series of injections

Product Name: Botox

Diagnosis	Chronic back pain [D] (Off-Label)
Approval Length	1 treatment session (series of injections) [L]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of low back pain

AND

2 Low back pain has lasted for greater than or equal to six (6) months

AND

3 Prescribed by or in consultation with one of the following specialists:

- Neurologist
- Neurosurgeon
- Orthopedist
- Pain specialist

AND

4 History of failure (at least 3 months), contraindication, or intolerance to both of the following conventional therapies: [23, 25, 26]

- At least one oral NSAID medication

- At least one opioid medication

AND

5 History of failure or inadequate response to one of the following: [23]

- Physical therapy
- Nonpharmacologic therapy (e.g., spinal manipulation, massage therapy, transcutaneous electrical nerve stimulation (TENS), acupuncture/acupressure, and surgery)

Product Name: Botox

Diagnosis	Chronic back pain [D] (Off-Label)
Approval Length	1 treatment session (series of injections) [L]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Confirmed improvement in symptoms with initial Botox treatment

AND

2 At least 3 months have or will have elapsed since the last series of injections

Notes	Authorization will not exceed more than two treatment sessions total per year (including initial authorization).

Product Name: Botox

Diagnosis	Achalasia (Off-Label)

Approval Length	6 Month [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of achalasia

AND

2 One of the following:

2.1 High risk of complication from or failure to one of the following: [9, 10]

- Pneumatic dilation
- Myotomy

OR

2.2 Prior dilation caused esophageal perforation

OR

2.3 Patient has an increased risk of dilation-induced perforation due to one of the following:

- Epiphrenic diverticulum
- Hiatal hernia

Product Name: Botox

Diagnosis	Achalasia (Off-Label)
Approval Length	6 Month [C]

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of improvement or reduction in symptoms of achalasia (i.e., dysphagia, regurgitation, chest pain)

AND

2 At least 6 months have or will have elapsed since the last series of injections [C]

Product Name: Botox

Diagnosis	All other diagnoses
Approval Length	6 months unless the FDA-approved treatment duration is less than 6 months. If FDA-approved treatment duration is less than 6 months, utilize the FDA-approved duration for authorization period.
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Both of the following:

1.1.1 Diagnosis is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert)

AND

1.1.2 Additional requirements listed in the “Indications and Usage” and “Dosage and Administration” sections of the prescribing information (or package insert) have been met (e.g.: first line therapies have been tried and failed, any testing requirements have been met, etc)

OR

1.2 Meets the off-label administrative guideline criteria

AND

2 History of failure, contraindication, or intolerance to two appropriate formulary alternatives (if available)

3 . Endnotes

A. Hyperhidrosis Disease Severity Scale • The HDSS is a 4-point scale designed to assess the severity of hyperhidrosis in everyday clinical practice or in clinical research and the effectiveness of treatment. • The HDSS can be administered by an interviewer or self-completed by the patient. • The HDSS assess disease severity based on the extent of sweating-related impairment of daily activities. (1) Question - My (underarm) sweating is never noticeable and never interferes with my daily activities, Score - 1; (2) Question - My (underarm) sweating is tolerable but sometimes interferes with my daily activities, Score - 2; (3) Question - My (underarm) sweating is barely tolerable and frequently interferes with my daily activities, Score - 3; (4) Question - My (underarm) sweating is intolerable and always interferes with my daily activities, Score - 4
B. This recommendation is based on results from the PREEMPT 2 trial. The primary endpoint of PREEMPT 2 was the mean change from baseline in frequency of headache days for the 28-day period ending with week 24. [31, 32]
C. Approximately 50% of achalasia patients relapse and require repeat treatments at 6 to 24-month intervals. [9]
D. An evidence-based review by the American Academy of Neurology (AAN) concluded that botulinum neurotoxin (BoNT) is possibly effective for the treatment of chronic

predominantly unilateral low back pain (LBP) [one Class II study]. The AAN recommends that BoNT may be considered as a treatment option for patients with chronic predominantly unilateral LBP (Level C). [26]

E. An evidence-based review by the AAN established BoNT as safe and effective for the treatment of neurogenic detrusor overactivity (NDO) in adults (one Class I study and one Class II study). Data on the use of BoNT is probably safe and effective for the treatment of detrusor sphincter dyssynergia (DSD) in patients with spinal cord inury (2 Class II studies). On basis of one Class I study, BoNT does not provide significant benefit for the treatment of DSD in patients with multiple sclerosis (MS). The AAN recommends that BoNT should be offered as a treatment option for neurogenic detrusor overacivity (Level A), and that BoNT should be considered for DSD in patients with spinal cord injury (Level B). [26]
F. BoNT is not effective in patients with DSD due to multiple sclerosis in a multicenter, double-blind, placebo-controlled trial; however, in patients with DSD due to spinal cord injury, open-label clinical studies showed improvements in urodynamic parameters [recommendation for DSD: Adult, Class IIb, Category B]. For NDO, the use of BoNT (refractory to antispasmodics) in a randomized, double-blind, placebo-controlled clinical trial of 59 patients (n = 53 with spinal cord injury and n = 6 with multiple sclerosis) showed significant improvement in daily incontinence episodes in weeks 1 through 24 (except for weeks 12 and 18) compared to placebo [recommendation for NDO: Adult, Class IIb, Category B]. [26]
G. The safety and effectiveness of Botox for hyperhidrosis in areas other than the axillae have not been established. [1]
H. Clinical benefit from prophylactic therapy may take as long as 2 to 3 months to manifest. [36, 40] Recommended first-line agents for the prevention of migraine headache are atenolol, nadolol, propranolol, timolol, amitriptyline, venlafaxine, topiramate, divalproex sodium, and sodium valproate. [36]
I. Safety and effectiveness have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) in seven placebo-controlled studies. [1] An evidence-based review by the American Academy of Neurology determined that, based on available evidence, Botox was probably ineffective in episodic migraine and tension-type headaches, and should not be considered in patients with these conditions. [26]
J. Amitriptyline is included on the 2013 Health Plan Employer Data and Information Set (HEDIS) list of high-risk medications in the elderly (greater than or equal to 65 years old). [37] Antimuscarinics (eg, darifenacin, fesotoredine, flavoxate, oxybutynin, solifenacin, tolterodine, trospium) and antispasmodics (eg, atropine) are included in the 2012 Beers Criteria for Potentially Inappropriate Medication Use in Older Adults greater than or equal to 65 years old. [38]
K. The effects of Botox in reducing the frequency of headache days in the PREEMPT trial and in the pooled analysis of the PREEMPT trials were very modest. Given the experience and evidence we have for other prophylactic treatments in the management of migraine, which are supported by national guidelines, it is reasonable to require failure with other prophylactic treatments before approving use of Botox. [36]
L. A single small randomized trial (n = 31) compared paravertebral injections of botulinum toxin with saline injections and found significant benefit of botulinum toxin up to eight weeks after injection. There is currently no consensus on number of injections or treatment length for low back pain. [26]

4 . References

1. Botox Prescribing Information. Allergan, Inc. January 2016.
2. McEvoy GK. AHFS Drug Information 2006. Bethesda, MD: American Society of Health-System Pharmacists, Inc; 2006.
3. United States Pharmacopeia Dispensing Information: Drug Information for the Health Care Professional. 25th ed. Greenwood Village, CO: Thomson MICROMEDEX; 2005.
4. American Academy of Neurology (AAN). Training guidelines for the use of botulinum toxin for the treatment of neurologic disorders. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 1994;44:2401-3.
5. American Academy of Neurology: Assessment: the clinical usefulness of botulinum toxin-A in treating neurologic disorders. Report of the Therapeutics and Technology Subcommittee of the American Academy of Neurology. Neurology 1990;40:1332-1336.
6. Charles PD. Botulinum neurotoxin serotype A: a clinical update on non-cosmetic uses. Am J Health Syst Pharm 2004;61:S11-23.
7. Lowe NJ, Glaser DA, Eadie N, Daggett S, Kowalski JW, Lai PY. Botulinum toxin type A in the treatment of primary axillary hyperhidrosis: a 52-week multicenter double-blind, randomized, placebo-controlled study of efficacy and safety. J Am Acad Dermatol. 2007;56:604-611.
8. Naumann M, Lowe NJ. Botulinum toxin type A in treatment of bilateral primary axillary hyperhidrosis: randomised, parallel group, double blind, placebo controlled trial. BMJ 2001;323:596-9.
9. Vaezi MF, Pandolfino JE, Vela MF. American College of Gastroenterology Practice Parameter Committee. Diagnosis and management of achalasia. Am J Gastroenterol advance online publication, 23 July 2013.
10. Pasricha PJ, et al. Intrasphincteric botulinum toxin for the treatment of achalasia. N Engl J Med 1995;332:774-8.
11. American Society of Colon and Rectal Surgeons. Practice Parameters for the Management of Anal Fissures (3rd Revision). Dis Colon Rectum 2010; 53: 1110–1115.
12. Brisinda G, et al. A comparison of injections of botulinum toxin and topical nitroglycerin ointment for the treatment of chronic anal fissure. N Engl J Med 1999;341:65-9.
13. Blitzer A, Brin MF, Steward CF. Botulinum toxin management of spasmodic dysphonia (laryngeal dystonia): a 12-year experience in more than 900 patients. Laryngoscope 1998;108:1435-41.
14. Koman LA, Mooney JF III, Smith BP, et al. Management of spasticity in cerebral palsy with botulinum-A toxin: report of a preliminary, randomized, double-blind trial. J Pediatr Orthop 1994;14:299-303.
15. Wissel J, Heinen F, Schenkel A et al. Botulinum toxin A in the management of spastic gait disorderes in children and young adults with cerebral palsy: a randomized, double-blind study of “high-dose” versus “low-dose” treatment. Neuropediatrics 1999;30:120-4.
16. Sutherland DH, Jaufman KR, Wyatt MP et al. Double-blind study of botulinum A toxin injections into the gastrocnemius muscle in patients with cerebral palsy. Gait Posture 1999;10:1-9.
17. Koman LA, Mooney JF III, Smith BP et al. BOTOX Study Group. Botulinum toxin type A neuromuscular blockade in the treatment of lower extremity spasticity in cerebral palsy: a randomized, double-blind, placebo-controlled trial. J Pediatr Orthop 2000;20:108-15.
18. Fehlings D, Rang M, Glazier J et al. An evaluation of botulinum-A toxin injections to improve upper extremity function in children with hemiplegic cerebral palsy.
19. Annese V, Bassotti G, Coccia G, et al. GIS-MAD Achalasia Study Group. A multi-centre randomized study of intrasphincteric botulinum toxin in patients with oesophageal achalasia. Gut 2000;46:597-600.

20. Mentes BB, Irkorucu O, Akin M, et al. Comparison of botulinum toxin injection and lateral internal sphincterotomy for the treatment of chronic anal fissure. Dis Colon Rectum 2003;46:232-7.
21. Cole R, Hallett M, Cohen LG. Double-blind trial of botulinum toxin for treatment of hand dystonia. Movement Disorders 1995;10(4):466-71.
22. Foster L, Clapp L, Erickson M, Jabbari B. Botulinum toxin A and chronic low back pain: a randomized, double blind study. Neurology 2001;56:1290-1293.
23. Ney JP, Difazio M, Sichani A, Monacci W, Foster L, Jabbari B. Treatment of chronic low back pain with successive injections of botulinum toxin A over 6 months: a prospective trial of 60 patients. Clin J Pain 2006;22(4):363-369.
24. van Tulder MW, Touray T, Furlan AD, Soloway S, Bouter LM. Muscle relaxants for nonspecific low back pain: a systematic review framework of the Cochrane Collaboration. Spine 2003;28(17):1978-1992.
25. MayoClinic. Back pain. Available at: www.Mayoclinic.com. Accessed April 23, 2007.
26. Naumann M, So Y, Argoff CE et al. Assessment: botulinum neurotoxin in the treatment of autonomic disorder and pain (an evidence-based review): report of the Therapeutics and Assessment Subcommittee of the American Academy of Neurology. Neurology 2008;70:1707-1714.
27. Schurch B, De Seze M, Denys P, et al. Botulinum toxin is a safe and effective treatment for neurogenic urinary incontinence: results of a single treatment, randomized, placebo controlled 6-month study. The Journal of Urology 2005;174:196-200.
28. Brashear A, Gordon MF, Elovic E, et al. Intramuscular injection of boltulinum toxin for the treatment of wrist and finger spasticity after a stroke. NEJM. 2002;347:395-400.
29. Childers MK, Brashear A, Jozefczyk P. Dose-dependent response to intramuscular botulinum toxin type A for upper-limb spasticity in patients after a stroke. Arch Phys Med Rehabil. 2004;85:1063-1069.
30. Royal College of Physicians, British Society of Rehabilitation Medicine, Chartered Society of Physiotherapy, Association of Chartered Physiotherapists Interested in Neurology. Spasticity in adults: management using botulinum toxin. National guidelines. London: RCP, 2009.
31. Aurora SK, Dodick DW, Turkel CC, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 1 trial. Cephalagia. 2010;30:793-803.
32. Diener HC, Dodick DW, Aurora SK, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. Cephalagia. 2010;30:804-814.
33. Dodick DW, Turkel CC, DeGryse RE, et al. OnabotulinumtoxinA for treatment of chronic migraine: pooled results from the double-blind, randomized, placebo-controlled phases of the PREEMPT clinical program. Headache. 2010;50:921-936.
34. Per clinical consultation with neurologist, January 7, 2011.
35. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean R, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults. Arch Intern Med. 2003;163:2716-2724.
36. Silberstein SD, Holland S, Freitag F, et al; Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology 2012 Apr 24;78(17):1337-45.
37. Use of High-Risk Medications in the Elderly (DAE). Summary of changes to HEDIS 2013. Available at: www.ncqa.org. Accessed June 11, 2013.

38. American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012 Apr;60(4):616-31.
39. FDA Supplement Approval. April 2015. http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2015/103000Orig1s5282ltr.pdf . Accessed May 21, 2015.
40. Loder E, Burch R, Rizzoli P.The 2012 AHS/AAN Guidelines for Prevention of Episodic Migraine: A Summary and Comparison With Other Recent Clinical Practice Guidelines. Headache 2012;52:930-945.
41. Per clinical consultation with neurologist, July 20, 2015.
42. American Academy of Neurology: Assessment: Botulinum neurotoxin for the treatment of movement disorders (an evidence-based review) Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2008;70:1699–1706.

Prior Authorization Guideline

GL-16521 Caprelsa (vandetanib)

Formulary OptumRx SP

Formulary Note

Approval Date 4/4/2016

Revision Date 4/4/2016

Technician Note :

P&T Approval Date: 7/12/2011; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Caprelsa (vandetanib)

Indications

Medullary Thyroid Cancer (MTC)

Indicated for the treatment of symptomatic or progressive MTC in patients with unresectable locally advanced or metastatic disease. Use Caprelsa in patients with indolent, asymptomatic or slowly progressing disease only after careful consideration of the treatment related risks of Caprelsa.

2 . Criteria

Product Name: Caprelsa

Approval Length	12 Months [A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of one of the following: [1,2]

- Metastatic medullary thyroid cancer (MTC)
- Unresectable locally advanced MTC

AND

2 One of the following: [1,2]

- Patient has symptomatic disease
- Patient has progressive disease

AND

3 Prescribed by or in consultation with one of the following:

- Oncologist
- Endocrinologist

Product Name: Caprelsa

Approval Length	12 Months [A]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Caprelsa therapy

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. Caprelsa treatment should be continued until patients are no longer benefiting from treatment or an unacceptable toxicity occurs. [1]

5 . References

1. Caprelsa Prescribing Information. AstraZeneca, March 2014.
2. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium: Vandetanib. Available at: http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=371. Accessed November 30, 2015.

Prior Authorization Guideline

GL-16323 Cayston (aztreonam for inhalation solution)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/25/2016

Technician Note :

P&T Approval Date: 6/22/2010; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Cayston (aztreonam for inhalation solution)

Indications

Cystic Fibrosis

Indicated to improve respiratory symptoms in cystic fibrosis (CF) patients with Pseudomonas aeruginosa. Safety and effectiveness have not been established in pediatric patients below the age of 7 years, patients with FEV1 < 25% or > 75% predicted, or patients colonized with Burkholderia cepacia. To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cayston and other antibacterial drugs, Cayston should be used only to treat patients with CF known to have Pseudomonas aeruginosa in the lungs.

2 . Criteria

Product Name: Cayston

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cystic fibrosis

AND

2 Patient has evidence of Pseudomonas aeruginosa in the lungs

AND

3 Patient is seven years of age or older

Product Name: Cayston

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cystic fibrosis

AND

2 Patient has evidence of Pseudomonas aeruginosa in the lungs

AND

3 Patient is seven years of age or older

AND

4 Patient is benefiting from treatment (i.e., improvement in lung function [forced expiratory volume in one second {FEV1}], decreased number of pulmonary exacerbations)

3 . References

1. Cayston Prescribing Information. Gilead Sciences, Inc., May 2014.

2. Retsch-Bogart GZ, Quittner AL, Gibson RL, et al. Efficacy and safety of inhaled aztreonam lysine for airway Pseudomonas in cystic fibrosis. Chest. 2009;135:1223-32.
3. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic Fibrosis Foundation Pulmonary Guideline. Pharmacologic approaches to prevention and eradication of initial Pseudomonas aeruginosa infection. Ann Am Thorac Soc. 2014;11(10):1640-50.

Prior Authorization Guideline

GL-17344 Cimzia (certolizumab pegol)

Formulary OptumRx SP

Formulary Note

Approval Date 11/19/2014

Revision Date 5/18/2016

Technician Note :

P&T Approval Date: 5/20/2008; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Cimzia (certolizumab pegol)

Indications

Crohn's Disease

Indicated for reducing signs and symptoms of Crohn's disease (CD) and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.

Rheumatoid Arthritis

Indicated for the treatment of adults with moderately to severely active rheumatoid arthritis. **Psoriatic Arthritis** Indicated for the treatment of adult patients with active psoriatic arthritis (PsA). **Ankylosing Spondylitis** Indicated for the treatment of adults with active ankylosing spondylitis.

2 . Criteria

Product Name: Cimzia

Diagnosis	Crohn’s disease
Approval Length	16 Week
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active Crohn’s disease

AND

2 History of failure, contraindication, or intolerance to one of the following conventional therapies: [14]

- 6-mercaptopurine (Purinethol)
- Azathioprine (Imuran)
- Corticosteroids (e.g., prednisone, methylprednisolone)

- Methotrexate (Rheumatrex, Trexall)

AND

3 Prescribed by or in consultation with a gastroenterologist

AND

4 Patient is not receiving Cimzia in combination with a biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)] [1]

AND

5 Patient is not receiving Cimzia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1]

Product Name: Cimzia

Diagnosis	Crohn's disease
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Cimzia therapy

AND

2 Patient is not receiving Cimzia in combination with a biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)] [1]

AND

3 Patient is not receiving Cimzia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1]

Product Name: Cimzia

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active RA

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication or intolerance to one non-biologic DMARDs [e.g., Rheumatrex/Trexall (methotrexate), Arava (leflunomide), Azulfidine (sulfasalazine)] [6,13]

AND

4 Patient is not receiving Cimzia in combination with a biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)] [1]

AND

5 Patient is not receiving Cimzia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1]

Product Name: Cimzia

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Cimzia therapy

AND

2 Patient is not receiving Cimzia in combination with a biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)] [1]

AND

3 Patient is not receiving Cimzia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1]

Product Name: Cimzia

Diagnosis	Psoriatic Arthritis
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active psoriatic arthritis

AND

2 Prescribed by or in consultation with one of the following:

- Dermatologist
- Rheumatologist

AND

3 Patient is not receiving Cimzia in combination with a biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)] [1]

AND

4 Patient is not receiving Cimzia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1]

Product Name: Cimzia

Diagnosis	Psoriatic Arthritis
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Cimzia therapy

AND

2 Patient is not receiving Cimzia in combination with a biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)] [1]

AND

3 Patient is not receiving Cimzia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1]

Product Name: Cimzia

Diagnosis	Ankylosing Spondylitis
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active ankylosing spondylitis

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to two NSAIDs [16, 17]

AND

4 Patient is not receiving Cimzia in combination with a biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)] [1]

AND

5 Patient is not receiving Cimzia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1]

Product Name: Cimzia

Diagnosis	Ankylosing Spondylitis
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Cimzia therapy

AND

2 Patient is not receiving Cimzia in combination with a biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)] [1]

AND

3 Patient is not receiving Cimzia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1]

3 . References

1. Cimzia Prescribing Information, UCB. October 2013.
2. Schreiber S, Rutgeerts P, Fedorak RN, et al. A randomized, placebo-controlled trial of certolizumab pegol (CDP870) for treatment of Crohn's disease. Gastroenterology. 2005; 129(3): 807-18.
3. Sandborn WJ, Feagan BG, Stoinov S, et al. Certolizumab pegol for the treatment of Crohn's disease. N Engl J Med. 2007 Jul 19; 357(3):228-38.
4. Schreiber WJ, Khaliq-Kareemi M, Lawrance IC, et al. Maintenance therapy with certolizumab pegol for Crohn's disease. N Engl J Med. 2007 Jul 19; 357(3):239-50
5. Lichtenstein GR, Abreu MT, Cohen R, Tremaine W. American Gastroenterological Association Institute medical position statement on corticosteroids, immunomodulators, and infliximab in inflammatory bowel disease. Gastroenterology 2006 Mar;130(3):935-9.
6. American College of Rheumatology 2008 Recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum.2008;59(6):762-784.
7. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases. Ann Rheum Dis. 2011;70(Suppl 1):i2-i36.
8. Keystone E, van der Heijde D, Mason Jr. D, et al. Certolizumab pegol plus methotrexate is significantly more effective than placebo plus methotrexate in active rheumatoid arthritis. Arthritis Rheum. 2008; 58(11): 3319-3329.
9. Fleischmann R, Vencovsky J, van Vollenhoven RF, et al. Efficacy and safety of certolizumab pegol monotherapy every 4 weeks in patients with rheumatoid arthritis failing previous disease-modifying antirheumatic therapy: the FAST4WARD study. Ann Rheum Dis. 2009; 68: 805-811.
10. Smolen J, Landewe RB, Mease P, et al. Efficacy and safety of certolizumab pegol plus methotrexate in active rheumatoid arthritis: the RAPID 2 study: A randomized controlled trial. Ann Rheum Dis. 2009; 68: 797-804.
11. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995;38:727-735.
12. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum. 1993; 36 (6): 729-740.
13. Per clinical consult with rheumatologist, June 30, 2011.
14. Lichtenstein GR, Hanauer SB, Sandborn WJ, and The Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn’s disease in adults. Am J Gastroenterol. 2009;104:465-483.
15. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College ofRheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012;64(5):625-39.
16. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of Ankylosing spondylitis. Ann Rheum Dis. 2011;70:896-904.

17. van der Heijde, Sieper J, Maksymowych WP, et al. 2010 update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. Ann Rheum Dis. 2011;70:905-908.
18. Kyle S, Chandler D, Griffiths EM, et al. Guideline for anti-TNF-? therapy in psoriatic arthritis. Rheumatology. 2005;44:390-397.
19. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011. Ann Rheum Dis. 2012;71(Supp II):i2–i45.

Prior Authorization Guideline

GL-17393 Colony-Stimulating Factors (CSFs)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/25/2016

Technician Note :

P&T Approval Date: 8/1/2006; P&T Revision Date: 2/25/2016 ** Effective 7/1/2016 **

1 . Indications

Drug Name: Neulasta (pegfilgrastim, G-CSF) **<u>Indications</u>** **Febrile Neutropenia (FN), Prophylaxis** Indicated to decrease the incidence of infection, as manifested by FN, in patients with nonmyeloid malignancies receiving myelosuppressive anti cancer drugs associated with a clinically significant incidence of FN.
Drug Name: Neupogen (filgrastim, G-CSF)

Indications

Febrile Neutropenia (FN), Prophylaxis

Indicated to decrease the incidence of infection, as manifested by FN, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever. A complete blood count (CBC) and platelet count should be obtained prior to chemotherapy, and twice per week during Neupogen therapy to avoid leukocytosis and to monitor the neutrophil count. In phase 3 clinical studies, Neupogen therapy was discontinued when the absolute neutrophil count (ANC) was greater than or equal to 10,000/mm^3 after the expected chemotherapy-induced nadir.

Patients with acute myeloid leukemia (AML) receiving induction or consolidation chemotherapy

Indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with AML.

Bone marrow transplant (BMT) - Neupogen use in cancer patients receiving BMT

Indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation. It is recommended that CBCs and platelet counts be obtained at a minimum of 3 times per week following marrow infusion to monitor the recovery of marrow reconstitution.

Patients undergoing peripheral blood progenitor cell (PBPC) collection and therapy

Indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis. Mobilization allows for the collection of increased numbers of progenitor cells capable of engraftment compared with collection by leukapheresis without mobilization or bone marrow harvest. After myeloablative chemotherapy, the transplantation of an increased number of progenitor cells can lead to more rapid engraftment, which may result in a decreased need for supportive care.

Patients with severe chronic neutropenia (SCN)

Indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia. It is essential that serial CBCs with differential and platelet counts, and an evaluation of bone marrow morphology and karyotype be performed prior to initiation of Neupogen therapy. The use of Neupogen prior to confirmation of SCN may impair diagnostic efforts and may thus impair or delay evaluation and treatment of an underlying condition, other than SCN, causing the neutropenia.

Off Label Uses

HIV-related neutropenia

Has been prescribed for HIV-related neutropenia. [11-15]

Hepatitis-C Interferon induced neutropenia

Neupogen has been prescribed for interferon-induced neutropenia in Hepatitis C virus infected patients [4-10]

Drug Name: Leukine (sargramostim, GM-CSF)

Indications

Patients with acute myeloid leukemia (AML) receiving induction or consolidation chemotherapy

Indicated for use following induction chemotherapy in older adults with AML to shorten time to neutrophil recovery and reduce the incidence of severe and life-threatening infections and infections resulting in death. The safety and efficacy of Leukine have not been assessed in patients with AML under 55 years of age.

Bone marrow transplant (BMT) - Leukine use in myeloid reconstitution after autologous BMT

Indicated for acceleration of myeloid recovery in patients with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's disease undergoing autologous BMT. After autologous BMT in patients with NHL, ALL, or Hodgkin's disease, Leukine has been found to be safe and effective in accelerating myeloid engraftment, decreasing median duration of antibiotic administration, reducing the median duration of infectious episodes and shortening the median duration of hospitalization. Hematologic response to Leukine can be detected by CBC with differential cell counts performed twice per week.

Bone marrow transplant (BMT) - Leukine use in myeloid reconstitution after allogeneic BMT

Indicated for acceleration of myeloid recovery in patients undergoing allogeneic BMT from HLA-matched related donors. Leukine has been found to be safe and effective in accelerating myeloid engraftment, reducing the incidence of bacteremia and other culture positive infections, and shortening the median duration of hospitalization.

Bone marrow transplant (BMT) - Leukine use in BMT failure or engraftment delay

Indicated in patients who have undergone allogeneic or autologous BMT in whom engraftment is delayed or has failed. Leukine has been found to be safe and effective in prolonging survival of patients who are experiencing graft failure or engraftment delay, in the presence or absence of infection, following autologous or allogeneic BMT. Survival benefit may be relatively greater in those patients who demonstrate one or more of the following characteristics: autologous BMT failure or engraftment delay, no previous total body irradiation, malignancy other than leukemia or a multiple organ failure (MOF) score less than or equal to 2. Hematologic response to Leukine can be detected by CBC with differential performed twice per week.

Patients undergoing peripheral blood progenitor cell (PBPC) collection and therapy

Indicated for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis. Mobilization allows for the collection of increased numbers of progenitor cells capable of engraftment as compared with collection without mobilization. After myeloablative chemotherapy, the transplantation of an increased number of progenitor cells can lead to more rapid engraftment, which may result in a decreased need for supportive care. Myeloid reconstitution is further accelerated by administration of Leukine following PBPC transplantation.

Drug Name: Granix (tbo-filgrastim, G-CSF)

Indications

Febrile Neutropenia (FN), prophylaxis

Indicated to reduce the duration of severe neutropenia in patients with non?myeloid malignancies receiving myelosuppressive anti?cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Drug Name: Zarxio (filgrastim-sndz, G-CSF)

Indications

Febrile Neutropenia (FN), Prophylaxis

Indicated to decrease the incidence of infection, as manifested by FN, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever

Patients with acute myeloid leukemia (AML) receiving induction or consolidation chemotherapy

Indicated for reducing the time to neutrophil recovery and the duration of fever, following

induction or consolidation chemotherapy treatment of adults with AML

Bone marrow transplant (BMT) - Zarxio use in cancer patients receiving BMT

Indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, eg, febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation

Patients undergoing peripheral blood progenitor cell (PBPC) collection and therapy

Indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis

Patients with severe chronic neutropenia (SCN)

Indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (eg, fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia

2 . Criteria

Product Name: Leukine, Neupogen, or Zarxio

Diagnosis	Bone Marrow/Stem Cell Transplant
Approval Length	3 months or duration of therapy
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by autologous or allogeneic BMT [2, 3]

OR

1.2 For mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis [2, 3]

OR

1.3 For peripheral stem cell transplant (PSCT) patients who have received myeloablative chemotherapy [2, 3]

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Leukine

Diagnosis	AML Induction or Consolidation Therapy
Approval Length	3 months or duration of therapy [C]
Guideline Type	Prior Authorization

Approval Criteria

1 For patients with AML following induction or consolidation chemotherapy [2, 3, 38, A]

AND

2 Age greater than or equal to 55 years [3, B]

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Neupogen or Zarxio

Diagnosis	AML Induction or Consolidation Therapy
Approval Length	3 months or duration of therapy [C]
Guideline Type	Prior Authorization

Approval Criteria

1 For patients with AML following induction or consolidation chemotherapy [2, 3, 38, A]

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Leukine, Neulasta, Neupogen, or Zarxio

Diagnosis	Neutropenia Associated with Cancer Chemotherapy - Dose Dense Chemotherapy
Approval Length	3 months or duration of therapy
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Patient is receiving National Cancer Institute's Breast Intergroup, INT C9741 dose dense chemotherapy protocol for primary breast cancer (see Table 2 in Background section)

[16-19, D, E]

OR

1.2 Patient is receiving a dose-dense chemotherapy regimen for which the incidence of FN is unknown [E]

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Granix, Leukine, Neulasta, Neupogen, or Zarxio

Diagnosis	Primary Prophylaxis of Chemotherapy-Induced Febrile Neutropenia (FN)
Approval Length	3 months or duration of therapy
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Patient receiving chemotherapy regimens associated with greater than 20% incidence of FN [16, 17, I]

OR

1.2 Both of the following:

1.2.1 Patient receiving chemotherapy regimen associated with 10-20% incidence of FN [16, J]

AND

1.2.2 One or more risk factors associated with chemotherapy-induced infection, FN, or neutropenia [16, 17, K]

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Granix, Leukine, Neulasta, Neupogen, or Zarxio

Diagnosis	Secondary Prophylaxis of Febrile Neutropenia
Approval Length	3 months or duration of therapy
Guideline Type	Prior Authorization

Approval Criteria

1 For patients receiving myelosuppressive anticancer drugs associated with neutropenia (ANC less than or equal to 500 cells/mm^3) [1-3, l]

AND

2 Patients with a history of FN during a previous course of chemotherapy [16, 17]

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Leukine, Neulasta, Neupogen, or Zarxio

Diagnosis	Treatment of Febrile Neutropenia (Off-label)
Approval Length	1 Month
Guideline Type	Prior Authorization

Approval Criteria

1 For patients receiving myelosuppressive anticancer drugs associated with neutropenia (ANC less than or equal to 500 cells/mm^3) [1-3, l]

AND

2 Patients with FN at high risk for infection-associated complications [16, 17]

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Neupogen or Zarxio

Diagnosis	Severe Chronic Neutropenia (SCN)
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 For patients with SCN (ie, congenital, cyclic, and idiopathic neutropenias with chronic ANC less than or equal to 500 cells/mm^3) [2, 16]

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Leukine, Neupogen, or Zarxio

Diagnosis	HIV-Related Neutropenia (Off-label)
Approval Length	6 months [11, 15, H]
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is infected with HIV virus [11- 13]

AND

2 ANC less than or equal to 1,000 (cells/mm3) [12, 13]

AND

3 Prescribed by or in consultation with one of the following:

- Hematologist/oncologist
- Infectious disease specialist

Product Name: Neupogen

Diagnosis	Hepatitis-C Treatment Related Neutropenia (Off-label)
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 All of the following:

1.1.1 Patients infected with Hepatitis C virus

AND

1.1.2 Patient is undergoing treatment with Peg-Intron (peginterferon alfa-2b) or Pegasys (peginterferon alfa-2a)

AND

1.1.3 Neutropenia (ANC less than or equal to 500 cells/mm3) after dose reduction of Peg-Intron or Pegasys

OR

1.2 Both of the following:

1.2.1 Patients who experience interferon-induced neutropenia (ANC less than or equal to 500 cells/mm3) due to treatment with Peg-Intron (peginterferon alfa-2b) or Pegasys (peginterferon alfa-2a)

AND

1.2.2 One of the following:

1.2.2.1 Patient with HIV co-infection

OR

1.2.2.2 Status post liver transplant

OR

1.2.2.3 Patient with established cirrhosis

AND

2 Prescribed by or in consultation with a hematologist/oncologist

3 . Endnotes

A. Currently there is no information available about the effect of longer acting pegylated G-CSF in patients with myeloid leukemias, therefore pegylated G-CSF should not be used in such patients outside of clinical trials. [17]
B. The safety and efficacy of Leukine in AML induction or consolidation in adults younger than 55 years old have not been established in clinical trials. [3]
C. Per hematology/oncology consultant and member of P&T, most cycles of induction or consolidation chemotherapy last ~ 1 month, but patients who complete therapy typically receive 1 induction and 2-3 consolidations, so re-approval would need to occur every month.
D. The safety and efficacy of pegylated G-CSF has not been fully established in the setting of dose-dense chemotherapy. [17]
E. Per hematology/oncology consultant and member of P&T in general, dose-dense regimens require growth factor support for chemotherapy administration. [16] Also, Neulasta is commonly used to support dose dense regimens in current community practice. It would be reasonable to allow Neulasta use [in the INT C9741 Protocol] and to broaden its use for other forms of dose dense chemotherapy.

F. The product information for both PEG-Intron and Pegasys recommends dose reduction in patients with neutropenia with an ANC level < 750 cells/mm^3. [22, 23]
G. Per GI consultant and member of P&T, his medical group of practicing hepatologists recommends Neupogen for a special subpopulation of patients with HIV infection, status post liver transplant, or established cirrhosis who experience interferon-induced neutropenia (ANC less than or equal to 500 cells/mm^3) due to treatment with Peg-Intron or Pegasys.
H. Guidelines issued by the U.S. Public Health Service (USPHS) and the Infectious Diseases Society of America (IDSA) recommend for HIV-related neutropenia, the length of therapy with G-CSF and GM-CSF is 2-4 weeks. [15]
I. Note: This list is NOT inclusive of all chemotherapy regimens with a high risk of FN: See Table 3 in Background section
J. Note: This list is NOT inclusive of all chemotherapy regimens with an intermediate risk of FN: See Table 4 in Background section
K. Risk factors are based on provider information, not the list in the table below. Examples of risk factors may include (but are NOT limited to): Risk factors associated with chemotherapy-induced infection, FN, or neutropenia • Age > 65 years [16, 17] • History of extensive prior chemotherapy or radiation therapy including large radiation ports [16, 17] • Previous episodes of FN [16, 17] • Administration of combined chemoradiotherapy [17] • Pre-existing neutropenia or bone marrow involvement with tumor [16, 17] • Pre-existing conditions [16] • Neutropenia • Active infection/open wounds • Recent surgery • Poor performance status [16, 17] • Poor renal function [16] • Liver dysfunction [16] • Poor nutritional status [17] • More advanced cancer [17] • Hypotension and multiorgan dysfunction (Sepsis syndrome) [16, 17] • Pneumonia [16] • Invasive fungal infection [16, 17] • Other clinically documented infections [16] • Hospitalization at the time of fever [16] • Anticipated prolonged (> 10 days) and profound neutropenia (< 100/mm^3) [17] • Uncontrolled primary disease [17] • Other serious comorbidities [17]
L. Note: This list is NOT all inclusive: See Table 5 in Background section

4 . References

1. Neulasta Prescribing Information. Amgen Inc., June 2011.
2. Neupogen Prescribing Information. Amgen Inc., September 2013.
3. Leukine Prescribing Information. .Bayer HealthCare Pharmaceuticals, April 2013.
4. Sulkowski M. Managing the hematologic complications of interferon/ribavirin. Clinical Care Options for Hepatitis Annual Update. Milford, MA: IMedoptions, 2003:101-102.
5. Soza A, Everhart JE, Gharny MG, et al. Neutropenia during combination therapy of interferon alfa and ribavirin for chronic hepatitis C. Hepatol. 2002;36:1273-1279.
6. Van Thiel DH, Faruki H. Combination treatment of advanced HCV associated liver disease with interferon and G-CSF. Hepatogastroenterol.1995;42:907-912.
7. Carreno V, Parra A, Navas S, Quiroga J. Granulocyte macrophage colony stimulating factors as adjuvant therapy for interferon alpha treatment of chronic hepatitis C. Cytokine. 1996;8:318-322.
8. Shiffman M, Hofmann, Luketic VA, Sanyal AJ. Use of granulocyte macrophage colony stimulating factor alone or in combination with interferon-alpha-2b for treatment of chronic hepatitis C. J Hepatol.1998;28:382-389.
9. Farmer D, Collantes R, Makay S, et al. Filgrastim for the neutropenia associated with combination therapy in chronic hepatitis C. Gastroenterol. 2005; 128(4, Suppl2):a-725.
10. Stein DF, McKenzie SD. Peg-interferon alfa-2b and ribavirin in treatment naïve African American patients infected with HCV genotype 1. Hepatol.2003;38(4):642A.

11. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed November 12, 2015.
12. Hermans P, Rozenbaum W, Jou A, et al. Filgrastim to treat neutropenia and support myelosuppressive medication dosing in HIV infections. G-CSF 92105 Study Group. AIDS 1996;10:1627-33.
13. Kuritzkes, DR, Parenti D, Ward DJ, et al. Filgrastim prevents severe neutropenia and reduces infective morbidity in patients with advanced HIV infection; results of a randomized, multicenter, controlled trial. AIDS 1998;12:65-74.
14. Levine AM, Karim R, Mack W, et al. Neutropenia in human immunodeficiency virus infection: data from the women's interagency HIV study. Arch Intern Med. 2006;166:405-410.
15. Centers for Disease Control and Prevention. Guidelines for Preventing Opportunistic Infections Among HIV-Infected Persons – 2002 Recommendations of the U.S. Public Health Service and the Infectious Disease Society of America. MMWR 2002;51(No. RR-8):1-52.
16. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Myeloid Growth Factors. v.1.2015. Available at: http://www.nccn.org/professionals/physician_gls/PDF/myeloid_growth.pdf. Accessed November 12, 2015.
17. Smith TJ, Khatcheressian J, Lyman GH, et al. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. J Clin Oncol. 2006;24:3187-205.
18. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology v.1.2016. Breast cancer. Available at: http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf. Accessed November 12, 2015.
19. Citron ML, Berry DA, Cirrincione C, et al. Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: first report of Intergroup Trial C9741/Cancer and Leukemia Group B trial. J Clin Oncol. 2003;21(8):1431-9.
20. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Prevention and Treatment of Cancer Related Infections v.2.2015. Available at: http://www.nccn.org/professionals/physician_gls/PDF/infections.pdf. Accessed November 12, 2015.
21. Benson CA, Kaplan JE, Masur H, Pau A, Holmes KK. Treating opportunistic infections among HIV-exposed and infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the Infectious Disease Society of America. MMWR Recomm Rep 2004;53(RR-15):1-118.
22. Pegasys Product Information. Roche Pharmaceuticals. August 2011.
23. Peg-Intron Product Information. Schering Corporation. June 2011.
24. American Gastroenterological Association. Medical Position Statement on the Management of Hepatitis C. Gastroenterol 2006;130:225-30.
25. Ghany MG, Strader DB, Thomas DL, Seeff LB; American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C: an update. Hepatology. 2009;49(4):1335-74.
26. Hudis CA, Schmitz. Dose-dense chemotherapy in breast cancer and lymphoma. Seminar in Oncol. 2004;31(Suppl 8):19-23.
27. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-Hodgkin’s Lymphoma. v.1.2016. Available at:

http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf Accessed November 12, 2015.
28. Nemunaitis J, Rosenfeld CS, Ash R, et al. Phase III Randomized, double-blind placebo-controlled trial of rhGM-CSF following allogenic bone marrow transplantation. Bone Marrow Transplant. 1995;72:949-54.
29. Nemunaitis J, Buckner CD, Appelbaum FR et al. Phase I/II trial of recombinant human granulocyte-macrophage colony-stimulating factor following allogeneic bone marrow transplantation. Blood. 1991;77:2065-71.
30. Nemunaitis J, Rabinowe SN, Singer JW et al. Recombinant granulocyte-macrophage colony-stimulating factor after autologous bone marrow transplantation for lymphoid cancer. N Engl J Med. 1991;324:1773-8.
31. Rabinowe SN, Neuberg D, Bierman PJ et al. Long-term follow-up of a phase III study of recombinant human granulocyte-macrophage colony-stimulating factor after autologous bone marrow transplantation for lymphoid malignancies. Blood. 1993;81:1903-8.
32. Grant SM, Heel RC. Recombinant granulocyte-macrophage colony-stimulating factor (rGM-CSF): a review of its pharmacological properties and prospective role in the management of myelosuppression. Drugs 1992;43:516-60.
33. McEvoy GK, ed. AHFS Drug Information 2006. Bethesda, MD: American Society of Health-System Pharmacists; 2006.
34. Nemunaitis J, Singer JW, Buckner CD et al. Use of recombinant human granulocyte-macrophage colony-stimulating factor in graft failure after bone marrow transplantation. Blood. 1990;76:245-53.
35. Rowe JN, Andersen JW, Mazza JJ et al. A randomized placebo-controlled phase III study of granulocyte-macrophage colony-stimulating factor in adult patients (> 55 to 70 years of age) with acute myelogenous leukemia: a study of the Eastern Cooperative Oncology Group (E1490). Blood. 1995;86:457-62.
36. Vogel CL, Wojtukiewicz MZ, Carroll RR, et al. First and subsequent cycle use of pegfilgrastim prevents febrile neutropenia in patients with breast cancer: a multicenter, double-blind, placebo-controlled phase III study. J Clin Oncol. 2005;23(6):1178-84.
37. Kuderer NM, Dale DC, Crawford J, Lyman GH. Impact of primary prophylaxis with granulocyte colony-stimulating factor on febrile neutropenia and mortality in adult cancer patients receiving chemotherapy: a systematic review. J Clin Oncol. 2007;25(21):3158-67.
38. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Acute Myeloid Leukemia v.1.2015. Available at: http://www.nccn.org/professionals/physician_gls/PDF/aml.pdf Accessed November 12, 2015.
39. Centers for Disease Control and Prevention. Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents: recommendations from CDC, the National Institutes of Health, and the Infectious Diseases Society of America. MMWR 2009;58(No. RR-4):1-216.
40. Granix Prescribing Information. Teva Pharmaceuticals USA, Inc., July 2013.
41. Zarxio Prescribing Information. Sandoz Inc., August 2015.

Prior Authorization Guideline

GL-15711 Cometriq (cabozantinib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/7/2013

Revision Date 3/26/2016

Technician Note :

P&T Approval Date: 2/19/2013; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Cometriq (cabozantinib)

Indications

Medullary thyroid cancer

Indicated for the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC).

Off Label Uses

Non-small cell lung cancer

Has activity against RET gene rearrangements in non-small cell lung cancer (NSCLC). [2]

2 . Criteria

Product Name: Cometriq

Diagnosis	Medullary Thyroid Cancer (MTC)
Approval Length	11 months [A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of one of the following: [1,2]

- Metastatic medullary thyroid cancer (MTC)
- Unresectable locally advanced MTC

AND

2 One of the following: [2]

- Patient has symptomatic disease
- Patient has progressive disease

AND

3 Prescribed by or in consultation with one of the following:

- Oncologist/hematologist
- Endocrinologist

Product Name: Cometriq

Diagnosis	Medullary Thyroid Cancer (MTC)
Approval Length	11 months [A]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Cometriq therapy

Product Name: Cometriq

Diagnosis	Non-Small Cell Lung Cancer (NSCLC) (off-label)
Approval Length	11 months [A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of non-small cell lung cancer (NSCLC) [2]

AND

2 Positive for RET gene rearrangements [2]

AND

3 Prescribed by or in consultation with an oncologist/hematologist

Product Name: Cometriq

Diagnosis	Non-Small Cell Lung Cancer (NSCLC) (off-label)
Approval Length	11 months [A]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Cometriq therapy

3 . Endnotes

A. In a phase 3 clinical trial of 330 patients, a statistically significant prolongation in progression free survival (PFS) was demonstrated among Cometriq-treated patients compared to those receiving placebo, with a median PFS time of 11.2 months and 4 months in the Cometriq and placebo arms, respectively. [1]

4 . References

1. Cometriq Prescribing Information. Exelixis Inc, November 2012.
2. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium: Cometriq Available at: http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/AgentList.aspx?aid=395. Accessed November 30, 2015.
3. Cometriq [Formulary Brief], South San Francisco, CA: Exelixis Inc.: December 2012.

Prior Authorization Guideline

GL-14508 Cotellic (cobimetinib)

Formulary OptumRx SP

Formulary Note

Approval Date 2/2/2016

Revision Date 2/2/2016

Technician Note :

P&T Approval Date: 1/27/2016 **Effective date 2-15-2016**

1 . Indications

Drug Name: Cotellic (cobimetinib)

Indications

Melanoma

Indicated for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib. Limitation of Use: Cotellic is not indicated for treatment of patients with wild-type BRAF melanoma.

2 . Criteria

Product Name: Cotellic*

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of unresectable or metastatic melanoma

AND

2 One of the following: [A]

2.1 Patient has a BRAF V600E mutation as detected by an FDA-approved test (e.g., cobas 4800 BRAF V600 Mutation Test) or performed at a facility approved by Clinical Laboratory Improvement Amendments (CLIA)

OR

2.2 Patient has a BRAF V600K mutation as detected by an FDA-approved test (e.g., cobas 4800 BRAF V600 Mutation Test) or performed at a facility approved by Clinical Laboratory Improvement Amendments (CLIA)

AND

3 Used in combination with vemurafenib** [1, 3, B]

AND

4 Prescribed by or in consultation with an oncologist

Notes	*Prior authorization may not apply depending on the plan. **This product may require prior authorization.

Product Name: Cotellic*

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has not experienced disease progression

AND

2 Patient has not experienced Grade 4 hemorrhagic event or a Grade 3 hemorrhagic event that does not improve within 4 weeks [1]

AND

3 Patient has not experienced asymptomatic absolute decrease in left ventricular ejection fraction (LVEF) from baseline of greater than 10% and less than the institutional lower limit of normal (LLN) that does not improve within 2 weeks [1]

AND

4 Patient has not experienced symptomatic LVEF decrease from baseline that persists for 4 weeks [1]

AND

5 Patient has not experienced serous retinopathy that does not improve within 4 weeks [1]

AND

6 Patient has not experienced Grade 4 liver abnormality or hepatotoxicity that does not improve within 4 weeks [1]

AND

7 Patient has not experienced Grade 4 creatine phosphokinase (CPK) elevation or any CPK elevation with myalgia that does not improve within 4 weeks [1]

AND

8 Patient has not experienced intolerable Grade 2, Grade 3, or Grade 4 photosensitivity that does not improve within 4 weeks [1]

AND **9** Patient has not experienced retinal vein occlusion [1] **AND** **10** Patient has not experienced any other intolerable Grade 2 or Grade 3 adverse event that does not improve within 4 weeks [1] **AND** **11** Patient has not experienced any recurrent Grade 4 adverse event [1]	
Notes	*Prior authorization may not apply depending on the plan

3 . Endnotes

A. Prior to starting treatment with Cotellic (cobimetinib), providers should confirm the BRAF V600 mutation using one of the available FDA approved tests. [4] The Cobas 4800 BRAF V600 Mutation Test is an FDA approved option and was used in the pivotal trial. [2, 5] The Cobas 4800 BRAF V600 Mutation Test is also listed as the FDA approved companion diagnostic device for Zelboraf (vemurafenib).
B. The National Comprehensive Cancer Network recommends Cotellic (cobimetinib) in combination with Zelboraf (vemurafenib) as a preferred treatment option (category 1) for BRAF mutated metastatic or unresectable melanoma. [3] Other preferred (category 1)

targeted therapy options include single agent Zelboraf (vemurafenib), single agent Tafinlar (dabrafenib), and combination treatment with Tafinlar (dabrafenib)/Mekinist (trametinib). Prior to the approval of Cotellic (cobimetinib), Mekinist (trametinib) was the only approved MEK inhibitor.

4 . References

1. Cotellic prescribing information. Genentech, Inc. November 2015.
2. Larkin J, Ascierto PA, Dréno B,et al. Combined vemurafenib and cobimetinib in BRAF-mutated melanoma. N Engl J Med. 2014;371(20):1867-76.
3. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Melanoma-Version 2.2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf. Accessed December 17, 2015.
4. U.S. Food and Drug Administration. (2015) [a]. FDA News Release: FDA approves Cotellic as part of combination treatment for advanced melanoma. Retrieved from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm471934.htm. Accessed 12/27/2015
5. U.S. Food and Drug Administration. (2015) [b]. List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools). Retrieved from: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm. Accessed 12/17/2015.

Prior Authorization Guideline

GL-16220 Cystaran (cysteamine)

Formulary OptumRx SP

Formulary Note

Approval Date 8/22/2013

Revision Date 5/24/2016

Technician Note :

P&T Approval Date: 8/20/2013; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Cystaran (cysteamine)

Indications

Corneal cystine crystal accumulation

Indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis.

2 . Criteria

Product Name: Cystaran

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cystinosis

AND

2 Diagnosis is confirmed by elevated leukocyte cystine levels (LCL), genetic analysis of the CTNS gene or corneal cystine crystal accumulation [A, 2-4]

AND

3 Patient is concomitantly receiving treatment with oral cysteamine

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. Cystinosis is a rare autosomal recessive disorder resulting in intracellular accumulation of cysteine in all organs and tissues. After the initial symptoms of failure to thrive and signs of renal Fanconi syndrome, a definitive diagnosis can be verified by measuring leukocyte cystine levels or genetic analysis of the CTNS gene. [2-4]

5 . References

1. Cystaran Prescribing Information. Sigma-Tau Pharmaceuticals, Inc., October 2012.
2. Emma F, Nesterva G, Langman C, et al. Nephropathic cystinosis: an international consensus document. Nephrol Dial Transplant (2014) 29: iv87–iv94.
3. Kleta R, Kaskel F, Dohil R, et al. Consensus statement: First NIH/Office of Rare Diseases Conference on Cystinosis: past, present, and future. Pediatric Neurology 2005. Accessed 5/6/13. Available at: https://cystinosis.org/images/research/article-library/overview/CRN_Research_UpdateJ.pdf.
4. Wilmer MJ, Schoeber JP, van den Heuvel LP, Levtchenko EN. Cystinosis: practical tools for diagnosis and treatment [educational review]. Pediatric Nephrology 2011; 26: 205-15.

Prior Authorization Guideline

GL-16950 Dacogen (decitabine)

Formulary OptumRx SP

Formulary Note

Approval Date 1/9/2014

Revision Date 4/11/2016

Technician Note :

P&T Approval Date: 12/5/2006; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Dacogen (decitabine)

Indications

Myelodysplastic Syndromes (MDS)

Indicated for treatment of patients with myelodysplastic syndromes including previously treated and untreated, de novo and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and Intermediate-1, Intermediate-2, and High-Risk International Prognostic Scoring System groups.

2 . Criteria

Product Name: Brand Dacogen*, Generic decitabine*

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of myelodysplastic syndrome

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Notes	*Prior authorization may not apply depending on the plan.

Product Name: Brand Dacogen*, Generic decitabine*

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on decitabine therapy

Notes	*Prior authorization may not apply depending on the plan.

3 . References

1. Dacogen Prescribing Information. MGI PHARMA, INC., March 2010.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology v1.2012. Myelodysplastic Syndromes. Available at: http://www.nccn.org/professionals/physician_gls/PDF/mds.pdf. Accessed July 3, 2012
3. Kantarjian H, Issa JPJ, Rosenfeld CS, et al. Decitabine Improves Patient Outcomes in Myelodysplastic Syndromes: Results of a Phase III Randomized Study. Cancer 2006; 106:1794-1803.
4. Saba HI, Lübbert M, Wijermans PW. Response Rate of Phase 2 and Phase 3 Trials of Decitabine (DAC) in Patients with Myelodysplastic Syndromes (MDS) [abstract]. Blood 2005; 106:2515.
5. American Cancer Society. Myelodysplastic Syndromes. February 10, 2014. Available at: http://www.cancer.org/acs/groups/cid/documents/webcontent/003122-pdf.pdf. Accessed 03/31/2015.
6. Conley AP, Stevenson W, Garcia-Manero G. Review of the response criteria for myelodysplastic syndrome. European Oncology. 2008; 54-56.
7. Fenaux P, Haase D, Sanz GF, et al. Myelodysplastic syndromes: ESMO clinical practice guidelines for diagnosis, treatment and follow up. Annals of Oncology. 2014;25(supplement 3):iii57-iii69.
8. Fenaux P, Mufti GJ, Hellstrom-Lindber E et al. Efficacy of azacitidine compared with that of conventional care regimens in the treatment of higher-risk myelodysplastic syndromes: a randomized, open-label, phase III study. Lancet Oncol. 2009;10:223-232.
9. Gurion R, Vidal L, Gafter-Gvili A et al. 5-azacitidine prolongs overall survival in patients with myelodysplastic syndrome- A systematic review and meta-analysis. Haematologica. 2010; 95:303-310.
10. Lubbert M, Suciu S, Baila L, et al. Low-dose decitabine versus best supportive care in elderly patients with intermediate- or high-risk myelodysplastic syndrome (MDS) ineligible for intensive chemotherapy: final results of the randomized phase III study of the European Organization for Research and Treatment of Cancer Leukemia Group and the German MDS Study Group. J Clin Oncol. 2011;29(15):1987-96.

Prior Authorization Guideline

GL-31898 Daklinza (daclatasvir)

Formulary OptumRx SP

Formulary Note

Approval Date 9/21/2016

Revision Date 9/21/2016

Technician Note :

P&T Approval Date: 7/27/2015; P&T Revision Date: 6/22/2016, 8/18/2016

1 . Indications

Drug Name: Daklinza (daclatasvir)

Indications

Chronic Hepatitis C (CHC) Indicated for use with sofosbuvir, with or without ribavirin, for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1 or genotype 3 infection. Limitations of Use: Sustained virologic response (SVR12) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

2 . Criteria

Product Name: Daklinza

Diagnosis	Chronic Hepatitis C - Genotype 1
Approval Length	12 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (eg, chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1

AND

2 Used in combination with Sovaldi (sofosbuvir)

AND

3 One of the following:

3.1 Patient is without decompensated cirrhosis and is not a liver transplant recipient

OR

3.2 Both of the following:

3.2.1 Patient has decompensated cirrhosis and/or is a liver transplant recipient

AND

3.2.2 Used in combination with ribavirin

AND

4 Prescribed by or in consultation with one of the following:

- Hepatologist
- Gastroenterologist
- Infectious disease specialist
- HIV specialist certified through the American Academy of HIV Medicine

AND

5 Patient has not failed a prior HCV NS5A-containing regimen (eg, Daklinza)

AND

6 One of the following:

6.1 History of contraindication or intolerance to both of the following:

- Harvoni therapy
- Zepatier therapy

OR

6.2 Patient is currently on Daklinza plus Sovaldi therapy

Product Name: Daklinza

Diagnosis	Chronic Hepatitis C - Genotype 3
Approval Length	12 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (eg, chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 3

AND

2 Used in combination with Sovaldi (sofosbuvir)

AND

3 One of the following:

3.1 Patient is without cirrhosis and is not a liver transplant recipient

OR

3.2 Both of the following:

3.2.1 Patient has cirrhosis (compensated or decompensated) and/or is a liver transplant recipient

AND

3.2.2 Used in combination with ribavirin

AND

4 Prescribed by or in consultation with one of the following:

- Hepatologist
- Gastroenterologist
- Infectious disease specialist
- HIV specialist certified through the American Academy of HIV Medicine

AND

5 Patient has not failed a prior HCV NS5A-containing regimen (eg, Daklinza)

AND

6 One of the following:

6.1 History of contraindication or intolerance to Epclusa

OR

6.2 Patient is currently on Daklinza plus Sovaldi therapy

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product may be subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . References

1. Daklinza Prescribing Information, Bristol-Myers Squibb, 2016.
2. American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. Recommendations for Testing, Managing, and Treating Hepatitis C. October 2015. http://www.hcvguidelines.org/full-report-view. Accessed March, 10 2015.

Prior Authorization Guideline

GL-14434 Darzalex (daratumumab)

Formulary OptumRx SP

Formulary Note

Approval Date 2/15/2016

Revision Date 2/15/2016

Technician Note :

P&T Approval Date: 1/27/2015 **Effective 2-15-2016**

1 . Indications

Drug Name: Darzalex (daratumumab)

Indications

Multiple Myeloma

Indicated for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

2 . Criteria

Product Name: Darzalex*

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple myeloma

AND

2 One of the following:

2.1 Patient has received at least three prior treatment regimens which included both of the following:

- Proteasome inhibitor (eg, bortezomib [Velcade], carfilzomib [Kyprolis])
- Immunomodulatory agent (eg, lenalidomide [Revlimid], thalidomide [Thalomid])

OR

2.2 Patient is double-refractory to a proteasome inhibitor and an immunomodulatory agent

AND

3 Prescribed by or in consultation with an oncologist/hematologist

Notes	*Product may be excluded depending on the plan.

Product Name: Darzalex*

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Patient does not show evidence of progressive disease while on Darzalex therapy	
Notes	*Product may be excluded depending on the plan.

3 . References

1. Darzalex Prescribing Information. Janssen Biotech, Inc., Horsham, PA. November 2015.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Multiple Myeloma-Version 2.2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed December 9, 2015.

Prior Authorization Guideline

GL-32266 Dysport (abobotulinum toxin type A)

Formulary OptumRx SP

Formulary Note

Approval Date 10/21/2016

Revision Date 10/21/2016

Technician Note :

P&T Approval Date: 8/18/2009; P&T Revision Date: 9/28/2016 **Effective 11/1/2016**

1 . Indications

Drug Name: Dysport (abobotulinum toxin type A)

Indications

Cervical dystonia Indicated for the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain in both toxin-naÃ¯ve and previously treated patients.

Glabellar lines Indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adult patients less than 65 years of age. Note: This indication is generally a plan exclusion. Drugs prescribed

to primarily improve or otherwise modify the memberâ€™s external appearance are excluded from coverage.

Upper limb spasticity Indicated for the treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors, wrist flexors and finger flexors.

Lower limb spasticity in pediatric patients Indicated for the treatment of lower limb spasticity in pediatric patients 2 years of age and older.

2 . Criteria

Product Name: Dysport

Diagnosis	Cervical Dystonia (also known as spasmodic torticollis)
Approval Length	3 months for a single dose (up to 500 units) [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cervical dystonia (also known as spasmodic torticollis)

Product Name: Dysport

Diagnosis	Cervical Dystonia (also known as spasmodic torticollis)
Approval Length	3 months for a single dose (up to 1000 units) [C]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Confirmed improvement in symptoms with initial Dysport treatment

AND

2 At least 3 months have elapsed since the last treatment with Dysport

Product Name: Dysport

Diagnosis	Upper or lower limb spasticity
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of upper or lower limb muscle spasticity as a result of CNS disorder or CNS injury [1, A]

Product Name: Dysport

Diagnosis	Upper or lower limb spasticity
Approval Length	3 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Confirmed improvement in symptoms with initial Dysport treatment

AND

2 At least 3 months have elapsed since the last treatment with Dysport [B]

3 . Endnotes

A. The efficacy and safety of Dysport for the treatment of upper limb spasticity was evaluated in a randomized trial (N=238) of patients who were at least 6 months poststroke or posttraumatic brain injury. Those receiving total abobotulinumtoxinA doses of 500 to 1000 units IM had significantly greater improvements from baseline in Modified Ashworth Scale (MAS) scores (improvement of -1.2 and -1.4) at week 4 compared with those receiving placebo (improvements of -0.3 for MAS). [1, 3] The Modified Ashworth Scale is a rehabilitation tool that measures spasticity in patients with lesions of the Central Nervous System using a 6-point scale ranging from 0 to 4. [5]
B. In the pivotal clinical trial, doses of 500 Units and 1000 Units were divided among selected muscles. Repeat treatment should be administered when the effect of a previous injection has diminished, but no sooner than 12 weeks after the previous injection. A majority of patients in clinical studies were retreated between 12-16 weeks; however some patients had a longer duration of response, ie, 20 weeks.[1]
C. Pivotal clinical studies have shown patients to receive retreatment for cervical dystonia in 250 unit steps to doses ranging from 250 units to 1000 units after an initial 500 unit dose. [1]

4 . References

1. Dysport Prescribing Information. Ipsen Biopharmaceuticals, Inc. July, 2016.
2. Truong D, Duane DD, Jankovic J, et al. Efficacy and safety of botulinum type A toxin (Dysport) in cervical dystonia: results of the first US randomized, double-blind, placebo-controlled study. Mov Disord. 2005;20(7):783-791.
3. DRUGDEX System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed August 25, 2015.

4. McCrory P, Turner-Stokes L, Baguley IJ et al. Botulinum toxin A for treatment of upper limb spasticity following stroke: A multi-centre randomized placebo-controlled study of the effects on quality of life and other person-centred outcomes. J Rehabil Med 2009; 41: 536â€“544.
5. Rehab Measures: Ashworth Scale / Modified Ashworth Scale. http://www.rehabmeasures.org/Lists/RehabMeasures/PrintView.aspx?ID=902. Accessed September 1, 2015.

Prior Authorization Guideline

GL-17396 Egrifta (tesamorelin)

Formulary OptumRx SP

Formulary Note

Approval Date 3/12/2013

Revision Date 5/25/2016

Technician Note :

P&T Approval Date: 2/15/2011; P&T Revision Date: 2/25/2016 ** Effective Date 7/1/2016 **

1 . Indications

Drug Name: Egrifta (tesamorelin)

Indications

Excess Abdominal Fat Reduction in HIV-associated Lipodystrophy

Indicated for the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy. Limitations of use: Since the long-term cardiovascular safety and potential long-term cardiovascular benefit of tesamorelin treatment have not been studies and are not known, careful consideration should be given whether to continue tesamorelin treatment in patients who do not show a clear efficacy response as judged by the degree of reduction in visceral adipose tissue measured by waist circumference or CT scan. Tesamorelin is not indicated for weight

loss management (weight neutral effect). There are no data to support improved compliance with anti-retroviral therapies in HIV-positive patients taking tesamorelin.

2 . Criteria

Product Name: Egrifta

Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of HIV-associated lipodystrophy

AND

2 Patient is greater than or equal to 18 years [A]

AND

3 One of the following: [B]

- Waist-circumference of greater than or equal to 95 cm (37.4 inches) in men
- Waist-circumference of greater than or equal to 94 cm (37 inches) for women

AND

4 One of the following: [B]

- Waist-to-hip ratio of greater than or equal to 0.94 for men
- Waist-to-hip ratio of greater than or equal to 0.88 for women

AND

5 Body mass index (BMI) of greater than 20 kg/m^2 [B]

AND

6 Fasting blood glucose (FBG) levels less than or equal to 150 mg/dL (8.33 mmol/L) [B]

AND

7 Patient has been on a stable regimen of antiretrovirals (e.g., NRTIs, NNRTI, Protease Inhibitors, Integrase Inhibitors) for at least 8 weeks [C]

Product Name: Egrifta

Approval Length	6 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria	

1 Documentation of clinical improvement (e.g., improvement in visceral adipose tissue [VAT], decrease in waist circumference, belly appearance, etc) while on Egrifta therapy

3 . Background

Benefit/Coverage/Program Information **Quantity Limit** This product is subject to a standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. Study sponsors requested a waiver for pediatric studies in children less than 18 years of age, and this waiver was granted by the FDA due to concerns that among patients with open epiphyses, excess growth hormone and IGF-1 may result in linear growth acceleration and excessive growth. [2]
B. Both pivotal studies included patients 18 to 65 years of age (mean age, 48 years) who met the waist circumference criteria [95 cm (37.4 inches) or greater for men; 94 cm (37 inches) or greater for women], who met the waist-to-hip ratio criteria (0.94 or greater for men; 0.88 or greater for women), who had a fasting blood glucose of less than 150 mg/dL (8.33 mmol/L) criteria, and who had been on a stable antiretroviral regimen for at least 8 weeks. Patients with a BMI (body mass index) of 20 kg/m^2 or less and patients with diabetes [fasting blood glucose (FBG) levels > 150 mg/dL] were among those excluded. [1, 3-6]
C. The 8 weeks of antiretroviral regimen listed in the criteria is based on the inclusion criteria in the pivotal study. [3-6]

5 . References

1. Egrifta (tesamorelin for injection) [package insert], EMD Serono, Inc, January 2013.
2. Egrifta FDA Medical Review, September 15, 2010. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/022505Orig1s000TOC.cfm. Accessed March 17, 2014.
3. Falutz J, Allas S, Blot K, Potvin D, et al. Metabolic effects of a growth hormone-releasing factor in patients with HIV. N Engl J Med. 2007;357:2359-2370.
4. Falutz J, Allas S, Mamputu JC, Potvin D, et al. Long-term safety and effects of tesamorelin, a growth hormone-releasing factor analogue, in HIV patients with abdominal fat accumulation. AIDS. 2008;22:1719-1728.
5. Falutz J, Mamputu JC, Potvin D, Moyle G, et al. Effects of tesamorelin (TH9507), a growth hormone-releasing factor analog, in HIV-infected patients with excess abdominal fat: a pooled analysis of two multicenter, double-blind placebo-controlled phase 3 trials with safety extension data. J Clin Endocrinol Metab. 2010;95:4291-4304.
6. Falutz J, Potvin D, Mamputu JC, Assaad H, et al. Effects of tesamorelin, a growth hormone-releasing factor, in HIV-infected patients with abdominal fat accumulation: a randomized placebo-controlled trial with a safety extension. J Acquir Immune Defic Syndr. 2010; 53(3):311-22.

Prior Authorization Guideline

GL-15512 Elaprase (idursulfase)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/7/2016

Technician Note :

P&T Approval Date: 7/30/2004; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Elaprase (idursulfase) [1]

Indications

Hunter Syndrome

Is indicated for patients with Hunter syndrome (Mucopolysaccharidosis II, MPS II). Elaprase has been shown to improve walking capacity in patients 5 years and older. In patients 16 months to 5 years of age, no data are available to demonstrate improvement in disease-related symptoms or long term clinical outcome; however, treatment with Elaprase has reduced spleen volume similarly to that of adults and children 5 years of age and older. The safety and efficacy of Elaprase have not been established in pediatric patients less than 16 months of age.

2 . Criteria

Product Name: Elaprase (idursulfase)

Approval Length	5 Year
Guideline Type	Prior Authorization
Approval Criteria **1** Diagnosis of Hunter syndrome (Mucopolysaccharidosis II, MPS II)	

3 . Definitions

Definition	Description
Elaprase (idursulfase)	Is a formulation of idursulfase, a purified form of human iduronate-2-sulfatase, a lysosomal enzyme. This enzyme hydrolyzes the 2-sulfate esters of terminal iduronate sulfate residues from the glycosaminoglycans (GAGs) dermatan sulfate and heparin sulfate in the lysosomes of various cell types.
Hunter syndrome	Is an X-linked recessive disease caused by insufficient levels of the lysosomal enzyme iduronate-2-sulfatase. Due to the missing or defective iduronate-2-sulfatase enzyme in patients with Hunter syndrome, GAGs progressively accumulate in the lysosomes of a variety of cells, leading to cellular

	engorgement, organomegaly, tissue destruction, and organ system dysfunction.
Treatment of Hunter syndrome	Patients with Elaprase provides exogenous enzyme for uptake into cellular lysosomes. Mannose-6-phosphate (M6P) residues on the oligosaccharide chains allow specific binding of the enzyme to the M6P receptors on the cell surface, leading to cellular internalization of the enzyme, targeting intra-cellular lysosome and catabolism of accumulated GAG.
Hunter Syndrome (Mucopolysaccharidosis II, MPS II)	Is inherited as an X-linked recessive trait that presents in either a mild (MPS IIB) or severe (MPS IIA) form. This rare genetic disease results in the deficiency of iduronate sulfatase enzyme found in lysosomes. These enzymes serve to breakdown or digest certain carbohydrates. The deficiency of iduronate sulfatase leads to an abnormal accumulation of complex carbohydrates (glycosaminoglycans or mucopolysaccharides) in tissues, such as the skeleton, joints, brain, spinal cord, heart, spleen, or liver. [5]

4 . References

1. Elaprase Prescribing Information. Shire Human Genetic Therapies, Inc. October 2015.

Prior Authorization Guideline

GL-17073 Empliciti (elotuzumab)

Formulary OptumRx SP

Formulary Note

Approval Date 1/28/2016

Revision Date 4/15/2016

Technician Note :

P&T Approval Date: 1/27/2016; P&T Revision Date: 5/19/2016 **Effective 6-15-2016**

1 . Indications

Drug Name: Empliciti (elotuzumab)

Indications

Multiple myeloma

Indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.

2 . Criteria

Product Name: Empliciti*

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple myeloma

AND

2 Patient has received at least one prior therapy for multiple myeloma [eg, Revlimid (lenalidomide), Thalomid (thalidomide), Velcade (bortezomib)]

AND

3 Used in combination with both of the following:

- Revlimid (lenalidomide)**
- Dexamethasone

AND

4 Prescribed by or in consultation with a hematologist/oncologist

Notes	*Product may be excluded depending on the plan. **This product may

	require prior authorization.

Product Name: Empliciti*

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Patient does not show evidence of progressive disease while on Empliciti therapy	
Notes	*Product may be excluded depending on the plan.

3 . References

1. Empliciti Prescribing Information. Bristol-Myers Squibb Company, Princeton, NJ. November 2015.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Multiple Myeloma-Version 3.2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed January 26, 2016.

Prior Authorization Guideline

GL-16819 Enbrel (etanercept)

Formulary OptumRx SP

Formulary Note

Approval Date 2/18/2015

Revision Date 4/14/2016

Technician Note :

P&T Approval Date: 5/15/2005; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Enbrel (etanercept)

Indications

Rheumatoid Arthritis (RA)

Indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis. Enbrel can be initiated in combination with methotrexate (MTX) or used alone.

Polyarticular Juvenile Idiopathic Arthritis

Indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients ages 2 and older.

Psoriatic Arthritis (PsA)

Indicated for reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis. Enbrel can be used with or without MTX.

Ankylosing Spondylitis (AS)

Indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

Plaque Psoriasis (PsO)

Indicated for the treatment of adult patients (18 years or older) with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

2 . Criteria

Product Name: Enbrel

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	12 months [1,4]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active RA

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication or intolerance to one nonbiologic disease modifying anti-rheumatic drug (DMARD) [e.g., methotrexate (Rheumatrex/Trexall), Arava (leflunomide), Azulfidine (sulfasalazine)] [5, 25]

AND

4 One of the following:

4.1 History of failure, contraindication, or intolerance to two of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Simponi (golimumab) or Simponi Aria (golimumab IV)

OR

4.2 For continuation of prior Enbrel therapy

AND

5 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

6 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

Product Name: Enbrel

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Enbrel therapy

AND

2 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

3 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

Product Name: Enbrel

Diagnosis	Polyarticular Juvenile Idiopathic Arthritis (JIA)

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active polyarticular juvenile idiopathic arthritis

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to one of the following nonbiologic disease modifying anti-rheumatic drugs (DMARDs): [24]

- Arava (leflunomide)
- methotrexate (Rheumatrex/Trexall)

AND

4 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

5 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

Product Name: Enbrel

Diagnosis	Polyarticular Juvenile Idiopathic Arthritis (JIA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Enbrel therapy

AND

2 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

3 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

Product Name: Enbrel

Diagnosis	Psoriatic Arthritis (PsA)
Approval Length	12 Month

Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active PsA

AND

2 Prescribed by or in consultation with one of the following:

- Dermatologist
- Rheumatologist

AND

3 One of the following:

3.1 History of failure, contraindication, or intolerance to two of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Simponi (golimumab)
- Stelara (ustekinumab)

OR

3.2 For continuation of prior Enbrel therapy

AND

4 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

5 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

Product Name: Enbrel

Diagnosis	Psoriatic Arthritis (PsA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Enbrel therapy

AND

2 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

3 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

Product Name: Enbrel

Diagnosis	Plaque Psoriasis
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderate to severe chronic plaque psoriasis [1, 13, 14, A]

AND

2 Prescribed by or in consultation with a dermatologist

AND

3 One of the following:

3.1 History of failure, contraindication, or intolerance to both of the following:

- Humira (adalimumab)
- Stelara (ustekinumab)

OR

3.2 For continuation of prior Enbrel therapy

AND

4 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

5 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

Product Name: Enbrel

Diagnosis	Plaque Psoriasis
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Enbrel therapy

AND

2 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

3 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

Product Name: Enbrel

Diagnosis	Ankylosing Spondylitis (AS)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active ankylosing spondylitis

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to two NSAIDs [15, 16, 26]

AND

4 One of the following:

4.1 History of failure, contraindication, or intolerance to two of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Simponi (golimumab)

OR

4.2 For continuation of prior Enbrel therapy

AND

5 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

6 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

Product Name: Enbrel

Diagnosis	Ankylosing Spondylitis (AS)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Enbrel therapy

AND

2 Patient is not receiving Enbrel in combination with a biologic DMARD [e.g., Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1,5]

AND

3 Patient is not receiving Enbrel in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,5]

3 . Endnotes

A. Patients who are candidates for systemic/and or phototherapy have significant disease, typically affecting 5% or more of the body surface area (BSA). Some of these candidates may also have less than 5% BSA affected but have psoriasis in vulnerable areas such as the face, genitals, hands, or feet (palmer-plantar), nails, scalp, or intertriginous areas. [23]

4 . References

1. Enbrel Prescribing Information. Amgen; March 2015
2. Moreland, L, Schiff, M, Baumgartner, S, et al. Etanercept therapy in rheumatoid arthritis. Ann Intern Med 1999;130:478-486.

3. Weinblatt M, Kremer J, Bankhurst A, et al. A trial of etanercept, a recombinant tumor necrosis factor receptor: Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate. NEJM 2005;340: 253-359.
4. Bathon J, Martin R, Fleischman R, et al. A comparison of etanercept and methotrexate in patients with early rheumatoid arthritis. NEJM 2000;343:1586-1593.
5. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012;64(5):625-639.
6. Pavy S. Constantin A, Pham T, et al. Methotrexate therapy for rheumatoid arthritis: clinical practice guidelines based on published evidence and expert opinions. Joint Bone Spine 2006; [Epub ahead of print]:1-8.
7. Ledingham J, Deighton C, on behalf of the British Society of Rheumatology Standards, Guidelines and Audit Working Group (SGAWG). Update on the British Society for Rheumatology guidelines for prescribing TNF-alpha blockers in adults with rheumatoid arthritis (update of previous guidelines of April 2001). Rheumatol 2005; 44: 157-163.
8. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995; 38(6):727-735.
9. Bulletin on the Rheumatic Diseases for evidence-based management of rheumatic disease, a publication of the arthritis foundation: Use of etanercept in children. Bulletin on the Rheumatic Dis 2000; 49 (12):1-4.
10. Giannini H, Ruperto N, Ravelli A, et al. Preliminary definition of improvement in juvenile arthritis. Arthritis Rheum 1997; 40(7):1202-9.
11. Lovell DJ, Giannini H, Reiff A, et al. Etanercept in children with polyarticular juvenile rheumatoid arthritis. N Engl J Med. 2000; 342(11): 763-9.
12. Kyle S, Chandler D, Griffiths EM, et al. Guideline for anti-TNF-? therapy in psoriatic arthritis. Rheumatology. 2005; 44(3):390-397.
13. Leonardi GL, Powers JL, Matheson RT, et al. Etanercept as monotherapy in patients with psoriasis. NEJM 2003; 349:2014-22.
14. Papp KA, Tyring S, Lahfa M, et al. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. Br J Dermatol. 2005;152:1304-1312.
15. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of Ankylosing spondylitis. Ann Rheum Dis. 2011;70:896-904.
16. British Society for Rheumatology (BSR) Guideline for Prescribing TNF? Blockers in Adults with Ankylosing Spondylitis. London: BSR; 2004 July: 1-21.
17. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011. Ann Rheum Dis. 2012;71(Suppl II):i2- i45
18. Felson D, Anderson JJ, Boers M, et al. The American College of Rheumatology preliminary core sets of disease activity measures for rheumatoid arthritis clinical trials. Arthritis & Rheumatism 1993; 36(6): 729-740.
19. Mease PJ, Kivitz AJ, Burch FX, et al. Etanercept treatment for psoriatic arthritis. Arthritis Rheum. 2004; 50(4): 2264-72.
20. U.S. Food and Drug Administration. MedWatch. 2008 Safety Alerts for Human Medical Products. Tumor necrosis factor-alpha blockers (TNF blockers), Cimzia (certolizumab pegol), Enbrel (etanercept), Humira (adalimumab), and Remicade (infliximab) September 2008.
21. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis section 4. Guidelines of care for the management and

treatment of psoriasis with traditional systemic agents. J Am Acad Dermatol. 2009;61:451-85.
22. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case based presentations and evidence-based conclusions. J Am Acad Dermatol. 2011;65(1):137-74.
23. Pariser DM, Bagel J, Gelfand JM, et al. National Psoriasis Foundation Clinical Consensus on Disease Severity. Arch Dermatol. 2007 Feb;143(2):239-42.
24. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011 Apr;63(4):465-82.
25. Per clinical consult with rheumatologist, June 30, 2011.
26. van der Heijde, Sieper J, Maksymowych WP, et al. 2010 update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. Ann Rheum Dis. 2011;70:905-908.
27. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012;64(5):625-39.

Prior Authorization Guideline

GL-17023 Erythropoietic Agents

Formulary OptumRx SP

Formulary Note

Approval Date 7/15/2015

Revision Date 4/25/2016

Technician Note :

P&T Approval Date: 3/17/2000; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Aranesp (darbepoetin alfa)

Indications

Anemia Due to Chronic Kidney Disease

Indicated for the treatment of anemia due to chronic kidney disease (CKD) including patients on dialysis and patients not on dialysis.

Anemia in Cancer Patients on Chemotherapy

Indicated for treatment of anemia in patients with non-myeloid malignancies where anemia is

due to the effect of concomitant myelosuppressive chemotherapy and upon initiation there is a minimum of 2 additional months of planned chemotherapy. Limitations of Use: Aranesp has not been shown to improve quality of life, fatigue, or patient well-being. Aranesp is not indicated for use: (1) In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy; (2) In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure; (3) As a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia.

Off Label Uses

Anemia in patients with Myelodysplastic Syndrome (MDS)

Have been used for the treatment of anemia in patients with MDS. [28]

Drug Name: Epogen (epoetin alfa) and Procrit (epoetin alfa)

Indications

Anemia Due to Chronic Kidney Disease

Indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC) transfusion.

Anemia Due to Zidovudine in HIV-infected Patients

Indicated for the treatment of anemia due to zidovudine (AZT) administered at less than or equal to 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of less than or equal to 500 mUnits/mL.

Anemia in Cancer Patients on Chemotherapy

Indicated for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy and upon initiation, there is a minimum of 2 additional months of planned chemotherapy. Limitations of Use: Epogen and Procrit have not been shown to improve quality of life, fatigue, or patient well-being. Epogen and Procrit are not indicated for use: (1) In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy; (2) In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure; (3) As a substitute for red blood cell (RBC) transfusions in patients who require immediate correction of anemia.

Reduction of Allogeneic Red Blood Cell Transfusions in Patients Undergoing Elective, Noncardiac, Nonvascular Surgery

Indicated to reduce the need for allogeneic RBC transfusions among patients with perioperative hemoglobin greater than 10 to less than or equal to 13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery. Epogen and Procrit are not indicated for patients who are willing to donate autologous blood preoperatively. Limitations of Use: Epogen and Procrit have not been shown to improve quality of life, fatigue, or patient well-being. Epogen and Procrit are not indicated for use: (1) In patients scheduled for surgery who are willing to donate autologous blood; (2) In patients undergoing cardiac or vascular surgery.

Off Label Uses

Anemia associated with HIV infection

Have been used for the treatment of anemia associated with HIV infection in patients not receiving zidovudine. [5, 30-33]

Anemia in Hepatitis C virus (HCV) infected patients due to combination therapy of ribavirin and interferon or peg-interferon

Have been used for the treatment of anemia in patients with hepatitis C virus (HCV) infection who are being treated with the combination of ribavirin and interferon or peginterferon alfa. [28]

Anemia in patients with Myelodysplastic Syndrome (MDS)

Have been used for the treatment of anemia in patients with MDS. [5,28]

Drug Name: Mircera (methoxy polyethylene glycol-epoetin beta)

Indications

Anemia Due to Chronic Kidney Disease

Indicated for the treatment of anemia due to chronic kidney disease (CKD) including patients on dialysis and patients not on dialysis. Mircera is not indicated and is not recommended: (1) In the treatment of anemia due to cancer chemotherapy; or (2) As a substitute for RBC transfusions in patients who require immediate correction of anemia. Mircera has not been shown to improve symptoms, physical functioning or health-related quality of life.

2 . Criteria

Product Name: Aranesp* or Procrit

Diagnosis	Anemia Due to Chronic Kidney Disease (CKD)
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic kidney disease (CKD)

AND

2 Verification of iron evaluation for adequate iron stores† [A, J]

AND

3 Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request: [1, 3, 9, 20-24, B]

- Hematocrit (Hct) < 30%
- Hemoglobin (Hgb) < 10g/dL

AND

4 One of the following:[1-3]

4.1 Patient is on dialysis

OR

4.2 All of the following:

4.2.1 Patient is NOT on dialysis

AND

4.2.2 The rate of hemoglobin decline indicates the likelihood of requiring a red blood cell (RBC) transfusion

AND

4.2.3 Reducing the risk of alloimmunization and/or other RBC transfusion-related risks is a goal

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Epogen* or Mircera

Diagnosis	Anemia Due to Chronic Kidney Disease (CKD)
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic kidney disease (CKD)

AND

2 Verification of iron evaluation for adequate iron stores † [A, J]

AND

3 Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request: [2, 9, 20-24, 41,B]

- Hematocrit (Hct) < 30%
- Hemoglobin (Hgb) < 10 g/dL

AND

4 One of the following: [2, 41]

4.1 Patient is on dialysis

OR

4.2 All of the following:

4.2.1 Patient is NOT on dialysis

AND

4.2.2 The rate of hemoglobin decline indicates the likelihood of requiring a red blood cell (RBC) transfusion

AND

4.2.3 Reducing the risk of alloimmunization and/or other RBC transfusion-related risks is a goal

AND

5 One of the following:

5.1 As continuation of therapy

OR

5.2 History of failure, contraindication, or intolerance to both of the following:

- Aranesp
- Procrit

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Aranesp*, Epogen*, Mircera, or Procrit

Diagnosis	Anemia due to CKD
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic kidney disease (CKD)

AND

2 Verification of anemia as defined by one of the following:

- Most recent or average hematocrit (Hct) over a 3-month period was less than or equal to 33% [1-3, 7]
- Most recent or average hemoglobin (Hgb) over a 3-month period was less than or equal to 11 g/dL [1-3, 7]

AND

3 One of the following: [1-3, 41]

- Decrease in the need for blood transfusion
- Hemoglobin (Hgb) increased greater than or equal to 1g/dL from pre-treatment level

AND

4 Verification of iron evaluation for adequate iron stores †[A, J]

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Procrit

Diagnosis	Anemia in HIV-infected patients
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Verification of iron evaluation for adequate iron stores† [3]

AND

2 Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request:

- Hemoglobin (Hgb) < 12 g/dL [17, 30-34, K]
- Hematocrit (Hct) < 36%

AND

3 Serum erythropoietin level less than or equal to 500 mU/mL [2,3,30,32]

AND

4 One of the following:

- Patient is receiving zidovudine (AZT) therapy [3]
- Diagnosis of HIV infection [off-label] [5, 17, 30-34]

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores.

Product Name: Epogen*

Diagnosis	Anemia in HIV-infected patients
Approval Length	6 Month
Therapy Stage	Initial Authorization

Guideline Type	Prior Authorization

Approval Criteria

1 Verification of iron evaluation for adequate iron stores † [2]

AND

2 Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request:

- Hemoglobin (Hgb) < 12 g/dL [17, 30-34, K]
- Hematocrit (Hct) < 36%

AND

3 Serum erythropoietin level less than or equal to 500 mU/mL [2,3,30]

AND

4 One of the following:

- Patient is receiving zidovudine (AZT) therapy [2]
- Diagnosis of HIV infection [off-label] [5, 17, 30-34]

AND

5 One of the following:

- As continuation of therapy
- History of use or unavailability of Procrit

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Epogen* or Procrit

Diagnosis	Anemia in HIV-infected patients
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Verification of anemia as defined by one of the following: [2, 3]

- Most recent or average hematocrit (Hct) over a 3-month period was below 36%
- Most recent or average hemoglobin (Hgb) over a 3-month period was below 12 g/dL

AND

2 One of the following: [2, 3]

- Decrease in the need for blood transfusion
- Hemoglobin (Hgb) increased greater than or equal to 1g/dL from pre-treatment level

Notes	*Product may be excluded depending on the plan.

Product Name: Aranesp* or Procrit

Diagnosis	Anemia in cancer patients on chemotherapy
Approval Length	3 month [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Verification that other causes of anemia have been ruled out [1, 3, L]

AND

2 Verification of anemia as defined by one of the following laboratory values collected within the prior two weeks of the request: [1, 3]

- Hematocrit (Hct) < 30%
- Hemoglobin (Hgb) < 10 g/dL

AND

3 Verification of iron evaluation for adequate iron stores † [1, 3, 8, G]

AND

4 Verification that the cancer is a non-myeloid malignancy [1-3, F]

AND

5 One of the following: [1, 3, D]

- Verification that the patient is concurrently on chemotherapy
- Patient will be receiving concomitant chemotherapy for a minimum of 2 months
- Verification that anemia is caused by cancer chemotherapy

AND

6 Erythropoiesis stimulating agents (e.g., Aranesp, Epogen, Procrit) will not be approved for the treatment of anemic patients with cancer who are not receiving cancer chemotherapy [1-3, 26]

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Epogen*

Diagnosis	Anemia in cancer patients on chemotherapy
Approval Length	3 Month [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Verification that other causes of anemia have been ruled out [2, L]

AND

2 Verification of anemia as defined by one of the following laboratory values collected within the prior two weeks of the request: [2]

- Hematocrit (Hct) < 30%
- Hemoglobin (Hgb) < 10 g/dL

AND

3 Verification of iron evaluation for adequate iron stores † [2, 8, G]

AND

4 Verification that the cancer is a non-myeloid malignancy [2, F]

AND

5 One of the following: [2, D]

- Verification that the patient is concurrently on chemotherapy
- Patient will be receiving concomitant chemotherapy for a minimum of 2 months
- Verification that anemia is caused by cancer chemotherapy

AND

6 One of the following:

6.1 As continuation of therapy

OR

6.2 History of failure, contraindication, or intolerance to both of the following:

- Aranesp
- Procrit

AND

7 Erythropoiesis stimulating agents (e.g., Aranesp, Epogen, Procrit) will not be approved for the treatment of anemic patients with cancer who are not receiving cancer chemotherapy. [2, 26]

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Aranesp*, Epogen*, or Procrit

Diagnosis	Anemia in cancer patients on chemotherapy
Approval Length	3 Month [C]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Verification of anemia as defined by one of the following laboratory values collected within the prior two weeks of the request: [1-3]

- Hemoglobin (Hgb) < 10 g/dL
- Hematocrit (Hct) < 30% [16, 26, 27]

AND

2 One of the following: [1-3]

- Decrease in the need for blood transfusion
- Hemoglobin (Hgb) increased greater than or equal to 1 g/dL from pre-treatment level

AND

3 One of the following: [D]

- Verification that the patient is concurrently on chemotherapy
- Patient will be receiving concomitant chemotherapy for a minimum of 2 months
- Verification that anemia is caused by cancer chemotherapy.

AND

4 Erythropoiesis stimulating agents (e.g., Aranesp, Epogen, Procrit) will not be approved for the treatment of anemic patients with cancer who are not receiving cancer chemotherapy. [1-3, 26]

Notes	*Product may be excluded depending on the plan.

Product Name: Procrit

Diagnosis	Preoperative use for reduction of allogeneic blood transfusion in patients undergoing surgery
Approval Length	1 month [3]
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is scheduled to undergo elective, non-cardiac, non-vascular surgery

AND

2 Hemoglobin (Hgb) is greater than 10 to less than or equal to 13 g/dL

AND

3 Patient is at high risk for perioperative transfusions

AND

4 Patient is unwilling or unable to donate autologous blood pre-operatively

AND

5 Verification of iron evaluation for adequate iron stores † [3]

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores.

Product Name: Epogen*

Diagnosis	Preoperative use for reduction of allogeneic blood transfusion in patients undergoing surgery
Approval Length	1 month [2]
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is scheduled to undergo elective, non-cardiac, non-vascular surgery

AND

2 Hemoglobin (Hgb) is greater than 10 to less than or equal to 13 g/dL

AND

3 Patient is at high risk for perioperative transfusions

AND

4 Patient is unwilling or unable to donate autologous blood pre-operatively

AND

5 Verification of iron evaluation for adequate iron stores † [2]

AND

6 One of the following:

- As continuation of therapy
- History of use or unavailability of Procrit

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Aranesp* or Procrit

Diagnosis	Anemia in Myelodysplastic Syndrome (MDS) patients [off-label] [4-6, 28]
Approval Length	3 months [I]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Myelodysplastic Syndrome (MDS) [4]

AND

2 One of the following: [4]

- Serum erythropoietin level less than or equal to 500 mU/mL
- Diagnosis of transfusion-dependent MDS

AND

3 Verification of iron evaluation for adequate iron stores † [4, A, H]

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Epogen*

Diagnosis	Anemia in Myelodysplastic Syndrome (MDS) patients [off-label] [4-6, 28]
Approval Length	3 months [I]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Myelodysplastic Syndrome (MDS) [4]

AND

2 One of the following: [4]

- Serum erythropoietin level less than or equal to 500 mU/mL
- Diagnosis of transfusion-dependent MDS

AND

3 Verification of iron evaluation for adequate iron stores † [4, A, H]

AND

4 One of the following:

4.1 As continuation of therapy

OR

4.2 History of failure, contraindication, or intolerance to both of the following:

- Aranesp
- Procrit

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Aranesp*, Epogen*, or Procrit

Diagnosis	Anemia in MDS patients (off-label)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Verification of anemia as defined by one of the following: [4, E]

- Most recent or average hematocrit (Hct) over a 3-month period was less than or equal to 36%
- Most recent or average hemoglobin (Hgb)over a 3-month period was less than or equal to 12 g/dL

AND

2 One of the following: [1-3]

- Decrease in the need for blood transfusion
- Hemoglobin (Hgb) increased greater than or equal to 1 g/dL from pre-treatment level

Notes	*Product may be excluded depending on the plan.

Product Name: Procrit

Diagnosis	Anemia in HCV-infected patients due to ribavirin in combination with interferon or peg-interferon [off-label] [28]
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of hepatitis C virus (HCV) infection [18, 28]

AND

2 Verification of iron evaluation for adequate iron stores † [3]

AND

3 Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request: [35-37, 39]

- Hematocrit (Hct) < 30%
- Hemoglobin (Hgb) < 10 g/dL

AND

4 Verification of both of the following:

4.1 Patient is receiving ribavirin

AND

4.2 Patient is receiving one of the following:

- interferon alfa-2b
- interferon alfacon-1
- peginterferon alfa-2b
- peginterferon alfa-2a

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores.

Product Name: Epogen*

Diagnosis	Anemia in HCV-infected patients due to ribavirin in combination with interferon or peg-interferon [off-label] [6]
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of hepatitis C viral (HCV) infection [18, 28]

AND

2 Verification of iron evaluation for adequate iron stores † [2]

AND

3 Verification of anemia as defined by one of the following laboratory values collected within 30 days of the request: [35-37, 39]

- Hematocrit (Hct) < 30%
- Hemoglobin (Hgb) < 10 g/dL

AND

4 Verification of both of the following:

4.1 Patient is receiving ribavirin [28]

AND

4.2 Patient is receiving one of the following:[28]

- interferon alfa-2b
- interferon alfacon-1
- peginterferon alfa-2b
- peginterferon alfa-2a

AND

5 One of the following:

• As continuation of therapy • History of use, or unavailability of Procrit

Notes	†Authorization will be given if physician is aware of iron deficiency and is taking steps to replenish iron stores. *Product may be excluded depending on the plan.

Product Name: Epogen* or Procrit

Diagnosis	Anemia due to HCV therapy
Approval Length	3 Months or if patient has demonstrated response to therapy, authorization will be issued for the full course of ribavirin therapy.
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Verification of anemia as defined by one of the following: [37]

- Most recent or average hematocrit (Hct) over a 3-month period was 36% or less
- Most recent or average hemoglobin (Hgb) over a 3-month period was 12 g/dL or less

AND

2 One of the following:[1-3]

- Decrease in the need for blood transfusion
- Hemoglobin (Hgb) increased greater than or equal to 1 g/dL from pre-treatment level

Notes	*Product may be excluded depending on the plan.

Product Name: Aranesp*, Epogen*, Mircera, or Procrit

Diagnosis	Erythropoietin Stimulating Agents - Off-Label Uses
Guideline Type	Prior Authorization

Approval Criteria

1 Off-label requests for Aranesp, Epogen, Mircera, or Procrit will be evaluated on a case-by-case basis by a clinical pharmacist.

AND

2 Requests for coverage in patients with Hgb greater than 10 g/dL or Hct greater than 30% will not be approved. [1-3, 41]

Notes	*Product may be excluded depending on the plan.

3 . Endnotes

A. Aranesp, Epogen, Mircera, and Procrit Prescribing Information recommend prior and during therapy, the patient's iron stores should be evaluated. Administer supplemental iron therapy when serum ferritin is less than 100 mcg/L or when serum transferrin saturation is less than 20%. The majority of patients with CKD will require supplemental iron during the course of ESA therapy. [1-3, 41]
B. Aranesp, Epogen, Mircera, and Procrit Prescribing Information states that dialysis, and non-dialysis patients with symptomatic anemia considered for therapy should have a Hgb < 10 g/dL. [1-3, 41]
C. ESA treatment duration for each course of chemotherapy includes the 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen. [26]

D. ESAs are not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure. [1-3]
E. NCCN panel recommends MDS patients aim for a target hgb level of less than or equal to 12 g/dL.[4]
F. The American Cancer Society definition of “non-myeloid malignancy” is any malignancy that is not a myeloid leukemia. Non-myeloid cancers include all types of carcinoma, all types of sarcoma, melanoma, lymphomas, lymphocytic leukemias (ALL and CLL), and multiple myeloma. [40]
G. Absolute iron deficiency is defined as ferritin <30 ng/mL and TSAT <20%. Functional iron deficiency in patients receiving ESAs is defined as ferritin 30-800 ng/mL and TSAT 20%-50%. No iron deficiency is defined as ferritin >800 ng/mL or TSAT greater or equal to 50%. [8]
H. Iron repletion needs to be verified before instituting Epo therapy. [4]
I. Detection of erythroid responses generally occurs within 6 to 8 weeks of treatment. If no response occurs in this time frame, this treatment should be considered a failure and discontinued. [4]
J. Iron stores evaluation is recommended to occur every month during initial erythropoietin treatment in adults with chronic kidney disease or at least every 3 months during stable ESA treatment or in patients with HD-CKD not treated with an erythropoietin. [7]
K. Anemia in HIV patients has been defined as hemoglobin less than 10 g/dL [17,31,32], hemoglobin less than 11 g/dL[17,33], or hemoglobin less than 12 g/dL. [30]
L. Examples of other anemias include: vitamin B12, folate or iron deficiency anemia, hemolysis, or gastrointestinal bleeding

4 . References

1. Aranesp Prescribing Information, Amgen Inc., December 2013.
2. Epogen Prescribing Information, Amgen Inc., April 2014.
3. Procrit Prescribing Information.Amgen Inc., December 2013.
4. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Myelodysplastic Syndromes v.2.2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed March 2, 2015.
5. AHFS Drug Information (2005) website. Available at: http://online.lexi.com/lco/action/doc/retrieve/docid/complete_ashp/414035#uses-nested-7. Accessed March 11, 2014.
6. USP DI (United States Pharmacopeia Drug Information) 2003. Epoetin, Systemic. Thomson MICROMEDEX.
7. National Kidney Foundation (NKF), NKF-K/DOQI Practice guidelines for anemia of chronic kidney disease: Update 2007. Available at: http://www.kidney.org/professionals/KDOQI/guidelines_anemia/index.htm. Accessed on July 9, 2012.
8. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Cancer- and Chemotherapy-induced Anemia v.2.2015. Available at: http://www.nccn.org/professionals/physician_gls/PDF/anemia.pdf. Accessed March 18, 2015.
9. Eschbach JW, Abdulhadi MH, Browne JE, et al. Recombinant human erythropoietin in anemic patients with end-stage renal disease. Ann Intern Med 1989;111:992-1000.
10. The US Recombinant Human Erythropoietin Predialysis Study Group. Double-blind, placebo-controlled study of the therapeutic use of recombinant human erythropoietin for

anemia associated with chronic renal failure in predialysis patients. Am J Kidney Dis 1991;18(3):50-9.
11. Fischl M, Galpin JE, Levine JD, et al. Recombinant human erythropoietin for patients with AIDS treated with zidovudine. N Eng J Med 1990;322:1488-93.
12. Glaspy J, Bukowski R, Steinberg D, et al. Impact of therapy with epoetin alfa on clinical outcomes in patients with nonmyeloid malignancies during cancer chemotherapy in community oncology practice. J Clin Oncol 1997;15(3):1218-34.
13. Vansteenkiste J, Pirker R, Massuti B et al. Aranesp 980297 Study Group. Double-blind, placebo-controlled, randomized phase III trial of darbepoetin alfa in lung cancer patients receiving chemotherapy. J Natl Cancer Inst. 2002;94(16):1211-20.
14. Faris PM, Ritter MA, Abels RI, et al. The effects of recombinant human erythropoietin on perioperative transfusion requirements in patients having a major orthopedic operation. J Bone and Joint Surgery 1996;78-A:62-72.
15. Goldberg MA, McCutchen JW, Jove M, et al. A safety and efficacy comparison study of two dosing regimens of epoetin alfa in patients undergoing major orthopedic surgery. Am J Orthopedics 1996;25(8):544-52.
16. Rizzo JD, Lichtin AE, Woolf SH, et al. Use of epoetin in patients with cancer: evidence-based clinical practice guidelines of the American Society of Clinical Oncology and the American Society of Hematology. Blood 2002;100(7):2303-20.
17. Volberding P, Levine A, Dieterich D, et al. Anemia in HIV infection: clinical impact and evidence-based management strategies. Clin Infect Dis 2004;38:1454-63.
18. Yee HS, Currie SL, Darling JM et al. Management and treatment of hepatitis c viral infection: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program Office. Am J Gastroenterol 2006;101:2360-78.
19. Weatherall MS, Sherry KM. An evaluation of the Spuncrit™ infra-red analyzer for measurement of haematocrit. Clin Lab Haem.1997;19:183-86.
20. AHRQ Evidence Report #29: Health Services/Technology Assessment Text. Use of erythropoietin for anemia in chronic renal failure. Available at: http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat1.chapter.42263. Accessed on January 27, 2007.
21. Remuzzi G, Ingelfinger JR. Correction of anemia–payoffs and problems. N Engl J Med. 2006;355:2144-6.
22. Drueke TB, Locatelli F, Clyne N,et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med. 2006 Nov 16;355(20):2071-84.
23. Singh AK, Szczech L, Tang KL, et al. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med 2006;355:2085-98.
24. Besarab A, Bolton WK, Browne JK, et al. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. N Engl J Med 1998;339:584-90.
25. Mandeep S, Thokozeni L, Douglas N, et al. Should patients with anemia and low normal or normal serum ferritin undergo colonoscopy? Am J Gastroenterol. 2007;102:82-88.
26. Centers for Medicare and Medicaid Services. Decision memo for erythropoiesis stimulating agents (ESAs) for non-renal disease indications (CAG-00383N). July 30, 2007.
27. Rizzo J, Brouwers M, Hurley P, et al.American Society of Clinical Oncology/American Society of Hematology Clinical Practice Guideline Update on the Use of Epoetin and Darbepoetin in Adult Patients With Cancer Available at: http://jco.ascopubs.org/content/early/2010/10/25/JCO.2010.29.2201.full.pdf+html. Accessed February 21, 2011.

28. DRUGDEX System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed March 11, 2014.
29. Groopman JE, Itri LM. Chemotherapy-induced anemia in adults: Incidence and treatment. J Natl Cancer Inst.1999;91 (19): 1616-34Available at: http://jnci.oxfordjournals.org/content/91/19/1616.full.pdf+html. Accessed March 18, 2011.
30. Grossman HA, Goon B, Bowers P, Leitz G. Once-weekly epoetin alfa dosing is as effective as three times-weekly dosing in increasing hemoglobin levels and is associated with improved quality of life in anemic HIV-infected patients. J Acquir Immune Defic Syndr. 2003;34(4):368-78.
31. Revicki DA, Brown RE, Henry DA, McNeill MV, Rios A, Watson T. Recombinant human erythropoietin and health-related quality of life of AIDS patients with anemia. J Acquir Immune Defic Syndr. 1994;7:474-84.
32. Phair JP, Abels RI, McNeill MV, Sullivan DJ. Recombinant human erythropoietin treatment: investigational new drug protocol for the anemia of the acquired immunodeficiency syndrome. Arch Intern Med. 1993;153:2668-75.
33. Saag MS, Bowers P, Leitz GJ, Levine AM. Once-weekly epoetin alfa improves quality of life and increases hemoglobin in anemic HIV+ patients. AIDS Res Hum Retroviruses. 2004;20(10):1037-45.
34. Hematologic manifestations of HIV infection: Anemia. UpToDate. Available at Uptodate.com. Accessed August 22, 2011.
35. UpToDate. Peginterferon and ribavirin for the treatment of chronic hepatitis C virus infection: Management of side effects. Available at: http://www.uptodate.com/contents/peginterferon-and-ribavirin-for-the-treatment-of-chronic-hepatitis-c-virus-infection-management-of-side-effects?source=search_result&search=treatment+of+hepatitis+c&selectedTitle=9%7E150. Accessed July 13, 2012.
36. American Gastroenterological Association technical review on the management of hepatitis C. Gastroenterology. 2006;130(1):231-64.
37. EASL Clinical Practice Guidelines: Management of hepatitis C virus infection. J Hepatol. 2011;55(2):245-64.
38. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney inter., Suppl. 2012; 2: 279–335. http://www.kdigo.org/clinical_practice_guidelines/pdf/KDIGO-Anemia%20GL.pdf. Accessed August 7, 2012.
39. Yee et al. Update on the Management and Treatment of Hepatitis C Viral Infection: Recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program Office. [published online ahead of print April 24 2012]. Am J Gastroentero. 2012. http://www.hepatitis.va.gov/pdf/2012HCV-guidelines.pdf. Accessed August 7, 2012.
40. The American Cancer Society website. Available at http://www.cancer.org/cancer/cancerglossary/index.aspx?letter=N. Accessed May 24, 2013.
41. Mircera Prescribing Information, Hoffman-La Roche, Inc., October 2014

Prior Authorization Guideline

GL-16306 Fabrazyme (agalsidase beta)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/21/2016

Technician Note :

P&T Approval Date: 2/20/2004; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Fabrazyme

Indications

Fabry disease

Indicated for use in patients with Fabry disease. Reduces globotriaosylceramide (GL-3) deposition in capillary endothelium of the kidney and certain other cell types.

2 . Criteria

Product Name: Fabrazyme

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Fabry disease [A]

3 . Endnotes

A. Is an X-linked lysosomal-storage disorder due to a deficiency of alpha-galactosidase A. In the glycosphingolipid catabolic pathway, this enzyme removes the third sugar residue, a galactose, attached to ceramide. Without this enzyme, globotriaosylceramide accumulates within the vascular epithelium, heart, kidneys, cornea, and other tissues, causing angiokeratomata, painful acroparesthesias, hypohidrosis, renal failure, and cardiac and cerebrovascular disease. [3]

4 . References

1. Fabrazyme® Prescribing Information. Genzyme Corporation, May 2010.
2. Eng CM et al. Safety and efficacy of recombinant human alpha galactosidase A replacement therapy in Fabry's disease. N Engl J Med 2001; 345(1) 9-16.
3. Fabry Disease Disease Monograph. Genzyme Corporation, 2001
4. Germain DP, Waldek S, Banikazemi M. et al. Sustained, long-term renal stabilization after 54 Months of agalsidase beta therapy in patients with Fabry disease. J Am Soc Nephrol 2007;18:1547-1557.
5. Banikazemi M, Jan Bultas, Waldek S et al. Agalsidase-beta therapy for advanced Fabry disease. Ann Intern Med. 2007;146:77-86.

Prior Authorization Guideline

GL-15520 Farydak (panobinostat)

Formulary OptumRx SP

Formulary Note

Approval Date 4/15/2015

Revision Date 4/21/2016

Technician Note :

P&T Approval Date: 4/14/2015; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Farydak (panobinostat)

Indications

Multiple Myeloma (MM)

Indicated, in combination with bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent. This indication is approved under accelerated approval based on progression free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

2 . Criteria

Product Name: Farydak

Approval Length	12 Month [1,A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple myeloma [2]

AND

2 Used in combination with both of the following: [2]

- Velcade (bortezomib)
- Dexamethasone

AND

3 Patient has received at least two prior treatment regimens which included both of the following: [2]*

- Velcade (bortezomib)
- Immunomodulatory agent [eg, Revlimid (lenalidomide), Thalomid (thalidomide)]

AND	
4 Prescribed by or in consultation with an oncologist/hematologist	
Notes	*The concomittant use of Velcade and an immunomodulatory agent constitutes as one of two required prior treatment regimens.

Product Name: Farydak

Approval Length	12 Month [1,A]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Farydak therapy

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. The median progression-free survival was significantly longer in the panobinostat group than in the placebo group (11.99 months [95% CI 10.33–12.94] vs 8.08 months [7.56–9.23]; hazard ratio [HR] 0.63, 95% CI 0.52–0.76; p<0.0001). [1]

5 . References

1. San-Miguel JF, Hungria VT, Yoon SS, et al. Panobinostat plus bortezomib and dexamethasone versus placebo plus bortezomib and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma: a multicentre, randomised, double-blind phase 3 trial. Lancet Oncol. 2014;15(11):1195-206.
2. Farydak Prescribing Information. Novartis Pharmaceuticals Corporation., February 2015.
3. National Comprehensive Cancer Network (NCCN), Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 3.2015. Available at: www.nccn.org. Accessed March 9, 2015.

Prior Authorization Guideline

GL-17149 Ferriprox (deferiprone)

Formulary OptumRx SP

Formulary Note

Approval Date 3/12/2013

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 4/10/2012; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Ferriprox (deferiprone)

Indications

Iron Overload

Indicated for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate. Approval is based on a reduction in serum ferritin levels. There are no controlled trials demonstrating a direct treatment benefit, such as improvement in disease-related symptoms, functioning, or increased survival. Limitation of use: Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with other chronic anemias.

2 . Criteria

Product Name: Ferriprox tablet, Ferriprox oral solution

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of transfusional iron overload due to thalassemia syndromes

AND

2 One of the following:

2.1 History of failure, defined by a serum ferritin > 2,500 mcg/L, to one of the following: [A]

- Desferal (deferoxamine)
- Exjade (deferasirox)
- Jadenu (deferasirox)

OR

2.2 History of contraindication or intolerance to one of the following:

- Desferal (deferoxamine)
- Exjade (deferasirox)
- Jadenu (deferasirox)

AND

3 Absolute neutrophil count (ANC) > 1.5 x 10^9/L

Product Name: Ferriprox tablet, Ferriprox oral solution

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has experienced greater than or equal to 20% decline in serum ferritin levels from baseline

AND

2 Absolute neutrophil count (ANC) > 1.5 x 10^9/L

3 . Endnotes

A. Failure to prior chelation therapy is defined as serum ferritin > 2,500 mcg/L. [1]

4 . References

1. Ferriprox Prescribing Information. ApoPharma USA, Inc., February 2015.
2. Ho PJ, Tay L, Linderman R, Catley L, Bowden DK. Australian guidelines for the assessment of iron overload and iron chelation in transfusion-dependent thalassaemia major, sickle cell disease and other congenital anaemias. Intern Med J. 2011;41(7):516-24.
3. Angelucci E, Barosi G, Camaschella C, et al. Italian Society of Hematology practice guidelines for the management of iron overload in thalassemia major and related disorders. Haematologica. 2008;93(5):741-52.
4. United Kingdom Thalassemia Society. Standards for the clinical care of children and adults with thalassemia in the UK. 2008. Available at http://www.ukts.org/pdfs/awareness/standards/ukts-standards-2008.pdf. Accessed December 27, 2012.
5. Nursing Practice Guidelines: Care of the Patient with Sickle Cell Disease and Iron Overlead. 2008 International Association of Sickle Cell Nurses and Physician Assistants. Available at: http://www.iascnapa.org/guidelines/Guidelines_IronOverload.pdf. Accessed on December 28, 2012.
6. Cavill I. Iron status as measured by serum ferritin: the marker and its limitations. Am J Kidney Dis. 1999 Oct;34(4 Suppl 2):S12-7.
7. Porter JB and Shah FT. Iron overload in thalassemia and related conditions: therapeutic goals and assessment of response to chelation therapies. 2010 Dec;24(6):1109-30.
8. Ferriprox Solution Prescribing Information. ApoPharma USA, Inc., September 2015.

Prior Authorization Guideline

GL-17357 Firmagon (degarelix)

Formulary OptumRx SP

Formulary Note

Approval Date 3/8/2013

Revision Date 5/31/2016

Technician Note :

P&T Approval Date: 5/18/2010; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Firmagon (degarelix)

Indications

Advanced Prostate Cancer

Indicated for treatment of patients with advanced prostate cancer.

2 . Criteria

Product Name: Firmagon

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced prostate cancer

AND

2 Prescribed by or in consultation with an oncologist

Product Name: Firmagon

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Firmagon therapy

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . References

1. Firmagon Prescribing Information. Ferring Pharmaceuticals Inc., March 2015.
2. Klotz L, Boccon-Gibod L, Shore ND, et al. The efficacy and safety of Firmagon: a 12-month, comparative, randomized, open-label, parallel-group phase III study in patients with prostate cancer. BJU Int. 2008;102:1531-1538.
3. National Cancer Comprehensive Network Clinical Practice Guidelines in Oncology: Prostate Cancer V.1.2015. http://www.nccn.org/professionals/physician_gls/PDF/prostate.pdf. Accessed September 16, 2015.

Prior Authorization Guideline

GL-17124 Gattex (teduglutide)

Formulary OptumRx SP

Formulary Note

Approval Date 3/12/2013

Revision Date 4/22/2016

Technician Note :

P&T Approval Date: 2/19/2013; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Gattex (teduglutide)

Indications

Short Bowel Syndrome

Indicated for the treatment of adult patients with short bowel syndrome who are dependent on parenteral support.

2 . Criteria

Product Name: Gattex

Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of short bowel syndrome

AND

2 Dependent on parenteral nutrition/intravenous (PN/IV) support for at least 12 consecutive months [A]

Product Name: Gattex

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Gattex therapy

3 . Endnotes

A. Twelve consecutive months on parenteral nutrition is an inclusion criterion in clinical trials. [1]

4 . References

1. Gattex Prescribing Information, NPS Pharmaceuticals, December 2012.
2. Van Gossum A, Cabre E, Hébuterne X, et al. ESPEN Guidelines on Parenteral Nutrition: gastroenterology. Clin Nutr. 2009;28(4):415-27.
3. Nightingale J, Woodward JM on behalf of the Small Bowel and Nutrition Committee of the British Society of Gastroenterology. Guidelines for management of patients with a short bowel. Gut. 2006;55 Suppl 4:iv1-12.
4. Buchman AL, Scolapio J, Fryer J. AGA technical review on short bowel syndrome and intestinal transplantation. Gastroenterology. 2003;124(4):1111-34.

Prior Authorization Guideline

GL-15595 Gaucher Disease Agents

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/25/2016

Technician Note :

P&T Approval Date: 11/20/2000;P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Cerezyme (imiglucerase for injection) **<u>Indications</u>** **Type 1 Gaucher Disease** Indicated for long-term enzyme replacement therapy for pediatric and adult patients with a confirmed diagnosis of type 1 Gaucher disease that results in one or more of the following conditions: · anemia · thrombocytopenia · bone disease · hepatomegaly or splenomegaly
Drug Name: Elelyso (taliglucerase alfa) for injection

Indications

Type 1 Gaucher Disease

Indicated for the treatment of patients with a confirmed diagnosis of Type 1 Gaucher disease.

Drug Name: VPRIV (velaglucerase alfa for injection)

Indications

Type 1 Gaucher Disease

Indicated for long-term enzyme replacement therapy (ERT) for patients with type 1 Gaucher disease

Drug Name: Cerdelga (eliglustat)

Indications

Type 1 Gaucher Disease

Indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1) who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs), or poor metabolizers (PMs) as detected by an FDA-cleared test

Drug Name: Zavesca (miglustat)

Indications

Type 1 Gaucher Disease

Indicated as monotherapy for the treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (eg, due to allergy, hypersensitivity, or poor venous access)

2 . Criteria

Product Name: Cerezyme, Elelyso, or VPRIV

Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Type 1 Gaucher disease

AND

2 Patient has evidence of symptomatic disease (e.g., moderate to severe anemia [A], thrombocytopenia [B], bone disease [C], hepatomegaly [D], or splenomegaly [D])

Product Name: Cerdelga

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is 18 years of age or older

AND

2 Diagnosis of Type 1 Gaucher disease

AND

3 Patient is an extensive metabolizer (EM), intermediate metabolizer (IM), or poor metabolizer (PM) of cytochrome P450 enzyme (CYP) 2D6 as detected by an FDA-cleared test

Product Name: Cerdelga

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient's condition has not progressed, as defined by ALL of the following:

- Hemoglobin level decreased greater than 1.5 g/dL from baseline
- Platelet count decreased greater than 25% from baseline
- Spleen volume increased greater than 25% from baseline
- Liver volume increased greater than 20% from baseline

Product Name: Zavesca

Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of mild to moderate Type 1 Gaucher disease [E]

AND

2 Patient is unable to receive enzyme replacement therapy due to one of the following conditions:

- Allergy or hypersensitivity to enzyme replacement therapy
- Poor venous access
- Unavailability of enzyme replacement therapy (e.g., Cerezyme, VPRIV) [F]

3 . Endnotes

A. Goals of treatment with anemia are to increase hemoglobin to greater than or equal to 12.0 g/dL for males (greater than 12 years of age), and to greater than or equal to 11.0 g/dL for both children (less than or equal to 12 years of age) and females (greater than 12 years of age). [6,8]
B. Moderate thrombocytopenia is defined as a platelet count of 60,000 to 120,000/microliter. A platelet count of 120,000/microliter to meet the criterion of thrombocytopenia is based on the upper end of the range that defines moderate thrombocytopenia. [6]
C. In bone disease, the goal is to lessen or eliminate bone pain and prevent bone crises. Bone disease can be diagnosed using MRI, bone scan, and X-ray. [6-8]
D. Hepatomegaly is defined as a liver mass of greater than 1.25 times normal value. Splenomegaly is defined as a splenic mass greater than the normal, and moderate splenomegaly is considered a spleen volume of greater than 5 and less than or equal to 15 times normal. [6]
E. Zavesca may be prescribed only by physicians knowledgeable in the management of Gaucher disease (GD). In order to prescribe Zavesca, physicians must read the letter to doctors from Actelion, then sign and fax the one-page physician statement affirming that they are qualified to manage patients with GD and that they have read the Zavesca review booklet containing the full prescribing information. Zavesca is dispensed exclusively by Accredo specialty pharmacy. [10]
F. Due to previous shortages of Cerezyme, and when VPRIV was unable to meet the demand for all patients, criteria for Zavesca was added to address unavailability of enzyme replacement therapy (ERT). [11] The European Working Group for Gaucher Disease released a position statement regarding the ERT shortage, stating that Zavesca

could be used in patients with mild and moderate forms of type 1 Gaucher disease, for whom ERT was unavailable. [9]

4 . References

1. Cerezyme Prescribing Information. Genzyme Corporation, December 2012.
2. Elelyso Prescribing Information. Pfizer Inc., November 2015.
3. VPRIV Prescribing Information. Shire Human Genetic Therapies, April 2015.
4. Cerdelga Prescribing Information. Genzyme Corporation, August 2014.
5. Zavesca Prescribing Information. Actelion Pharmaceuticals US Inc., February 2014.
6. Pastores GM et al. Therapeutic goals in the treatment of Gaucher disease. Semin Hematol 2004;41(4 Suppl 5):4-14
7. Weinreb NJ, Aggio MC, Andersson HC, et al. Gaucher disease type 1: revised recommendations on evaluations and monitoring for adult patients. Semin Hematol 2004;41(suppl 5):15-22.
8. Weinreb N, Taylor J, Cox T, Yee J, vom Dahl S. A benchmark analysis of the achievement of therapeutic goals for type 1 Gaucher disease patients treated with imiglucerase. Am J Hematol.2008;83:890-895.
9. Hollak CE, vom Dahl S, Aerts JM, et al. Force majeure: therapeutic measures in response to restricted supply of imiglucerase (Cerezyme) for patients with Gaucher disease. Blood Cells Mol Dis. 2010;44(1):41-7.
10. Actelion Pharmaceuticals US, Inc. Zavesca (miglustat). Available at: http://www.zavesca.com/hcp-home.asp. Accessed on July 23, 2015.
11. Per clinical consultation with geneticist, November 11, 2010

Prior Authorization Guideline

GL-17249 Gazyva (obinutuzumab)

Formulary OptumRx SP

Formulary Note

Approval Date 2/24/2014

Revision Date 6/3/2016

Technician Note :

P&T Approval Date: 2/18/2014; P&T Revision Date: 4/27/2016

1 . Indications

Drug Name: Gazyva (obinutuzumab)

Indications

Chronic Lymphocytic Leukemia (CLL)

Gazyva, in combination with chlorambucil, is indicated for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL).

Follicular Lymphoma (FL)

Gazyva, in combination with bendamustine followed by Gazyva monotherapy, is indicated for

the treatment of patients with follicular lymphoma (FL) who relapsed after, or are refractory to, a rituximab-containing regimen.

2 . Criteria

Product Name: Gazyva

Diagnosis	Chronic Lymphocytic Leukemia (CLL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Chronic Lymphocytic Leukemia (CLL)

AND

2 Used in combination with chlorambucil [1, 2, 3, 4]

AND

3 Patient is previously untreated for CLL [1, 2, 3, 4]

AND

4 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Gazyva

Diagnosis	Chronic Lymphocytic Leukemia (CLL)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Gazyva therapy

Product Name: Gazyva

Diagnosis	Follicular Lymphoma (FL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of follicular lymphoma (FL)

AND

2 Will be used in combination with bendamustine for six cycles prior to maintenance

treatment with Gazyva monotherapy [1-3]

AND

3 Relapsed or refractory to a rituximab-containing regimen [1-2,A]

AND

4 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Gazyva

Diagnosis	Follicular Lymphoma (FL)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Gazyva therapy

3 . Endnotes

A. NCCN supports use of obinutuzumab in the treatment of follicular lymphoma as maintenance therapy for rituximab refractory disease in patients with indications for treatment as second-line extended dosing. [3]

4 . References

1. Gazyva Prescribing Information, Genentech Inc., November 2013.
2. NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed April 5, 2016.
3. National Comprehensive Cancer Network. Practice Guidelines in Oncology – v.2.2016. Non-Hodgkin's Lymphoma. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf. Accessed April 5, 2016.
4. Goede V, Fischer K, Humphrey K, et al. Obinutuzumab (GA101) plus chlorambucil (Clb) or rituximab (R) plus Clb versus Clb alone in patients with chronic lymphocytic leukemia (CLL) and preexisting medical conditions (comorbidities): final stage 1 results of the CLL11 (BO21004) phase III trial. J Clin Oncol. 2013;31 (suppl; abstr 7004).

Prior Authorization Guideline

GL-7297 Geodon (ziprasidone mesylate) injection

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/30/2013

Technician Note :

CPS Approval Date: 11/25/2002; CPS Revision Date: 5/15/2012

1 . Indications

Drug Name: Geodon (ziprasidone mesylate) injection (intramuscular)

Indications

Acute agitation [1]

Is indicated for the treatment of acute agitation in schizophrenic patients for whom treatment with Geodon is appropriate and who need intramuscular antipsychotic medication for rapid control of the agitation. "Psychomotor agitation" is defined in DSM-IV as "excessive motor activity associated with a feeling of inner tension." Schizophrenic patients experiencing agitation often manifest behaviors that interfere with their diagnosis and care, e.g., threatening behaviors, escalating or urgently distressing behavior, or self-exhausting behavior, leading clinicians to the

use of intramuscular antipsychotic medications to achieve immediate control of the agitation. The efficacy of intramuscular Geodon for acute agitation in schizophrenia was established in single-day controlled trials of schizophrenic inpatients. Since there is no experience regarding the safety of administering Geodon intramuscular to schizophrenic patients already taking oral Geodon, the practice of co-administration is not recommended.

2 . Criteria

Product Name: Geodon injection

Approval Length	3 Day
Guideline Type	Non-Preferred
Approval Criteria **1** Diagnosis of schizophrenia **AND** **2** Treatment of acute agitation for rapid control	
Notes	NOTE TO PRESCRIBER: If long-term therapy is indicated, oral Geodon should replace the intramuscular administration as soon as possible. [1]

3 . Dosing

Drug Name	Description

Geodon Injection	10 to 20 mg administered intramuscularly as required up to the maximum dose of 40 mg per day. Doses of 10 mg may be administered every 2 hours; doses of 20 mg may be administered every 4 hours up to a maximum of 40mg/day. Intramuscular administration of Geodon for more than 3 consecutive days have not been studied. If long-term therapy is indicated, oral Geodon should replace the intramuscular administration as soon as possible.

4 . Availability

Drug Name	Description
Geodon® Injection:	20 mg/mL as powder for injection

5 . Background

Clinical Practice Guidelines

American Psychiatric Association [2]
Schizophrenia (2004)

Table 1. Acute phase treatment of schizophrenia

Patient Profile	Consider Medication from		
	Group 1	Group 2	Group 3
First episode		X	
Persistent suicidal ideation or behavior			X
Persistent hostility and aggressive behavior			X
Tardive dyskinesia		X*	X
History of sensitivity to extrapyramidal side effects		X (except higher doses of	

		Risperdal)	
History of sensitivity to prolactin elevation		X (except Risperdal)	
History of sensitivity to weight gain, hyperglycemia, or hyperlipidemia		X (Geodon or Abilify)	

Group 1 = Typical (first-generation) antipsychotic agents

Group 2 = Abilify, Geodon, Risperdal, Seroquel, or Zyprexa

Group 3 = Clozaril

*All drugs in group 2 may not be equal in their potential to induce tardive dyskinesia

Stable phase treatment of schizophrenia

- Most patients who develop schizophrenia and related psychotic disorders are at very high risk of relapse in the absence of antipsychotic treatment.
- Antipsychotic medications substantially reduce the risk of relapse in the stable phase of illness and are strongly recommended.
- Indefinite maintenance antipsychotic medication is recommended for patients who have had multiple prior episodes or two episodes within 5 years. In patients for whom antipsychotic medications have been prescribed, monitoring for signs and symptoms of impending or actual relapse is recommended.

6 . References

1. Geodon® Prescribing information, Pfizer Inc. December 2010.
2. American Psychiatric Association. Practice guidelines for the treatment of patients with schizophrenia (2nd edition). Am J Psychiatry. 2004;161(2 Suppl):1-56.

3. Lesem MD, Zajecka JM, Swift RH, et al. Intramuscular ziprasidone, 2 mg versus 10 mg, in the short-term management of agitated psychotic patients. J Clin Psychiatry 2001; 62:12–18.
4. Daniel DG, Potkin SG, Reeves KR, et al. Intramuscular (IM) ziprasidone 20 mg is effective in reducing acute agitation associated with psychosis: a double-blind, randomized trial. Psychopharmacology 2001; 155:128–134.

Prior Authorization Guideline

GL-30250 Gilotrif (afatinib)

Formulary OptumRx SP

Formulary Note

Approval Date 7/8/2016

Revision Date 7/8/2016

Technician Note :

P&T Approval Date: 10/8/2013; P&T Revision Date: 6/22/2016. **Effective 7/15/2016**

1 . Indications

Drug Name: Gilotrif (afatinib)

Indications

EGFR Mutation-Positive, Metastatic Non-Small Cell Lung Cancer (NSCLC) Indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test. Limitation of Use: Safety and efficacy of Gilotrif have not been established in patients whose tumors have other EGFR mutations.

Previously Treated, Metastatic Squamous Non-Small Cell Lung Cancer (NSCLC) Indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy.

2 . Criteria

Product Name: Gilotrif

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced or metastatic (stage IIIB or IV) non-small cell lung cancer

and

2 One of the following:

2.1 Both of the following:

2.1.1 Patient has known active epidermal growth factor receptor (EGFR) exon 19 deletions, exon 21 (L858R) substitution, exon 18 (G719X, G719) or exon 20 (S7681) mutations as confirmed by an FDA-approved test or at a Clinical Laboratory Improvement Amendments-approved facility

and

2.1.2 Gilotrif will be used as first-line treatment

OR

2.2 Disease progressed after platinum-based chemotherapy

and

3 Prescribed by or in consultation with an oncologist

Product Name: Gilotrif

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Gilotrif therapy

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . References

1. Gilotrif Prescribing Information. Boehringer Ingelheim Pharmaceuticals, Inc., April 2016.

Prior Authorization Guideline

GL-16906 Gleevec (imatinib mesylate)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/20/2016

Technician Note :

P&T Approval Date: 8/24/2001; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Gleevec (imatinib mesylate)

Indications

Chronic myelogenous/myeloid leukemia (CML)

Indicated for the treatment of newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase. Gleevec is also indicated for the treatment of patients with Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.

Acute lymphoblastic leukemia/ Acute lymphoblastic lymphoma (ALL)

Indicated for the treatment of adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL). Gleevec is also indicated for the treatment of pediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) in combination with chemotherapy.

Myelodysplastic/myeloproliferative diseases (MDS/MPD)

Indicated for the treatment of adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements.

Aggressive systemic mastocytosis (ASM)

Indicated for the treatment of adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation or with c-Kit mutational status unknown.

Hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL)

Indicated for the treatment of adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRa fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRa fusion kinase negative or unknown.

Dermatofibrosarcoma protuberans (DFSP)

Indicated for the treatment of adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP).

Gastrointestinal stromal tumors (GIST)

Indicated for the treatment of patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST). Gleevec is also indicated for the adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positive GIST.

2 . Criteria

Product Name: Brand Gleevec, Generic imatinib

Diagnosis	Chronic Myelogenous/Myeloid Leukemia (CML)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Philadelphia chromosome-positive chronic myelogenous/myeloid leukemia (Ph+CML)

AND

2 Patient is found to be Philadelphia chromosome positive or BCR-ABL positive as detected by bone marrow cytogenetics, FISH or PCR

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Brand Gleevec, Generic imatinib

Diagnosis	Acute lymphoblastic leukemia/ Acute lymphoblastic lymphoma (ALL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL)

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Brand Gleevec, Generic imatinib

Diagnosis	Myelodysplastic Disease (MDS)/Myeloproliferative Disease (MPD)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of myelodysplastic/myeloproliferative disease (MDS/MPD)

AND

2 Disease is associated with platelet-derived growth factor receptor (PDGFR) gene rearrangements

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Brand Gleevec, Generic imatinib

Diagnosis	Aggressive Systemic Mastocytosis (ASM)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of aggressive systemic mastocytosis (ASM)

AND

2 One of the following:

2.1 Patient is without the D816V c-Kit mutation

OR

2.2 c-Kit mutational status is unknown

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Brand Gleevec, Generic imatinib

Diagnosis	Hypereosinophilic Syndrome (HES) and/or Chronic Eosinophilic Leukemia (CEL)

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of at least one of the following:

- Hypereosinophilic syndrome (HES)
- Chronic eosinophilic leukemia (CEL)

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Brand Gleevec, Generic imatinib

Diagnosis	Dermatofibrosarcoma Protuberans (DFSP)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of unresectable, recurrent, or metastatic dermatofibrosarcoma protuberans (DFSP)

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Brand Gleevec, Generic imatinib

Diagnosis	Gastrointestinal Stromal Tumors (GIST)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of gastrointestinal stromal tumors (GIST)

AND

2 One of the following:

2.1 Patient has documented c-KIT (CD117) positive unresectable or metastatic malignant GIST

OR

2.2 Both of the following:

2.2.1 Patient had resection of c-KIT (CD117) positive GIST

AND

2.2.2 Gleevec (imatinib) will be used as adjuvant therapy

AND
3 Prescribed by or in consultation with an oncologist

Product Name: Brand Gleevec, Generic imatinib

Diagnosis	All diagnoses listed above
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Gleevec therapy

3 . References

1. Gleevec Prescribing Information. Novartis Pharmaceuticals Corporation, January 2015.
2. Imatinib mesylate Prescribing Information. Sun Pharmaceutical Industries, Inc. January 2016.

Prior Authorization Guideline

GL-17380 Gonadotropin-Releasing Hormone Agonists

Formulary OptumRx SP

Formulary Note

Approval Date 10/14/2015

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 12/12/2005; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Lupron Depot (leuprolide acetate) 7.5 mg, Lupron Depot 3-Month 22.5 mg, Lupron Depot 4-Month 30 mg, Lupron Depot 6-Month 45 mg, Eligard (leuprolide acetate), Trelstar (triptorelin pamoate), and Vantas (histrelin acetate) **Indications** **Prostate Cancer** Indicated for the palliative treatment of advanced prostatic cancer.
Drug Name: Lupron Depot 3.75 mg and 3-Month 11.25 mg

Indications

Endometriosis

Indicated for the management of endometriosis, including pain relief and reduction of endometriotic lesions. They are also indicated, with norethindrone acetate 5 mg daily, for initial management of endometriosis and for management of recurrence of symptoms. Duration of initial treatment or retreatment should be limited to 6 months.

Uterine Leiomyomata (Fibroids)

Indicated, concomitantly with iron therapy, for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata. The clinician may wish to consider a 1 month trial period on iron alone as some patients will respond to iron alone. Lupron Depot may be added if the response to iron alone is considered inadequate. The recommended duration of therapy with Lupron Depot 3.75 mg is up to three months. Experience with Lupron Depot 3.75 mg in females has been limited to women 18 years of age and older. Recommended therapy for Lupron Depot 3-Month 11.25 mg is a single injection. Lupron Depot 3-Month 11.25 mg dosage formulation is indicated only for women for whom three months of hormonal suppression is deemed necessary. Experience with Lupron Depot 3-Month 11.25 mg in females has been limited to women 18 years of age and older treated for no more than 6 months.

Drug Name: Leuprolide acetate

Indications

Prostate Cancer

Indicated for the palliative treatment of advanced prostatic cancer.

Central Precocious Puberty (CPP)

Indicated for the treatment of children with CPP. Children should be selected using the following criteria: (a) Clinical diagnosis of CPP (idiopathic or neurogenic) with onset of secondary sexual characteristics earlier than 8 years in females and 9 years in males; (b) Clinical diagnosis should be confirmed prior to initiation of therapy: (1) Confirmation of diagnosis by a pubertal response to a gonadotropin releasing hormone (GnRH) stimulation test. The sensitivity and methodology of this assay must be understood.; (2) Bone age advanced one year beyond the chronological age.; and (c) Baseline evaluation should also include: (1) Height and weight measurements; (2) Sex steroid levels; (3) Adrenal steroid level to exclude congenital adrenal hyperplasia; (4) Beta human chorionic gonadotropin level to rule out a chorionic gonadotropin secreting tumor; (5) Pelvic/adrenal/testicular ultrasound to rule out a steroid secreting tumor; (6) Computerized tomography of the head to rule out intracranial tumor.

Off Label Uses

Infertility

Used for controlled ovarian hyperstimulation to enhance the in vitro fertilization-embryo transfer (IVF-ET) procedure. [28]

Drug Name: Lupaneta Pack (leuprolide acetate inj; norethindrone acetate tablets) 3.75 mg and 3-Month 11.25 mg

Indications

Endometriosis

Indicated for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms. Limitation of use: Duration of use is limited due to concerns about adverse impact on bone mineral density. The initial treatment course of Lupaneta is limited to 6 months. A single retreatment course of not more than 6 months may be administered after the initial course of treatment if symptoms recur. Use of Lupaneta for longer than a total of 12 months is not recommended.

Drug Name: Supprelin LA (histrelin acetate)

Indications

Central precocious puberty (CPP)

Indicated for the treatment of children with CPP. Children with CPP (neurogenic or idiopathic) have an early onset of secondary sexual characteristics (earlier than 8 years of age in females and 9 years of age in males). They also show a significantly advanced bone age that can result in diminished adult height attainment. Prior to initiation of treatment a clinical diagnosis of CPP should be confirmed by measurement of blood concentrations of total sex steroids, luteinizing hormone (LH) and follicle stimulating hormone (FSH) following stimulation with a GnRH analog, and assessment of bone age versus chronological age. Baseline evaluations should include height and weight measurements, diagnostic imaging of the brain (to rule out intracranial tumor), pelvic/testicular/adrenal ultrasound (to rule out steroid secreting tumors), human chorionic gonadotropin levels (to rule out a chorionic gonadotropin secreting tumor), and adrenal steroids to exclude congenital adrenal hyperplasia.

Drug Name: Lupron Depot-Ped (leuprolide acetate)

Indications

Central precocious puberty (CPP)

Indicated in the treatment of children with central precocious puberty (CPP). CPP is defined as early onset of secondary sexual characteristics (generally earlier than 8 years of age in girls and 9 years of age in boys) associated with pubertal pituitary gonadotropin activation. It may show a significantly advanced bone age that can result in diminished adult height. Prior to initiation of treatment a clinical diagnosis of CPP should be confirmed by measurement of blood concentrations of luteinizing hormone (LH) (basal or stimulated with a GnRH analog), sex steroids, and assessment of bone age versus chronological age. Baseline evaluations should include height and weight measurements, diagnostic imaging of the brain (to rule out intracranial tumor), pelvic/testicular/adrenal ultrasound (to rule out steroid secreting tumors), human chorionic gonadotropin levels (to rule out a chorionic gonadotropin secreting tumor), and adrenal steroid measurements to exclude congenital adrenal hyperplasia.

2 . Criteria

Product Name: Lupron Depot (3.75 mg and 11.25 mg)

Diagnosis	Endometriosis
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of endometriosis

AND

2 One of the following: [28, 30]

2.1 History of inadequate pain control response following a trial of at least 6 months, or history of intolerance or contraindication to one of the following:

- Danazol
- Combination (estrogen/progesterone) oral contraceptive
- Progestins

OR

2.2 Patient has had surgical ablation to prevent recurrence

Product Name: Lupron Depot (3.75 mg and 11.25 mg)

Diagnosis	Endometriosis [10, 18, 20]
Approval Length	6 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Recurrence of symptoms following a trial of at least 6 months with leuprolide acetate

AND

2 Used in combination with one of the following:

- Norethindrone 5 mg daily
- Other “add-back” sex-hormones
- Other bone-sparing agents

Product Name: Lupron Depot (3.75 mg and 11.25 mg)

Diagnosis	Uterine Leiomyomata (Fibroids) - For the reduction of the size of fibroids [off-label]
Approval Length	4 Month
Guideline Type	Prior Authorization

Approval Criteria

1 For use prior to surgery to reduce the size of fibroids to facilitate a surgical procedure (e.g., myomectomy, hysterectomy) [20]

Product Name: Lupron Depot (3.75 mg and 11.25 mg)

Diagnosis	Uterine Leiomyomata (Fibroids) - Anemia
Approval Length	3 Month
Guideline Type	Prior Authorization

Approval Criteria

1 For the treatment of anemia

AND

2 Anemia is caused by uterine leiomyomata (fibroids)

AND

3 Patient has tried and had an inadequate response to at least 1 month of monotherapy with iron

AND

4 Used in combination with iron therapy

AND

5 For use prior to surgery

Product Name: Generic leuprolide acetate, Lupron Depot-Ped, Supprelin LA

Diagnosis	Central Precocious Puberty (CPP)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of central precocious puberty (idiopathic or neurogenic)

AND

2 Early onset of secondary sexual characteristics in one of the following:

- Females less than 8 years of age
- Males less than 9 years of age

AND

3 Advanced bone age of at least one year compared with chronological age

AND

4 One of the following:

4.1 Both of the following:

- Patient has undergone gonadotropin-releasing hormone agonist (GnRHa) testing
- Peak luteinizing hormone (LH) level above pre-pubertal range

OR

4.2 Patient has a random LH level in the pubertal range

AND

5 One of the following:

5.1 Patient had one of the following diagnostic evaluations to rule out tumors, when suspected:

- Diagnostic imaging of the brain (MRI or CT scan) (in patients with symptoms suggestive of a brain tumor or in those 6 years of age or younger)
- Pelvic/testicular/adrenal ultrasound (if steroid levels suggest suspicion)
- Adrenal steroids to rule out congenital adrenal hyperplasia (when pubarche precedes thelarche or gonadarche)

OR

5.2 Patient has no suspected tumors

AND

6 Prescribed by or in consultation with a pediatric endocrinologist

Product Name: Generic leuprolide acetate, Lupron Depot-Ped, Supprelin LA

Diagnosis	Central Precocious Puberty (CPP)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 LH levels have been suppressed to pre-pubertal levels

AND

2 Prescribed by or in consultation with a pediatric endocrinologist

Product Name: Generic leuprolide acetate*

Diagnosis	Treatment of Infertility [off-label]
Approval Length	2 Month [A] (or per plan benefit design)
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of infertility

AND

2 Used as part of an assisted reproductive technology (ART) protocol

Notes	*Please consult client-specific resources to confirm whether benefit exclusions should be reviewed for medical necessity.

Product Name: Eligard, Generic leuprolide acetate, Trelstar, Vantas

Diagnosis	Prostate Cancer
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced or metastatic prostate cancer [B-C]

AND

2 History of failure, contraindication, or intolerance to one of the following:

- Lupron Depot (7.5 mg, 22.5 mg, 30 mg, or 45 mg)
- Zoladex (goserelin acetate implant)

Product Name: Lupron Depot (7.5 mg, 22.5 mg, 30 mg and 45 mg)

Diagnosis	Prostate Cancer
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization
Approval Criteria **1** Diagnosis of advanced or metastatic prostate cancer [18, 25, 32, B-C]	

Product Name: Eligard, Generic leuprolide acetate, Lupron Depot (7.5 mg, 22.5 mg, 30 mg and 45 mg), Trelstar, Vantas

Diagnosis	Prostate Cancer
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Patient does not show evidence of progressive disease while on therapy	

Product Name: Lupaneta Pack

Diagnosis	Endometriosis
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of endometriosis

AND

2 One of the following: [28, 30]

2.1 History of inadequate pain control response following a trial of at least 6 months, or history of intolerance or contraindication to one of the following:

- Danazol
- Combination (estrogen/progesterone) oral contraceptive
- Progestins

OR

2.2 Patient has had surgical ablation to prevent recurrence

Product Name: Lupaneta Pack

Diagnosis	Endometriosis
Approval Length	6 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Recurrence of symptoms following a trial of at least 6 months with leuprolide therapy

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

These products are subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. Sixty days would be a reasonable length of authorization for this indication. [29]
B. Micromedex recommends the off-label use of Lupron Depot and generic leuprolide acetate for clinically localized prostate cancer (Recommendation: Adult, Class IIb; Strength of Evidence: Adult, Category B) and for neoadjuvant treatment of prostate cancer (Recommendation: Adult, Class IIb; Strength of Evidence: Adult, Category B). [18] For clinically localized prostate cancer: A 6-month course of androgen-suppression therapy (AST) added to radiation therapy provided improved survival benefits compared with radiation therapy (RT) alone in men with clinically localized prostate cancer (p = 0.04), based on a randomized controlled trial (n = 206). [18] As neoadjuvant treatment in prostate cancer: In comparison to 3 months of neoadjuvant hormonal therapy (leuprolide and flutamide) for prostate cancer, 8 months of such treatment resulted in a reduced incidence of positive margins when prostatectomy was performed (n = 547); optimal duration of therapy appears to be longer than 3 months. [18]
C. The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium [32] recommends the use of Lupron Depot, Eligard, Trelstar, and Vantas in prostate cancer for the following: (1) Adjuvant treatment with or without external beam radiation therapy (EBRT) if positive lymph nodes were found during pelvic lymph node dissection [NCCN Category: 1; 2B for combination with EBRT]. (2) Initial androgen deprivation therapy (ADT) for 4-6 months in combination with EBRT with or without brachytherapy for patients in the intermediate risk group [NCCN Category: 2A]. (3) Initial ADT for 2-3 years in combination with EBRT (a) with or without brachytherapy for patients in the high or very high risk group or (b) for metastatic disease (any T, N1) [NCCN Category: 1; 2A for combination with brachytherapy]. (4) Initial ADT for (a)

patients in the very high risk group who are not candidates for definitive therapy or (b) metastatic disease [NCCN Category: 2A]. (5) Used for radical prostatectomy biochemical failure as (a) ADT with EBRT for disease without distant metastases or (b) ADT with or without EBRT for distant metastatic disease [NCCN Category: 2A]. (6) Used following radiation therapy in patients with biochemical failure or positive digital rectal examination (a) with a negative biopsy and no distant metastases or (b) who are not candidates for local therapy [NCCN Category: 2A]. (7) Used as a single agent or in combination with an antiandrogen (a) for progressive disease or low-volume metastatic disease or (b) docetaxel for high-volume metastatic disease [NCCN Category: 2A].

5 . References

1. Leuprolide acetate Prescribing Information. Teva Pharmaceuticals USA, August 2014.
2. Lupron Depot (7.5 mg) Prescribing Information. Abbvie Inc., June 2014.
3. Vantas Prescribing Information. Endo Pharmaceuticals Solutions Inc., July 2014.
4. Lupron Depot (3.75 mg) Prescribing Information. AbbVie Inc., October 2013.
5. Lupron Depot (3-Month 11.25 mg) Prescribing Information. AbbVie Inc., October 2013.
6. Sharifi R, Knoll D, Smith J, Kramolowsky E. Leuprolide acetate (30 mg depot every 4 months) in the treatment of advanced prostate cancer. Adult Urol. 1998;51:271-276.
7. Crawford ED, Eisenberger MA, McLeod DG, et al. A controlled trial of leuprolide with and without flutamide in prostatic carcinoma. N Engl J Med 1989;321:419-424.
8. Seidenfeld J, Samson DJ, Hasselblad V, et al. Single therapy androgen suppression in men with advanced prostate cancer: a systemic review and meta-analysis. Ann Inter Med. 2000;132:566-577.
9. Hornstein MD, Surrey ES, Weisberg GW, et al. Leuprolide acetate depot and hormonal add-back in endometriosis: a 12-month study. Lupron Add-Back Study Group. Obstet Gynecol 1998;91:16-24.
10. Friedman AJ, Harrison-Atlas D, Barbieri RL, et al. A randomized, placebo-controlled, double-blind study evaluating the efficacy of leuprolide acetate depot in the treatment of uterine leiomyomata. Fertil Steril 1989;51:251-256.
11. Ohyama K, Tanaka T, Tachibana K, et al. Timing for discontinuation of treatment with a long-acting gonadotropin-releasing hormone analog in girls with central precocious puberty. TAP-144SR CPP Study Group. Endocr J 1998;45:351-356.
12. Carel JC, Roger M, Ispas S, et al. Final height after long-term treatment with triptorelin slow release for central precocious puberty: importance of statural growth after interruption of treatment. J Clin Endo Society. 1999;84:1973-1978.
13. Oerter KE, Manasco PK, Barnes KM, Jones J, Hill S, Culter GB. Effects of luteinizing hormone-releasing hormone agonists on final height in luteinizing hormone-releasing hormone-dependent precocious puberty. Act Paed. 1993: Suppl 388:62-68.
14. National Cancer Institute. Prostate cancer PDQ: Treatment, health professional version. Available at: http://www.cancer.gov/cancertopics/pdq/treatment/prostate/healthprofessional/allpages. Accessed September 22, 2015.
15. Partsch CJ, Sippell WG. Treatment of central precocious puberty. Best Pract Res Clin Endocrinol Metobol. 2002;16:165-189.
16. American College of Obstetricians and Gynecologists. ACOG practice bulletin. Alternatives to hysterectomy in the management of leiomyomas. Obstet Gynecol.2008;112(2 Pt 1):387-400.
17. American College of Obstetricians and Gynecologists (ACOG). Management of endometriosis. Available at:

http://www.guideline.gov/summary/summary.aspx?doc_id=3961&nbr=3099&string=endometriosis. Accessed September 22, 2015.
18. DRUGDEX System [Internet database]. Greenwood Village, Colorado: Thomson Micromedex. Updated periodically. Accessed September 22, 2015.
19. Surrey ES, Voigt B, Fournet N, Judd HL. Prolonged gonadotropin-releasing hormone agonist treatment of symptomatic endometriosis: the role of cyclic sodium etidronate and low dose norethindrone "add-back" therapy. Fertil Steril. 1995;63:747-755.
20. Lethaby A, Vollenhoven B, Sowter M. Pre-operative GnRH analogue therapy before hysterectomy or myomectomy for uterine fibroids. Cochrane Database Syst Rev. 2001;(2):CD000547.
21. Supprelin LA Prescribing Information. Endo Pharmaceutical Solutions Inc., June 2013.
22. Eugster E, Clarke W, Kletter G, et al. Efficacy and safety of histrelin subdermal implant in children with central precocious puberty: a multicenter trial. J Clin Endocrinol Metab. 2007;92:1697-704.
23. Pain management of endometriosis: conservative approach is first-line treatment. Press release available at: http://www.acog.org/About-ACOG/News-Room/News-Releases/2010/Pain-Management-of-Endometriosis. Accessed September 24, 2015.
24. Levine GN, D'amio AV, Berger P, Clark PE, et al. Androgen-deprivation therapy in prostate cancer and cardiovascular risk: A science advisory from the American Heart Association, American Cancer Society, and American Urological Association, endorsed by the American Society of Radiation Oncology. CA Cancer J Clin. 2010;60(3):194-201. Epub 2010 Feb 2.
25. Lupron Depot (22.5 mg, 30 mg, 45 mg) Prescribing Information. AbbVie Inc., June 2014.
26. Eligard Prescribing Information. Tolmar Pharmaceuticals Inc., May 2015.
27. Trelstar Prescribing Information. Actavis Pharma, Inc., July 2014.
28. Practice bulletin no. 114: management of endometriosis. Obstet Gynecol. 2010 Jul;116(1):223-36.
29. Per clinical consult with reproductive endocrinologist, April 10, 2013.
30. MCG Care Guidelines. Ambulatory Care 17th Edition. Gonadotropin-releasing Hormone (GnRH) Agonists. Available at http://careweb.careguidelines.com/ed17/index.html. Accessed on April 5, 2013.
31. Lupaneta Pack Prescribing Information. AbbVie Inc., June 2015.
32. National Comprehensive Cancer Network Drugs and Biologics Compendium (NCCN Compendium). Available at: http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed September 29, 2015.
33. Lupron Depot-Ped Prescribing Information. AbbVie Inc., June 2013.

Prior Authorization Guideline

GL-17298 Growth Hormones

Formulary OptumRx SP

Formulary Note

Approval Date 4/3/2013

Revision Date 5/18/2016

Technician Note :

P&T Approval Date: 3/17/2000; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Genotropin, Humatrope, Norditropin, Nutropin/Nutropin AQ/Nutropin AQ NuSpin, Omnitrope, Saizen, and Zomacton **<u>Indications</u>** **Pediatric Growth Hormone Deficiency** Indicated for the long-term treatment of pediatric patients who have growth failure due to inadequate secretion of normal endogenous growth hormone.
Drug Name: Genotropin and Omnitrope

Indications

Prader-Willi Syndrome (PWS)

Indicated for the treatment of pediatric patients who have growth failure due to Prader-Willi Syndrome (PWS). The diagnosis of PWS should be confirmed by appropriate genetic testing.

Small for Gestational Age (SGA)

Indicated for the treatment of growth failure in children born small for gestational age (SGA) who fail to manifest catch-up growth by age 2.

Drug Name: Norditropin and Humatrope

Indications

Small for Gestational Age (SGA)

Indicated for the treatment of children with short stature born small for gestational age (SGA) with no catch-up growth by age 2-4 years.

Drug Name: Genotropin, Humatrope, Norditropin, Nutropin/Nutropin AQ/Nutropin AQ NuSpin, and Omnitrope

Indications

Turner Syndrome

Indicated for the treatment of short stature associated with Turner syndrome.

Drug Name: Humatrope

Indications

SHOX Deficiency

Indicated for the treatment of short stature or growth failure in children with short stature homeobox-containing gene (SHOX) deficiency.

Drug Name: Nutropin/Nutropin AQ/Nutropin AQ NuSpin

Indications

Chronic Renal Insufficiency

Indicated for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation. Therapy should be used in conjunction with optimal management of chronic renal insufficiency.

Drug Name: Genotropin, Humatrope, Nutropin/Nutropin AQ/Nutropin AQ NuSpin, and Omnitrope

Indications

Idiopathic Short Stature

Indicated for the long-term treatment of idiopathic short stature, also called non-growth hormone-deficient short stature, defined by height SDS less than or equal to -2.25, and associated with growth rates unlikely to permit attainment of adult height in the normal range, in pediatric patients whose epiphyses are not closed and for whom diagnostic evaluation excludes other causes associated with short stature that should be observed or treated by other means. **Please Note: The request for growth hormone (GH) injections to treat idiopathic short stature (ISS) is not authorized. There is no consensus in current peer-reviewed medical literature regarding the indications, efficacy, safety, or long-term consequences of GH therapy in children with ISS who are otherwise healthy.

Drug Name: Norditropin

Indications

Noonan Syndrome

Indicated for the treatment of pediatric patients with short stature associated with Noonan Syndrome.

Drug Name: Genotropin, Humatrope, Norditropin, Nutropin/Nutropin AQ/Nutropin AQ NuSpin, Omnitrope, and Saizen

Indications

Adult Growth Hormone Deficiency

Indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency who meet either of the following two criteria: Adult-Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation, or trauma; Childhood-Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes. In general, confirmation of the diagnosis of adult growth hormone deficiency in both groups usually requires an appropriate growth hormone stimulation test. However, confirmatory growth hormone stimulation testing may not be required in patients with congenital/genetic growth hormone deficiency or multiple pituitary hormone deficiencies due to organic disease.

Drug Name: Serostim

Indications

AIDS Wasting or Cachexia

Indicated for the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance. Concomitant antiretroviral therapy is necessary.

Drug Name: Zorbtive

Indications

Short Bowel Syndrome

Indicated for the treatment of short Bowel Syndrome in patients receiving specialized nutritional support. Zorbtive therapy should be used in conjunction with optimal management of Short Bowel Syndrome. Specialized nutritional support may consist of a high carbohydrate, low-fat diet, adjusted for individual patient requirements and preferences. Nutritional supplements may be added according to the discretion of the treating physician. Optimal management of Short Bowel Syndrome may include dietary adjustments, enteral feedings, parenteral nutrition, fluid and micronutrient supplements, as needed.

2 . Criteria

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Pediatric Growth Hormone Deficiency (GHD)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 One of the following: [12]

1.1.1 Both of the following:

- Infant is < 4 months of age
- Infant has growth deficiency

OR

1.1.2 History of neonatal hypoglycemia associated with pituitary disease

OR

1.1.3 Diagnosis of panhypopituitarism

OR

1.2 All of the following:

1.2.1 Diagnosis of pediatric GH deficiency as confirmed by one of the following: [10, 11, 12]

1.2.1.1 Height is documented by one of the following (utilizing age and gender growth charts related to height):

- Height is > 2.0 standard deviations [SD] below midparental height
- Height is > 2.25 SD below population mean (below the 1.2 percentile for age and gender)

OR

1.2.1.2 Growth velocity is > 2 SD below mean for age and gender

OR

1.2.1.3 Delayed skeletal maturation of > 2 SD below mean for age and gender (e.g., delayed > 2 years compared with chronological age)

AND

1.2.2 Documentation of one of the following: [28]

1.2.2.1 Both of the following:

- Patient is male
- Bone age < 16 years

OR

1.2.2.2 Both of the following:

- Patient is female
- Bone age < 14 years

AND

1.2.3 One of the following:

1.2.3.1 Both of the following: [10, 11, 12]

1.2.3.1.1 Patient has undergone two of the following provocative GH stimulation tests:

- Arginine

- Clonidine
- Glucagon
- Insulin
- Levodopa
- Growth hormone releasing hormone

AND

1.2.3.1.2 Both GH response values are < 10 mcg/L

OR

1.2.3.2 Both of the following: [11]

1.2.3.2.1 Patient is < 1 year of age

AND

1.2.3.2.2 One of the following is below the age and gender adjusted normal range as provided by the physician's lab: [A, 13, 14]

- Insulin-like Growth Factor 1 (IGF-1/Somatomedin-C)
- Insulin Growth Factor Binding Protein-3 (IGFBP-3)

AND

1.2.4 Pediatric GH dosing will be utilized as defined by the prescribing information

AND

2 Prescribed by or in consultation with an endocrinologist

Notes	Includes children who have undergone brain radiation. If patient is a Transition Phase Adolescent or Adult who had childhood onset GH deficiency, utilize criteria for Transition Phase Adolescent or Adult GH Deficiency. NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton

Diagnosis	Pediatric Growth Hormone Deficiency (GHD)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 One of the following: [12]

1.1.1 Both of the following:

- Infant is < 4 months of age
- Infant has growth deficiency

OR

1.1.2 History of neonatal hypoglycemia associated with pituitary disease

OR

1.1.3 Diagnosis of panhypopituitarism

OR

1.2 All of the following:

1.2.1 Diagnosis of pediatric GH deficiency as confirmed by one of the following: [10, 11, 12]

1.2.1.1 Height is documented by one of the following (utilizing age and gender growth charts related to height):

- Height is > 2.0 standard deviations [SD] below midparental height
- Height is > 2.25 SD below population mean (below the 1.2 percentile for age and gender)

OR

1.2.1.2 Growth velocity is > 2 SD below mean for age and gender

OR

1.2.1.3 Delayed skeletal maturation of > 2 SD below mean for age and gender (e.g., delayed > 2 years compared with chronological age)

AND

1.2.2 Documentation of one of the following: [28]

1.2.2.1 Both of the following:

- Patient is male
- Bone age < 16 years

OR

1.2.2.2 Both of the following:

- Patient is female
- Bone age < 14 years

AND

1.2.3 One of the following:

1.2.3.1 Both of the following: [10, 11, 12]

1.2.3.1.1 Patient has undergone two of the following provocative GH stimulation tests:

- Arginine

- Clonidine
- Glucagon
- Insulin
- Levodopa
- Growth hormone releasing hormone

AND

1.2.3.1.2 Both GH response values are < 10 mcg/L

OR

1.2.3.2 Both of the following: [11]

1.2.3.2.1 Patient is < 1 year of age

AND

1.2.3.2.2 One of the following is below the age and gender adjusted normal range as provided by the physician's lab: [A, 13, 14]

- Insulin-like Growth Factor 1 (IGF-1/Somatomedin-C)
- Insulin Growth Factor Binding Protein-3 (IGFBP-3)

AND

1.2.4 Pediatric GH dosing will be utilized as defined by the prescribing information

AND

2 Prescribed by or in consultation with an endocrinologist

AND

3 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Notes	Includes children who have undergone brain radiation. If patient is a Transition Phase Adolescent or Adult who had childhood onset GH deficiency, utilize criteria for Transition Phase Adolescent or Adult GH Deficiency. NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Pediatric Growth Hormone Deficiency (GHD)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with an endocrinologist

Notes	Includes children who have undergone brain radiation. If patient is a Transition Phase Adolescent or Adult who had childhood onset GH deficiency, utilize criteria for Transition Phase Adolescent or Adult GH Deficiency.

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton

Diagnosis	Pediatric Growth Hormone Deficiency (GHD)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Notes	Includes children who have undergone brain radiation. If patient is a Transition Phase Adolescent or Adult who had childhood onset GH deficiency, utilize criteria for Transition Phase Adolescent or Adult GH Deficiency.

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Prader-Willi Syndrome [off-label]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Prader-Willi Syndrome [10, 11]

AND

2 Prescribed by or in consultation with an endocrinologist

Product Name: Genotropin, Humatrope [off-label], Omnitrope, or Zomacton [off-label]

Diagnosis	Prader-Willi Syndrome
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Prader-Willi Syndrome [10, 11]

AND

2 Prescribed by or in consultation with an endocrinologist

AND

3 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Prader-Willi Syndrome [off-label]

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Evidence of positive response to therapy (e.g., increase in total lean body mass, decrease in fat mass)

OR

1.2 Both of the following:

1.2.1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

1.2.2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

2 Prescribed by or in consultation with an endocrinologist

Product Name: Genotropin, Humatrope [off-label], Omnitrope, or Zomacton [off-label]

Diagnosis	Prader-Willi Syndrome
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Evidence of positive response to therapy (e.g., increase in total lean body mass, decrease in fat mass)

OR

1.2 Both of the following:

1.2.1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

1.2.2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

2 Prescribed by or in consultation with an endocrinologist

AND

3 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Growth Failure in Children Small for Gestational Age (SGA) [off-label]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of SGA based on demonstration of catch up growth failure in the first 24 months of life using a 0-36 month growth chart as confirmed by the following criterion: [10]

1.1 One of the following is below the 3rd percentile for gestational age (more than 2 SD below population mean):

- Birth weight
- Birth length

AND

2 Height remains less than or equal to 3rd percentile (more than 2 SD below population

mean) [10]

AND

3 Prescribed by or in consultation with an endocrinologist

Notes	NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton [off-label]

Diagnosis	Growth Failure in Children Small for Gestational Age (SGA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of SGA based on demonstration of catch up growth failure in the first 24 months of life using a 0-36 month growth chart as confirmed by the following criterion: [10]

1.1 One of the following is below the 3rd percentile for gestational age (more than 2 SD below the population mean):

- Birth weight
- Birth length

AND

2 Height remains less than or equal to 3rd percentile (more than 2 SD below population mean) [10]

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Notes	NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Growth Failure in Children Small for Gestational Age (SGA) [off-label]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained

- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with an endocrinologist

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton [off-label]

Diagnosis	Growth Failure in Children Small for Gestational Age (SGA)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Turner Syndrome [off-label for Saizen] or Noonan Syndrome [off-label except for Norditropin]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pediatric growth failure associated with one of the following: [10, 28]

1.1 Both of the following:

1.1.1 Turner Syndrome (Gonadal Dysgenesis)

AND

1.1.2 Documentation of both of the following:

- Patient is female
- Bone age < 14 years

OR

1.2 Both of the following:

1.2.1 Noonan Syndrome

AND

1.2.2 Documentation of one of the following:

1.2.2.1 Both of the following:

- Patient is male
- Bone age < 16 years

OR

1.2.2.2 Both of the following:

- Patient is female
- Bone age < 14 years

AND

2 Height is below the 5th percentile on growth charts for age and gender [10]

AND

3 Prescribed by or in consultation with an endocrinologist

Notes	NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton [off-label]

Diagnosis	Turner Syndrome [off-label for Zomacton] or Noonan Syndrome [off-label]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pediatric growth failure associated with one of the following: [10, 28]

1.1 Both of the following:

1.1.1 Turner Syndrome (Gonadal Dysgenesis)

AND

1.1.2 Documentation of both of the following:

- Patient is female
- Bone age < 14 years

OR

1.2 Both of the following:

1.2.1 Noonan Syndrome

AND

1.2.2 Documentation of one of the following:

1.2.2.1 Both of the following:

- Patient is male
- Bone age < 16 years

OR

1.2.2.2 Both of the following:

- Patient is female
- Bone age < 14 years

AND

2 Height is below the 5th percentile on growth charts for age and gender [10]

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Notes	NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen [off-label]

Diagnosis	Turner Syndrome [off-label for Saizen] or Noonan Syndrome [off-label except for Norditropin]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with an endocrinologist

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton [off-label]

Diagnosis	Turner Syndrome [off-label for Zomacton] or Noonan Syndrome [off-label]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Short-Stature Homeobox (SHOX) Gene Deficiency [off-label]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pediatric growth failure with short stature homeobox (SHOX) gene deficiency as confirmed by genetic testing [2]

AND

2 Documentation of one of the following: [28]

2.1 Both of the following:

- Patient is male

- Bone age < 16 years

OR

2.2 Both of the following:

- Patient is female
- Bone age < 14 years

AND

3 Prescribed by or in consultation with an endocrinologist

Notes	NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.

Product Name: Genotropin [off-label], Humatrope, Omnitrope [off-label], or Zomacton [off-label]

Diagnosis	Short-Stature Homeobox (SHOX) Gene Deficiency
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pediatric growth failure with short stature homeobox (SHOX) gene deficiency as confirmed by genetic testing [2]

AND

2 Documentation of one of the following: [28]

2.1 Both of the following:

- Patient is male
- Bone age < 16 years

OR

2.2 Both of the following:

- Patient is female
- Bone age < 14 years

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Notes	NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Short-Stature Homeobox (SHOX) Gene Deficiency [off-label]
Approval Length	12 Month

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with an endocrinologist

Product Name: Genotropin [off-label], Humatrope, Omnitrope [off-label], or Zomacton [off-label]

Diagnosis	Short-Stature Homeobox (SHOX) Gene Deficiency
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen [off-label]

Diagnosis	Growth Failure associated with Chronic Renal Insufficiency

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pediatric growth failure associated with chronic renal insufficiency [10]

AND

2 Documentation of one of the following: [28]

2.1 Both of the following:

- Patient is male
- Bone age < 16 years

OR

2.2 Both of the following:

- Patient is female
- Bone age < 14 years

AND

3 Prescribed by or in consultation with one of the following:

- Endocrinologist
- Nephrologist

Notes	NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton

Diagnosis	Growth Failure associated with Chronic Renal Insufficiency [off-label]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pediatric growth failure associated with chronic renal insufficiency [10]

AND

2 Documentation of one of the following: [28]

2.1 Both of the following:

- Patient is male
- Bone age < 16 years

OR

2.2 Both of the following:

- Patient is female
- Bone age < 14 years

AND

3 Prescribed by or in consultation with one of the following:

- Endocrinologist
- Nephrologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Notes	NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen [off-label]

Diagnosis	Growth Failure associated with Chronic Renal Insufficiency
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with one of the following:

- Endocrinologist
- Nephrologist

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton

Diagnosis	Growth Failure associated with Chronic Renal Insufficiency [off-label]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Height increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [28]

- Previous height and date obtained
- Current height and date obtained

AND

2 Both of the following:

- Expected adult height not attained
- Documentation of expected adult height goal

AND

3 Prescribed by or in consultation with one of the following:

- Endocrinologist
- Nephrologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Adult Growth Hormone Deficiency
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization
Approval Criteria	

1 Diagnosis of adult GH deficiency as a result of one of the following: [10, 12, 27]

1.1 Clinical records supporting a diagnosis of childhood-onset GHD

OR

1.2 Both of the following:

1.2.1 Adult-onset GHD

AND

1.2.2 Clinical records documenting that hormone deficiency is a result of hypothalamic-pituitary disease from organic or known causes (e.g., damage from surgery, cranial irradiation, head trauma, or subarachnoid hemorrhage)

AND

2 One of the following: [10, 12, 27]

2.1 Both of the following:

2.1.1 Patient has undergone one of the following GH stimulation tests to confirm adult GH deficiency:

- Insulin tolerance test (ITT)
- Arginine & GHRH (GHRH+ARG)
- Glucagon
- Arginine (ARG)

AND

2.1.2 One of the following peak GH values:

- ITT less than or equal to 5 µg/L
- GHRH + ARG (less than or equal to 11 µg/L if body mass index [BMI] < 25 kg/m^2; less than or equal to 8 µg/L if BMI greater than or equal to 25 and < 30 kg/m^2; less than or equal to 4 µg/L if BMI greater than or equal to 30 kg/m^2)
- Glucagon less than or equal to 3 µg/L
- ARG less than or equal to 0.4 µg/L

OR

2.2 Both of the following:

2.2.1 Documented deficiency of three of the following anterior pituitary hormones:

- Prolactin
- Adrenocorticotropic hormone (ACTH)
- Thyroid stimulating hormone (TSH)
- Follicle-stimulating hormone/luteinizing hormone (FSH/LH)

AND

2.2.2 IGF-1/Somatomedin-C level is below the age and gender adjusted normal range as provided by the physician's lab

AND

3 One of the following:

3.1 Diagnosis of panhypopituitarism

OR

3.2 Both of the following:

3.2.1 Other diagnosis

AND

3.2.2 Both of the following:

- Not used in combination with aromatase inhibitors (e.g., Arimidex [anastrazole], Femara [letrazole])
- Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate], Depo-Testosterone [testosterone cypionate])

AND

4 Adult GH dosing will be utilized as defined by the prescribing information

AND

5 Prescribed by or in consultation with an endocrinologist

Notes	Use the following criteria for child- and adult-onset with pituitary disease; use Isolated GHD in Adult criteria for patients without pituitary disease.

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton [off-label]

Diagnosis	Adult Growth Hormone Deficiency
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of adult GH deficiency as a result of one of the following: [10, 12, 27]

1.1 Clinical records supporting a diagnosis of childhood-onset GHD

OR

1.2 Both of the following:

1.2.1 Adult-onset GHD

AND

1.2.2 Clinical records documenting that hormone deficiency is a result of hypothalamic-pituitary disease from organic or known causes (e.g., damage from surgery, cranial irradiation, head trauma, or subarachnoid hemorrhage)

AND

2 One of the following: [10, 12, 27]

2.1 Both of the following:

2.1.1 Patient has undergone one of the following GH stimulation tests to confirm adult GH deficiency:

- Insulin tolerance test (ITT)
- Arginine & GHRH (GHRH+ARG)
- Glucagon
- Arginine (ARG)

AND

2.1.2 One of the following peak GH values:

- ITT less than or equal to 5 µg/L
- GHRH + ARG (less than or equal to 11 µg/L if body mass index [BMI] < 25 kg/m^2; less than or equal to 8 µg/L if BMI greater than or equal to 25 and < 30 kg/m^2; less than or equal to 4 µg/L if BMI greater than or equal to 30 kg/m^2)
- Glucagon less than or equal to 3 µg/L

- ARG less than or equal to 0.4 µg/L

OR

2.2 Both of the following:

2.2.1 Documented deficiency of three of the following anterior pituitary hormones:

- Prolactin
- ACTH
- TSH
- FSH/LH

AND

2.2.2 IGF-1/Somatomedin-C level is below the age and gender adjusted normal range as provided by the physician's lab

AND

3 One of the following:

3.1 Diagnosis of panhypopituitarism

OR

3.2 Both of the following:

3.2.1 Other diagnosis

AND

3.2.2 Both of the following:

- Not used in combination with aromatase inhibitors (e.g., Arimidex [anastrazole], Femara [letrazole])
- Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate],

Depo-Testosterone [testosterone cypionate])

AND

4 Adult GH dosing will be utilized as defined by the prescribing information

AND

5 Prescribed by or in consultation with an endocrinologist

AND

6 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Notes	Use the following criteria for child- and adult-onset with pituitary disease; use Isolated GHD in Adult criteria for patients without pituitary disease.

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Adult Growth Hormone Deficiency
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Evidence of ongoing monitoring as demonstrated by documentation within the past 12 months of an IGF-1/Somatomedin C level [10, 12, 27]

AND

2 One of the following:

2.1 Diagnosis of panhypopituitarism

OR

2.2 Both of the following:

2.2.1 Other diagnosis

AND

2.2.2 Both of the following:

- Not used in combination with aromatase inhibitors (e.g., Arimidex [anastrazole], Femara [letrazole])
- Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate], Depo-Testosterone [testosterone cypionate])

AND

3 Continued use of adult GH dosing as defined by the prescribing information

AND

4 Prescribed by or in consultation with an endocrinologist

Notes	Use the following criteria for child- and adult-onset with pituitary disease; use Isolated GHD in Adult criteria for patients without pituitary disease.

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton [off-label]

Diagnosis	Adult Growth Hormone Deficiency
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Evidence of ongoing monitoring as demonstrated by documentation within the past 12 months of an IGF-1/Somatomedin C level [10, 12, 27]

AND

2 One of the following:

2.1 Diagnosis of panhypopituitarism

OR

2.2 Both of the following:

2.2.1 Other diagnosis

AND

2.2.2 Both of the following:

- Not used in combination with aromatase inhibitors (e.g., Arimidex [anastrazole], Femara [letrazole])
- Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate], Depo-Testosterone [testosterone cypionate])

AND

3 Continued use of adult GH dosing as defined by the prescribing information

AND

4 Prescribed by or in consultation with an endocrinologist

AND

5 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Notes	Use the following criteria for child- and adult-onset with pituitary disease; use Isolated GHD in Adult criteria for patients without pituitary disease.

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Transition Phase Adolescent Patients

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Adult GH dosing will be utilized as defined by the prescribing information (additional information may be found in the AACE 2009 treatment guideline) [27]

AND

2 One of the following: [27]

- Attained expected adult height
- Closed epiphyses on bone radiograph

AND

3 One of the following: [27]

3.1 Both of the following:

3.1.1 Documentation of high risk of GH deficiency due to GH deficiency in childhood from one of the following:

3.1.1.1 Embryopathic/congenital defects

OR

3.1.1.2 Genetic mutations

OR

3.1.1.3 Irreversible structural hypothalamic-pituitary disease

OR

3.1.1.4 Panhypopituitarism

OR

3.1.1.5 Deficiency of three of the following anterior pituitary hormones:

- ACTH
- TSH
- Prolactin
- FSH/LH

AND

3.1.2 One of the following:

3.1.2.1 IGF-1/Somatomedin-C level is below the age and gender adjusted normal range as provided by the physician's lab

OR

3.1.2.2 All of the following:

3.1.2.2.1 Patient does not have a low IGF-1/Somatomedin C level

AND

3.1.2.2.2 Discontinued GH therapy for at least 1 month

AND

3.1.2.2.3 Patient has undergone one of the following GH stimulation tests after discontinuation of therapy for at least 1 month:

- ITT
- GHRH+ARG
- ARG
- Glucagon

AND

3.1.2.2.4 One of the following peak GH values:

- ITT less than or equal to 5 µg/L
- GHRH + ARG (less than or equal to 11 µg/L if body mass index [BMI] < 25 kg/m^2; less than or equal to 8 µg/L if BMI greater than or equal to 25 and < 30 kg/m^2; less than or equal to 4 µg/L if BMI greater than or equal to 30 kg/m^2)
- Glucagon less than or equal to 3 µg/L
- ARG less than or equal to 0.4 µg/L

OR

3.2 All of the following:

3.2.1 At low risk of severe GH deficiency (e.g., due to isolated and/or idiopathic GH deficiency)

AND

3.2.2 Discontinued GH therapy for at least 1 month

AND

3.2.3 Patient has undergone one of the following GH stimulation tests after discontinuation of therapy for at least 1 month:

- ITT
- GHRH + ARG
- ARG
- Glucagon

AND

3.2.4 One of the following peak GH values:

- ITT less than or equal to 5 µg/L
- GHRH + ARG (less than or equal to 11 µg/L if body mass index [BMI] < 25 kg/m^2; less than or equal to 8 µg/L if BMI greater than or equal to 25 and < 30 kg/m^2; less than or equal to 4 µg/L if BMI greater than or equal to 30 kg/m^2)
- Glucagon less than or equal to 3 µg/L
- ARG less than or equal to 0.4 µg/L

AND

4 Prescribed by or in consultation with an endocrinologist

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton

Diagnosis	Transition Phase Adolescent Patients
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Adult GH dosing will be utilized as defined by the prescribing information (additional information may be found in the AACE 2009 treatment guideline) [27]

AND

2 One of the following: [27]

- Attained expected adult height
- Closed epiphyses on bone radiograph

AND

3 One of the following: [27]

3.1 Both of the following:

3.1.1 Documentation of high risk of GH deficiency due to GH deficiency in childhood from one of the following:

3.1.1.1 Embryopathic/congenital defects

OR

3.1.1.2 Genetic mutations

OR

3.1.1.3 Irreversible structural hypothalamic-pituitary disease

OR

3.1.1.4 Panhypopituitarism

OR

3.1.1.5 Deficiency of three of the following anterior pituitary hormones:

- ACTH
- TSH
- Prolactin
- FSH/LH

AND

3.1.2 One of the following:

3.1.2.1 IGF-1/Somatomedin-C level is below the age and gender adjusted normal range as provided by the physician's lab

OR

3.1.2.2 All of the following:

3.1.2.2.1 Patient does not have a low IGF-1/Somatomedin C level

AND

3.1.2.2.2 Discontinued GH therapy for at least 1 month

AND

3.1.2.2.3 Patient has undergone one of the following GH stimulation tests after discontinuation of therapy for at least 1 month:

- ITT
- GHRH + ARG
- ARG
- Glucagon

AND

3.1.2.2.4 One of the following peak GH values:

- ITT less than or equal to 5 µg/L
- GHRH + ARG (less than or equal to 11 µg/L if body mass index [BMI] < 25 kg/m^2; less than or equal to 8 µg/L if BMI greater than or equal to 25 and < 30 kg/m^2; less than or equal to 4 µg/L if BMI greater than or equal to 30 kg/m^2)
- Glucagon less than or equal to 3 µg/L
- ARG less than or equal to 0.4 µg/L

OR

3.2 All of the following:

3.2.1 At low risk of severe GH deficiency (e.g., due to isolated and/or idiopathic GH deficiency)

AND

3.2.2 Discontinued GH therapy for at least 1 month

AND

3.2.3 Patient has undergone one of the following GH stimulation tests after discontinuation of therapy for at least 1 month:

- ITT
- GHRH + ARG
- ARG
- Glucagon

AND

3.2.4 One of the following peak GH values:

- ITT less than or equal to 5 µg/L
- GHRH + ARG (less than or equal to 11 µg/L if body mass index [BMI] < 25 kg/m^2; less than or equal to 8 µg/L if BMI greater than or equal to 25 and < 30 kg/m^2; less than or equal to 4 µg/L if BMI greater than or equal to 30 kg/m^2)
- Glucagon less than or equal to 3 µg/L
- ARG less than or equal to 0.4 µg/L

AND

4 Prescribed by or in consultation with an endocrinologist

AND

5 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Transition Phase Adolescent Patients
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Evidence of positive response to therapy (e.g., increase in total lean body mass, exercise capacity or IGF-1 and IGFBP-3 levels)

AND

2 Continued use of adult GH dosing as defined by the prescribing information (additional information may be found in the AACE 2009 treatment guideline)

AND

3 Prescribed by or in consultation with an endocrinologist

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton

Diagnosis	Transition Phase Adolescent Patients
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Evidence of positive response to therapy (e.g., increase in total lean body mass, exercise capacity or IGF-1 and IGFBP-3 levels)

AND

2 Continued use of adult GH dosing as defined by the prescribing information (additional information may be found in the AACE 2009 treatment guideline)

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Product Name: Serostim

Diagnosis	Human Immunodeficiency Virus (HIV)-Associated Cachexia
Approval Length	3 Month
Therapy Stage	Initial Authorization

Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of HIV-associated wasting syndrome or cachexia [7, 15, 29]

AND

2 One of the following: [7, 15, 29]

2.1 Unintentional weight loss of > 10% over the last 12 months

OR

2.2 Unintentional weight loss of > 7.5% over the last 6 months

OR

2.3 Loss of 5% body cell mass (BCM) within 6 months

OR

2.4 Body mass index (BMI) < 20 kg/m^2

OR

2.5 All of the following

- Patient is male
- BCM < 35% of total body weight
- BMI < 27 kg/m^2

OR

2.6 All of the following

- Patient is female
- BCM < 23% of total body weight
- BMI < 27 kg/m^2

AND

3 Nutritional evaluation since onset of wasting first occurred [7, 15, 29]

AND

4 Patient has not had weight loss as a result of other underlying treatable conditions (e.g., depression, mycobacterium avium complex, chronic infectious diarrhea, or malignancy with the exception of Kaposi's sarcoma limited to skin or mucous membranes) [7, 15, 29]

AND

5 Anti-retroviral therapy has been optimized to decrease the viral load [7, 15, 29]

Product Name: Serostim

Diagnosis	Human Immunodeficiency Virus (HIV)-Associated Cachexia
Approval Length	6 months [D]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Evidence of positive response to therapy (i.e., greater than or equal to 2% increase in body weight and/or BCM) [22, 23]

AND

2 One of the following targets or goals has not been achieved: [22, 23]

- Weight
- BCM
- BMI

Product Name: Zorbtive

Diagnosis	Short Bowel Syndrome
Approval Length	4 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Short Bowel Syndrome [9, 16]

AND

2 Patient is currently receiving specialized nutritional support (e.g., intravenous parenteral nutrition, fluid, and micronutrient supplements) [9, 16]

AND

3 Patient has not previously received 4 weeks of treatment with Zorbtive [9, 16]	
Notes	NOTE: Treatment with Zorbtive will not be authorized beyond 4 weeks. Administration for more than 4 weeks has not been adequately studied.

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Isolated Growth Hormone Deficiency in Adults
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documented deficiency of GH defined by a failure to produce a peak serum GH > 5 mcg/L after provocative pharmacologic stimulation by two of the following tests: [27]

- Insulin
- L-arginine
- Glucagon

AND

2 Both of the following:

- Not used in combination with aromatase inhibitors (e.g., Arimidex [anastrazole], Femara [letrazole])
- Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate], Depo-Testosterone [testosterone cypionate])

AND

3 Prescribed by or in consultation with an endocrinologist

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton [off-label]

Diagnosis	Isolated Growth Hormone Deficiency in Adults
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documented deficiency of GH defined by a failure to produce a peak serum GH > 5 mcg/L after provocative pharmacologic stimulation by two of the following tests: [27]

- Insulin
- L-arginine
- Glucagon

AND

2 Both of the following:

- Not used in combination with aromatase inhibitors (e.g., Arimidex [anastrazole], Femara [letrazole])
- Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate], Depo-Testosterone [testosterone cypionate])

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

Diagnosis	Isolated Growth Hormone Deficiency in Adults
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Evidence of ongoing monitoring as demonstrated by documentation within the past 12 months of an IGF-1/Somatomedin C level [10, 12, 27]

AND

2 Both of the following:

- Not used in combination with aromatase inhibitors (e.g., Arimidex [anastrazole], Femara [letrazole])
- Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate], Depo-Testosterone [testosterone cypionate])

AND

3 Prescribed by or in consultation with an endocrinologist

Product Name: Genotropin, Humatrope, Omnitrope, or Zomacton [off-label]

Diagnosis	Isolated Growth Hormone Deficiency in Adults
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Evidence of ongoing monitoring as demonstrated by documentation within the past 12 months of an IGF-1/Somatomedin C level [10, 12, 27]

AND

2 Both of the following:

- Not used in combination with aromatase inhibitors (e.g., Arimidex [anastrazole], Femara [letrazole])
- Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate], Depo-Testosterone [testosterone cypionate])

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

3 . Endnotes

A. Several recent review articles in the literature have suggested that GH stimulation tests should no longer be used to diagnose GHD.[13,14] The authors argue that GH stimulation test may have side effects, lack precision, accuracy, and do not predict response to GH therapy. It has been suggested that newer diagnostic procedures such as serum IGF-1, IGFBP-3 concentrations, genetic testing and neuroimaging could provide an alternative approach to the diagnosis of GHD in childhood.
B. Overall, there are no observable differences in the results obtained among the different preparations as long as the regimen follows currently approved daily injections. Many of the products are available in a variety of injection devices that are meant to make administration more appealing and easier. Currently, there is no evidence that clinical outcome differs among the various injection systems, although there may be patient and parent preferences for some of these devices. [11]
C. Even a 5% weight loss in persons with HIV infection indicates a poor prognosis. [2]
D. Patients with HIV-associated wasting may begin an initial 12-week course of therapy with Serostim, 6 mg/day s.c. The clinician should monitor treatment responses by obtaining serial body weights and BCM measurements by BIA. A positive response to therapy probably should be considered as a 2% increase in body weight and/or BCM. Maintenance therapy may continue on a monthly basis as long as wasting is still evident. Once BCM has normalized, therapy can be stopped, with the patient being observed for an 8-week period. Over these 8 weeks, body weight, BCM, and any appearance of wasting symptoms can be monitored. If wasting reappears, therapy can be restarted. [22]

4 . References

1. Genotropin Prescribing Information. Pfizer, September 2014.
2. Humatrope Prescribing Information. Lilly, April 2015.
3. Norditropin Prescribing Information. NovoNordisk, January 2015.
4. Nutropin, Prescribing Information.Genentech, April 2012.
5. Omnitrope Prescribing Information. Sandoz Inc., October 2014.
6. Saizen Prescribing Information. Serono, June 2014.
7. Serostim Prescribing Information. Serono, June 2014.
8. Zomacton Prescribing Information. Ferring Pharmaceuticals Inc., March 2015.
9. Zorbtive Prescribing Information. Serono, January 2012.
10. Gharib H, Cook DM et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for GH use in adults and children-2003 update. Endocr Pract. 2003;9(1):64-76.
11. Wilson TA, Rose SA, Cohen P, et al. Update on guidelines for the use of GH in children: The Lawson Wilkins pediatric endocrinology society drug and therapeutics committee. J Pediatrics 2003 (Oct): 415-21
12. GH Research society. Consensus guidelines for the diagnosis and treatment of GH deficiency in childhood and adolescence: Summary statement. J Clin Endocinol Metab. 2000; 85: 3990-93.
13. Badaru A, Wilson DM. Alternatives to growth hormone stimulation testing in children. Trends Endocrinol Metab 2004;15(6):252-8.
14. Gandrud LM, Wilson DM. Is growth hormone stimulation testing in children still appropriate? Growth Horm IGF Res 2004;14(3):185-94.
15. Corcoran C, Grinspoon S. Treatment for wasting in patients with the acquired immunodeficiency syndrome. N Engl J Med 1999; 340 (22):1740-50.
16. Byrne TA, Wilmore DW, Iyer K et al. Growth hormone, glutamine, and an optimal diet reduces parenteral nutrition in patients with short bowel syndrome. Ann Surg 2005;242:655-61.
17. Wilton P, Gunnarson R. Clinical experience with Genotropin in growth hormone deficient children. Acta Paediatr Scand Suppl. 1988;343:95-101.
18. Macgillivray MH, Baptista J, Johanson A. Outcome of a four-year randomized study of daily versus three times weekly somatropin treatment in prepubertal naive growth hormone-deficient children. Genentech Study Group. J Clin Endocrinol Metab. 1996;81(5):1806-9.
19. Pavia C. Spanish multicenter clinical trial of recombinant growth hormone produced in mammalian cells for treatment of growth failure due to idiopathic growth hormone deficiency. Spanish Multicenter Study Group. Horm Res. 1992;37 Suppl 2:22-7.
20. Fine RN, Kohaut EC, Brown D, et al. Growth after recombinant human growth hormone treatment in children with chronic renal failure: report of a multicenter randomized double-blind placebo-controlled study. Genentech Cooperative Study Group. Pediatr. 1994 Mar;124(3):374-82.
21. Job JC, Landier F. Three-year results of treatment with growth hormone, alone or associated with oxandrolone, in girls with Turner syndrome. The Kabi Collaborative Study Group. Horm Res. 1991;35(6):229-33.
22. Polsky B, Kotler D, Steinhart C. HIV-associated wasting in the HAART era: guidelines for assessment, diagnosis, and treatment. AIDS Patient Care STDS. 2001;15:411-23.
23. Polsky B, Kotler D, Steinhart C. Treatment guidelines for HIV-associated wasting. HIV Clin Trials. 2004;5:50-61.
24. Nemechek P, Polsky B, Gottlieb M. Treatment guidelines for HIV-associated wasting. Mayo Clin Proc. 2000;75:386-394.

25. Jacobs, D. Laboratory Test Handbook: Concise With Disease Index, 3rd Edition. Lexi-Comp, 2004.
26. Nutropin AQ/Nutropin AQ NuSpin Prescribing Information. Genentech, June 2014.
27. Cook DM, Yuen KC. et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in growth hormone-deficient adults and transition patients -2009 update. Endocr Pract. 2009;15(suppl 2):1-29. Available at: http://www.aace.com/pub/pdf/guidelines/GrowthHormoneGuidelines.pdf. Accessed January 21, 2014.
28. Mauras N, Attie KM, Reiter EO, Saenger P, Baptista J. High dose recombinant human growth hormone (GH) treatment of GH-deficient patients in puberty increases near-final height: a randomized, multicenter trial. Genentech, Inc., Cooperative Study Group. J Clin Endocrinol Metab. 2000;85(10):3653-60.
29. HIV Clinical Resource. General Nutrition, weight loss and wasting syndrome. Available at http://www.hivguidelines.org/clinical-guidelines/adults/general-nutrition-weight-loss-and-wasting-syndrome/. Accessed July 11, 2012.

Prior Authorization Guideline

GL-17105 H.P. Acthar Gel (repository corticotropin)

Formulary OptumRx SP

Formulary Note

Approval Date 4/10/2013

Revision Date 4/22/2016

Technician Note :

P&T Approval Date: 5/19/2009; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: H.P. Acthar Gel (repository corticotropin injection)

Indications

Infantile spasms

Indicated as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age.

Exacerbations of Multiple Sclerosis

Indicated for the treatment of acute exacerbations of multiple sclerosis in adults. Controlled

clinical trials have shown H.P. Acthar Gel to be effective in speeding the resolution of acute exacerbations of multiple sclerosis. However, there is no evidence that it affects the ultimate outcome or natural history of the disease.

Rheumatic Disorders

As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: Psoriatic arthritis, Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy), Ankylosing spondylitis.

Collagen Diseases

During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis).

Dermatologic Diseases

Severe erythema multiforme, Stevens-Johnson syndrome.

Allergic States

Serum sickness.

Ophthalmic Diseases

Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis; optic neuritis; chorioretinitis; anterior segment inflammation.

Respiratory Diseases

Symptomatic sarcoidosis

Edematous State

To induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus.

Off Label Uses

Opsoclonus-Myoclonus Syndrome (OMS, Kinsbourne Syndrome) [2-9]

Has been used for short-term treatment of opsoclonus-myoclonus syndrome.

2 . Criteria

Product Name: H.P. Acthar Gel

Diagnosis	Infantile Spasms (West Syndrome)
Approval Length	4 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of infantile spasms (West Syndrome)

AND

2 Prescribed by or in consultation with a neurologist

AND

3 Patient is less than 2 years of age

Product Name: H.P. Acthar Gel

Diagnosis	Multiple Sclerosis
Approval Length	3 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of acute exacerbation of multiple sclerosis

AND

2 Prescribed by or in consultation with a neurologist

AND

3 History of failure, contraindication, or intolerance to treatment with two corticosteroids (e.g., prednisone, methylprednisolone)

Product Name: H.P. Acthar Gel

Diagnosis	Opsoclonus-Myoclonus Syndrome (off-label)
Approval Length	3 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of opsoclonus-myoclonus syndrome

AND

2 Prescribed by or in consultation with a neurologist

Product Name: H.P. Acthar Gel

Diagnosis	Other FDA-Approved Indications

Approval Length	3 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of one of the following:

1.1 Rheumatic disorders: As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in one of the following:

- Psoriatic arthritis
- Rheumatoid arthritis
- Juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy)
- Ankylosing spondylitis

OR

1.2 Collagen diseases: During an exacerbation or as maintenance therapy in selected cases of one of the following:

- Systemic lupus erythematosus
- Systemic dermatomyositis (polymyositis)

OR

1.3 One of the following dermatologic diseases:

- Severe erythema multiforme
- Stevens-Johnsons syndrome

OR

1.4 Allergic states:

- Serum sickness

OR

1.5 Ophthalmic diseases: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa, such as one of the following:

- Keratitis
- Iritis
- Iridocyclitis
- Diffuse posterior uveitis and choroiditis
- Optic neuritis
- Chorioretinitis
- Anterior segment inflammation

OR

1.6 Respiratory diseases:

- Symptomatic sarcoidosis

OR

1.7 Edematous state: To induce a diuresis or a remission of one of the following:

- Proteinuria in the nephrotic syndrome without uremia of the idiopathic type
- Proteinuria due to lupus erythematosus

AND

2 Prescribed by or in consultation with one of the following specialists:

- Rheumatic disorders: rheumatologist
- Collagen diseases: rheumatologist
- Dermatologic diseases: dermatologist
- Allergic states: allergist, immunologist
- Ophthalmic diseases: optometrist, ophthalmologist
- Respiratory diseases: pulmonologist
- Edematous state: nephrologist, rheumatologist

AND

3 Treatment of the requested condition is supported by two articles from major peer reviewed medical journals that present data from randomized controlled trials supporting the proposed use or uses as generally safe and effective unless there is clear and convincing contradictory evidence presented in a major peer-reviewed medical journal

AND

4 History of failure, contraindication, or intolerance to two corticosteroids (e.g., prednisone, methylprednisolone), each given for a trial of at least two weeks

3 . References

1. H.P. Acthar Gel Prescribing Information. Questcor Pharmaceuticals, Inc., January 2015.
2. Pranzatelli M. The immunopharmacology of the opsoclonus-myoclonus syndrome. Clin Neuropharm. 1996;19: 1-47.
3. Pranzatelli M. The neurobiology of the opsoclonus-myoclonus syndrome. Clin Neuropharm. 1992;15:186-228.
4. Pranzatelli M, Chun K, Moxness M, Tate E, Allison T. Cerebrospinal fluid ACTH and cortisol in opsoclonus-myoclonus: effect of therapy. Pediatr Neurol. 2005;33:121-126.
5. Pranzatelli M. The immunopharmacology of the opsoclonus-myoclonus syndrome. Clin Neuropharm. 1996;19:1-47.
6. Prazantelli M, Tate E, Travelstead A, Longee D. Immunologic and clinical response to rituximab in a child wth opsoclonus-myoclonus syndrome. Pediatrics. 2005;115:e115-e119.
7. Opsoclonus-Myoclonus U.S.A. and International. National Pediatric Myoclonus Center. Available at: www.omsusa.org. Accessed on October 21, 2015.
8. Xiong H, Peng J, Zhang YH, Bao XH, et al. Clinical diagnosis and therapy of opsoclonus-myoclonus syndrome. Zhonghua Er Ke Za Zhi. 2008 Aug;46(8):570-3.
9. National Institute of Neurological Disorders and Stroke (NINDS): Opsoclonus Myoclonus Information Page. Last updated February 14, 2007. Available at: www.ninds.nih.gov/disorders/opsoclonus_myoclonus/opsoclonus_myoclonus.htm. Accessed October 21, 2015.

Prior Authorization Guideline

GL-15354 Halaven (eribulin mesylate)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 3/23/2016

Technician Note :

P&T Approval Date: 4/5/2011; P&T Revision Date: 3/23/2016. **Effective 4-15-2016**

1 . Indications

Drug Name: Halaven (eribulin mesylate)

Indications

Metastatic Breast Cancer

Indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease. Prior therapy should have included an anthracycline and a taxane in either the adjuvant or metastatic setting.

Liposarcoma Indicated for the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

2 . Criteria

Product Name: Halaven

Diagnosis	Breast cancer
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of breast cancer

AND

2 Disease is one of the following: [1-3]

- Recurrent
- Metastatic

AND

3 Previous treatment with both of the following:

- One anthracycline [eg, doxorubicin, Ellence (epirubicin)]
- One taxane [eg, paclitaxel, Taxotere (docetaxel)]

AND

4 Prescribed by or in consulation with an oncologist

Product Name: Halaven

Diagnosis	Breast cancer
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Halaven therapy

Product Name: Halaven

Diagnosis	Liposarcoma
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of liposarcoma

AND

2 Disease is one of the following:

- Unresectable
- Metastatic

AND

3 Previous treatment with one anthracycline-containing regimen

AND

4 Prescribed by or in consulation with an oncologist

Product Name: Halaven

Diagnosis	Liposarcoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Halaven therapy

3 . References

1. Halaven Prescribing Information. Eisai Inc., January 2016.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Breast Cancer v.1.2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed March 8, 2016.
3. National Comprehensive Cancer Network. Drugs & Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=367. Accessed March 8, 2016.
4. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Soft Tissue Sarcoma v.2.2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed March 8, 2016.

Prior Authorization Guideline

GL-17345 Herceptin (trastuzumab)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/18/2016

Technician Note :

P&T Approval Date: 9/8/2000; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Herceptin (trastuzumab)

Indications

Adjuvant Breast Cancer

Indicated for adjuvant treatment of HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer • as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel • with docetaxel and carboplatin • as a single agent following multi-modality anthracycline based therapy.

Metastatic breast cancer

Indicated: • In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer • As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease.

Metastatic Gastric Cancer

Indicated in combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2 overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, who have not received prior treatment for metastatic disease.

2 . Criteria

Product Name: Herceptin

Diagnosis	Adjuvant or Neoadjuvant Breast Cancer
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of HER2-overexpressing of breast cancer [A]

AND

2 One of the following treatment regimens:

- Adjuvant treatment
- Used in combination with Perjeta (pertuzumab)

AND

3 Baseline cardiac assessment including history, physical examination, and one or more of the following: [1,C]

- electrocardiogram (EKG)
- echocardiogram
- multiple gated acquisition angiographies (MUGA) scan

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Herceptin

Diagnosis	Metastatic Breast Cancer
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of HER2-overexpressing of breast cancer [A]

AND

2 Disease is metastatic

AND

3 One of the following treatment regimens:

- Used in combination with a taxane
- Used as a single agent in a patient who has received one or more chemotherapy regimens for metastatic disease
- Used in combination with Perjeta (pertuzumab)

AND

4 Baseline cardiac assessment including history, physical examination, and one or more of the following: [1, C]

- electrocardiogram (EKG)
- echocardiogram
- multiple gated acquisition angiographies (MUGA) scan

AND

5 Prescribed by or in consultation with an oncologist

Product Name: Herceptin

Diagnosis	Metastatic Breast Cancer
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Herceptin therapy

Product Name: Herceptin

Diagnosis	Metastatic Gastric Cancer
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of HER2-overexpressing gastric or gastroesophageal junction adenocarcinoma (locally advanced, recurrent, or metastatic) [1, A, B]

AND

2 Used in combination with one of the following treatment regimens: [1, 13]

- Adrucil (5-fluorouracil)
- Platinol (cisplatin) and Xeloda (capecitabine)

AND

3 Baseline cardiac assessment including history, physical examination, and one or more of the following: [1, C]

- electrocardiogram (EKG)
- echocardiogram

- multiple gated acquisition angiographies (MUGA) scan

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Herceptin

Diagnosis	Metastatic Gastric Cancer
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Herceptin therapy

3 . Endnotes

A. Detection of HER2 protein overexpression is necessary for selection of patients appropriate for Herceptin therapy because these are the only patients studied and for whom benefit has been shown. Due to differences in tumor histopathology, use FDA-approved tests for the specific tumor type (breast or gastric/gastroesophageal adenocarcinoma) to assess HER2 protein overexpression and HER2 gene amplification. Tests should be performed by laboratories with demonstrated proficiency in the specific technology being utilized. Improper assay performance, including use of suboptimally

fixed tissue, failure to utilize specified reagents, deviation from specific assay instructions, and failure to include appropriate controls for assay validation, can lead to unreliable results. Several FDA-approved commercial assays are available to aid in the selection of breast cancer and metastatic gastric cancer patients for Herceptin therapy. Users should refer to the package inserts of specific assay kits for information on the Intended Use, and the validation and performance of each assay. Limitations in assay precision make it inadvisable to rely on a single method to rule out potential Herceptin benefit. Assessment of HER2 protein overexpression and HER2 gene amplification in metastatic gastric cancer should be performed using FDA-approved tests specifically for gastric cancers due to differences in gastric vs. breast histopathology, including incomplete membrane staining and more frequent heterogeneous expression of HER2 seen in gastric cancers. Study 7 demonstrated that gene amplification and protein overexpression were not as well correlated as with breast cancer. Treatment outcomes for metastatic gastric cancer (Study 7) are based on HER2 gene amplification (FISH) and HER 2 protein overexpression (IHC) test results. [1]

B. Herceptin is indicated for the treatment of HER-2 overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma. A pivotal study included patients previously untreated for metastatic gastric or gastroeophageal junction adenocarcinoma. [1]
C. Herceptin can cause left ventricular cardiac dysfunction, arrhythmias, hypertension, disabling cardiac failure, cardiomyopathy, and cardiac death. Withhold Herceptin for greater than or equal to 16% absolute decrease in LVEF from pre-treatment values or an LVEF value below institutional limits of normal and ? 10% absolute decrease in LVEF from pretreatment values. The safety of continuation or resumption of Herceptin in patients with Herceptin-induced left ventricular cardiac dysfunction has not been studied. Conduct thorough cardiac assessment, including history, physical examination, and determination of LVEF by echocardiogram or MUGA scan. The following schedule is recommended: Baseline LVEF measurement immediately prior to initiation of Herceptin; LVEF measurements every 3 months during and upon completion of Herceptin; Repeat LVEF measurement at 4 week intervals if Herceptin is withheld for significant left ventricular cardiac dysfunction; LVEF measurements every 6 months for at least 2 years following completion of Herceptin as a component of adjuvant therapy. [1]

4 . References

1. Herceptin Prescribing Information, Genentech October 2010.
2. DRUGDEX System [internet database]. Greenwood Village, Colorado: Thomson Micromedex®. Last modified February 6, 2009.
3. Romond EH, Perez EA, Bryant John, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. N Engl J Med. 2005;353(16):1673-1683.
4. Cobleigh MA, Vogel CL, Tripathy D, et al. Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease. J Clin Oncol. 1999; 17(9):2639-48.
5. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. N Engl J Med. 2001; 344(11):783-92.
6. Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. J Engl J Med. 2005;353(16):1659-1672.
7. National Comprehensive Cancer Network (NCCN), Clinical Practice Guidelines in Oncology.-v.2.2011. Breast Cancer. Available at:

http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf. Accessed December 15, 2010
8. The American Joint Committee on Cancer (AJCC) TNM system, last reviewed 9/2008. Available at: http://www.cancer.org/docroot/CRI/content/CRI_2_4_3X_How_is_breast_cancer_staged_5.asp?sitearea=. Accessed April 10, 2009
9. Breast Cancer fact sheet. Available at: http://www.gene.com/gene/products/education/oncology/breastcancerfact.jsp. Accessed April 10, 2009
10. Perez EA, Romond EH, Suman VJ. Updated results of the combined analysis of NCCTG N9831 and NSABP B-31 adjuvant chemotherapy with/without trastuzumab in patients with HER2-positive breast cancer. J Clin Oncol. 2007;25(185) (suppl): 512
11. Slamon D, Eiermann W, Robert N et al. Phase III trial comparing AC-T with AC-TH and with TCH in the adjuvant treatment of HER2-positive early breast cancer patients: second interim efficacy analysis. Breast Cancer Res Treat. 2006;100 (suppl 1):53
12. Smith I, Procter M, Gelber RD. 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER-2 positive breast cancer: a randomized controlled trial. Lancet. 2007;369:29-36
13. National Comprehensive Cancer Network (NCCN), Clinical Practice Guidelines in Oncology.-v.2.2010. Gastric Cancer. Available at: www.nccn.org/professionals/physician_gls/PDF/gastric.pdf. Accessed December 15, 2010

Prior Authorization Guideline

GL-30121 Hetlioz (tasimelteon)

Formulary OptumRx SP

Formulary Note

Approval Date 8/8/2016

Revision Date 8/8/2016

Technician Note :

P&T Approval Date: 4/8/2014: P&T Revision Date: 7/27/2016; ** Effective 7/1/2016 **

1 . Indications

Drug Name: Hetlioz (tasimelteon)

Indications

Non-24-Hour Sleep-Wake Disorder (Non-24) Indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24)

2 . Criteria

Product Name: Hetlioz

Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of non-24-hour sleep-wake disorder (also known as free-running disorder, free-running or non-entrained type circadian rhythm sleep disorder, or hypernychthemeral syndrome) [2,6-8,A]

and

2 Patient is totally blind (has no light perception) [2-12,B,C]

and

3 Prescribed by or in consultation with a specialist in sleep disorders [3-4,6,D]

Product Name: Hetlioz

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Hetlioz therapy

3 . Endnotes

A. The International Classification of Sleep Disorders (an official publication of the American Academy of Sleep Medicine) defines non-24-hour sleep-wake disorder as a circadian rhythm sleep disorder characterized by complaints of insomnia or excessive sleepiness related to abnormal synchronization between the 24-hour light-dark cycle and the endogenous circadian rhythms of sleep and wake propensity. [2] Patients with non-24 experience a chronic steady pattern comprising 1- to 2-hour daily delays in sleep onset and wake times. As incremental phase delays in sleep occur, the complaint will consist of difficulty initiating sleep at night coupled with oversleeping into the daytime hours or inability to remain awake in the daytime. Therefore, over long periods of time, patients alternate between being symptomatic and asymptomatic, depending on the degree of synchrony between their internal biologic rhythm and the 24-hour world. [2] The condition is very rare in normally sighted people, but quite common in the totally blind who have no access to the entraining effects of the light-dark cycle. [3] Of the estimated 1.3 million legally blind individuals in the United States, approximately 130,000 have no light perception. Epidemiologic studies have found that 57-70% of this totally blind sub-population suffer from non-24. [4-5] Non-24 is considered a chronic condition and markedly decreases the quality of life for patients. To varying extents, individuals with non-24 are unable to function in scheduled social activities or hold conventional jobs. [2,5]
B. Hetlioz was granted orphan drug designation by the Food and Drug Administration (FDA). Per the FDA approval letter, this new drug application (NDA) provides for the use of Hetlioz in the treatment of non-24-hour sleep-wake disorder in blind patients without light perception. [9]
C. Hetlioz was approved on the basis of two pivotal, randomized, double-masked, placebo-controlled, multicenter, parallel-group studies in totally blind patients with non-24-hour sleep-wake disorder. [1,10,12] The Safety and Efficacy of Tasimelteon (SET) Trial [1,10,12] was conducted in 84 totally blind patients with non-24, aged 21-84 years. Subjects received either Hetlioz 20 mg or placebo, one hour prior to bedtime, at the same time every night for up to 6 months. The Randomized-withdrawal study of the Efficacy and Safety of Tasimelteon to treat non-24 (RESET) Trial [1,11-12] was conducted in 20 entrained totally blind patients with non-24, aged 28-70 years. Subjects were treated for approximately 12 weeks with Hetlioz 20 mg one hour prior to bedtime,

at the same time every night. Patients in whom the calculated time of peak melatonin level (melatonin acrophase) occurred at approximately the same time of day (in contrast to the expected daily delay) during the run-in phase were randomized to receive placebo or continue treatment with Hetlioz 20 mg for 8 weeks.

D. Given the wide range of available dosing regimens for melatonin [3], the variability in response time to treatment with tasimelteon and melatonin [3-4], and the need for consistent monitoring and evaluation of patients' sleep-related symptoms [3-4,6], tasimelteon must be prescribed by or in consultation with a specialist in sleep disorders.

4 . References

1. Hetlioz Prescribing Information. Vanda Pharmaceuticals, Inc., December 2014.
2. The International Classification of Sleep Disorders, Revised: Diagnostic & Coding Manual. Westchester, IL: American Academy of Sleep Medicine; 2001.
3. Sack RL, Auckley D, Auger RR, et al. Circadian rhythm sleep disorders: Part II, advanced sleep phase disorder, delayed sleep phase disorder, free-running disorder, and irregular sleep-wake rhythm. Sleep 2007;30(11):1484-1501.
4. Hetlioz Formulary Submission Dossier. Vanda Pharmaceuticals, Inc., March 2014.
5. Vanda Pharmaceuticals, Inc. About Non-24. Available at: http://www.non-24.com/about-non-24.php. Accessed on July 23, 2015.
6. Morgenthaler TI, Lee-Chiong T, Alessi C, et al. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders: an American Academy of Sleep Medicine report. Sleep 2007;30(11):1445-1459.
7. National Sleep Foundation. Non-24-hour Sleep Wake Disorder Facts and Prevalence. Available at: http://sleepfoundation.org/non-24/facts_prevalence.html. Accessed on July 23, 2015.
8. Circadian Sleep Disorders Network. Non-24-Hour Sleep-Wake Disorder Questions and Answers. Available at: http://www.circadiansleepdisorders.org/docs/N24-QandA.php. Accessed on July 23, 2015.
9. Food and Drug Administration Center for Drug Evaluation and Research. New Drug Approval 205677. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2014/205677Orig1s000ltr.pdf. Accessed on July 23, 2015.
10. Lockley SW, Dressman MA, Xiao C, et al. Tasimelteon treatment entrains the circadian clock and demonstrates a clinically meaningful benefit in totally blind individuals with non-24-hour circadian rhythms [Poster abstract no. FP26-6]. 95th Annual Meeting of the Endocrine Society; 15â€“18 Jun 2013; San Francisco, CA.
11. Lockley SW, Dressman MA, Xiao C, Licamele L, Polymeropoulos MH. RESET study demonstrates that tasimelteon maintains entrainment of melatonin and cortisol in totally blind individuals with non-24-hour circadian rhythms [Poster abstract no. SUN-137]. 95th Annual Meeting of the Endocrine Society; 15â€“18 Jun 2013; San Francisco, CA.
12. Dhillon S, Clarke M. Tasimelteon: First Global Approval. Drugs 2014;74(4):505-511.

Prior Authorization Guideline

GL-32052 Humira (adalimumab)

Formulary OptumRx SP

Formulary Note

Approval Date 10/5/2016

Revision Date 10/5/2016

Technician Note :

P&T Approval Date: 3/17/2003; P&T Revision Date: 9/28/2016 **Effective 10/15/2016**

1 . Indications

Drug Name: Humira (adalimumab)

Indications

Rheumatoid arthritis (RA) Indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage and improving physical function in adult patients with moderately to severe active rheumatoid arthritis (RA). Humira can be used alone or in combination with methotrexate (MTX) or other DMARDs.

Juvenile idiopathic arthritis (JIA) Indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients ages 2 years of age and

older. Humira can be used alone or in combination with MTX.

Psoriatic arthritis (PsA) Indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage and improving physical function in patients with psoriatic arthritis. Humira can be used alone or in combination with DMARDs.

Plaque psoriasis Indicated for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate. Humira should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

Ankylosing spondylitis (AS) Indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

Adult Crohnâ€™s disease (CD) Indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohnâ€™s disease who have had an inadequate response to conventional therapy. Humira is indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.

Pediatric Crohnâ€™s disease Indicated for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active Crohnâ€™s disease who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate.

Ulcerative Colitis Indicated for inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP). The effectiveness of Humira has not been established in patients who have lost response to or were intolerant to TNF blockers.

Hidradenitis Suppurativa Indicated for the treatment of moderate to severe hidradenitis suppurativa.

Uveitis (UV) Indicated for the treatment of non-infectious intermediate, posterior and panuveitis in adult patients.

2 . Criteria

Product Name: Humira

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active RA

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to one nonbiologic disease modifying anti-rheumatic drug (DMARD) [e.g., methotrexate (Rheumatrex/Trexall), Arava (leflunomide), Azulfidine (sulfasalazine)] [6, 29]

AND

4 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

5 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Humira therapy.

AND

2 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

3 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Juvenile Idiopathic Arthritis (JIA)
Approval Length	12 Month

Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderate to severely active polyarticular JIA

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to one of the following nonbiologic disease modifying anti-rheumatic drugs (DMARDs): [34]

- Arava (leflunomide)
- methotrexate (Rheumatrex/Trexall)

AND

4 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

5 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz

(tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Juvenile Idiopathic Arthritis (JIA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Humira therapy

AND

2 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

3 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Psoriatic Arthritis (PsA)
Approval Length	12 Months [15]
Therapy Stage	Initial Authorization

Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active PsA

AND

2 Prescribed by or in consultation with one of the following:

- Dermatologist
- Rheumatologist

AND

3 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

4 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

AND

5 Patient is not receiving Humira in combination with a phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]. [1, 6]

Product Name: Humira

Diagnosis	Psoriatic Arthritis (PsA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Humira therapy

AND

2 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

3 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

AND

4 Patient is not receiving Humira in combination with a phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]. [1, 6]

Product Name: Humira

Diagnosis	Plaque Psoriasis [1, 5]

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderate to severe chronic plaque psoriasis [A]

AND

2 Prescribed by or in consultation with a dermatologist

AND

3 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

4 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

AND

5 Patient is not receiving Humira in combination with a phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]. [1, 6]

Product Name: Humira

Diagnosis	Plaque Psoriasis [1, 5]
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Humira therapy

AND

2 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

3 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

AND

4 Patient is not receiving Humira in combination with a phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]. [1, 6]

Product Name: Humira

Diagnosis	Ankylosing Spondylitis
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active ankylosing spondylitis

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to two NSAIDs [20, 30]

AND

4 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

5 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Ankylosing Spondylitis
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Humira therapy

AND

2 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

3 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Crohnâ€™s disease [1-4]
Approval Length	12 Month

Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active Crohnâ€™s disease [3, B]

AND

2 One of the following:

2.1 History of failure, contraindication, or intolerance to one of the following conventional therapies: [28]

- 6-mercaptopurine (Purinethol)
- Azathioprine (Imuran)
- Corticosteroids (e.g., prednisone, methylprednisolone)
- Methotrexate (Rheumatrex, Trexall)

OR

2.2 History of failure (i.e., lost response) or intolerance to Remicade (infliximab) [1]

AND

3 Prescribed by or in consultation with a gastroenterologist

AND

4 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

5 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Crohnâ€™s disease
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Humira therapy

AND

2 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

3 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Ulcerative Colitis
Approval Length	12 Week
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active ulcerative colitis

AND

2 History of failure, contraindication, or intolerance to one of the following conventional therapies: [32]

- 6-mercaptopurine (Purinethol)
- Aminosalicylate [e.g., mesalamine (Asacol, Pentasa, Rowasa), olsalazine (Dipentum), sulfasalazine (Azulfidine, Sulfazine)]
- Azathioprine (Imuran)
- Corticosteroids (e.g., prednisone, methylprednisolone)

AND

3 Prescribed by or in consultation with a gastroenterologist

AND

4 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

5 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Ulcerative Colitis
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 For patients who initiated Humira therapy within the past 12 weeks: Documentation of clinical remission or significant clinical benefit by eight weeks (Day 57) of therapy

OR

1.2 For patients who have been maintained on Humira therapy for longer than 12 weeks: Documentation of positive clinical response to Humira therapy.

AND

2 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

3 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Hidradenitis Suppurativa
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderate to severe hidradenitis suppurativa (i.e., Hurley Stage II or III)

AND

2 Prescribed by or in consultation with a dermatologist

AND

3 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

4 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Hidradenitis Suppurativa
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Humira therapy

AND

2 Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

3 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Uveitis (UV)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of non-infectious uveitis

AND

2 Uveitis is classified as one of the following:

- intermediate
- posterior
- panuveitis

AND

3 Prescribed by or in consultation with one of the following:

- ophthalmologist
- rheumatologist

AND

4 Patient is not receiving Humira in combination with a biologic DMARD [eg, Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

5 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

Diagnosis	Uveitis (UV)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Humira therapy.

AND

2 Patient is not receiving Humira in combination with a biologic DMARD [eg, Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]

AND

3 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

3 . Endnotes

A. Patients who are candidates for systemic/and or phototherapy have significant disease, typically affecting 5% or more of the body surface area (BSA). Some of these candidates may also have less than 5% BSA affected but have psoriasis in vulnerable areas such as the face, genitals, hands, or feet (palmer-plantar), nails, scalp, or intertriginous areas. [26]
B. In the CLASSIC-I trial, moderate to severe Crohn's disease was defined as a Crohn's Disease Activity Index (CDAI) score between 220 and 450, inclusive. [3]

4 . References

1. Humira Prescribing Information. Abbott Laboratories, July 2016.
2. Sandborn WJ, Rutgeerts P, Enns R, et al. Adalimumab induction therapy for Crohnâ€™s disease previously treated with infliximab: a randomized trial Ann Intern Med. 2007 Jun 19;146(12):829-38.
3. Hanauer SB, Sandborn WJ, Rugeerts P, et al. Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohnâ€™s disease: the CLASSIC-I trial. Gastroenterol. 2006;130:323-333.
4. Sandborn WJ, Hanauer SB, Rutgeerts P, et al. Adalimumab for maintenance treatment of Crohn's disease: results of the CLASSIC II Trial. Gut. 2007 Sep;56(9):1232-9.
5. Menter A, Tyring SK, Gordon K, et al. Adalimumab therapy for moderate to severe psoriasis: A randomized, controlled III trial. J Am Acad Dermatol. 2008 Jan;58(1):106-15.
6. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012;64(5):625-639.
7. Furst DE, Breedveld FC, Kadlden JR, et al. Updated consensus statement on biological agents, specifically tumor necrosis factor alpha (TNF-alpha) blocking agents and interleukin-1 receptor antagonist (IL-1ra), for the treatment of rheumatic diseases. Ann Rheum Dis. 2004;63 (Suppl II):ii2-ii12.
8. Van de Putte LBA, Atkins C, Malaise C, et al. Efficacy and safety of adalimumab as monotherapy in patients with rheumatoid arthritis for whom previous disease modifying antirheumatic drug treatment has failed. Ann Rheum Dis. 2004;63:508-516.
9. Pavy S, Constatin A, Pham T, et al. Methotrexate therapy for rheumatoid arthritis: clinical practice guidelines based on published evidence and expert opinion. Joint Bone Spine. 2006;73:388-95.

10. Scott DL, Kingsley GH, Ch. B. Tumor necrosis factor inhibitors of rheumatoid arthritis. N Engl J Med. 2006;355:704-12.
11. Weinblatt M, KeystoneE, Furst D, et al. The ARMADA Trial. Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate. Arthritis Rheum 2003;48:35-45.
12. Ledingham J, Deighton C, behalf of the British Society of Rheumatology Standards, Guidelines and Audit Working Group (SGAWG). Rheum. 2005;44:157-163.
13. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995;38:727-735.
14. Keystone E, Kavanaugh A, Sharp J, et al. Radiographic, clinical, and functional outcomes of treatment with adalimumab (a human anti-tumor necrosis factor monoclonal antibody) in patients with active rheumatoid arthritis receiving concomitant methotrexate therapy. Arthritis Rheum. 2004;50:1400-1411.
15. Mease PJ, Gladman DD, Ritchlin CT, et al. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis. Arthritis Rheum. 2005;52:3279-3289.
16. Kyle S, Chandler D, Griffiths EM, et al. Guideline for anti-TNF-alpha therapy in psoriatic arthritis. Rheumatology. 2005;44:390-397.
17. Hanauer SB, Sandborn W, and the Practice Parameters Committee of the American College of Gastroenterology. Practice Guidelines: Management of Crohnâ€™s disease in adults. Am J Gastroenterol. 2001; 96(3):635-643.
18. Lichtenstein GR, Abreu MT, Cohen R, Tremaine W. American Gastroenterological Association Institute medical position statement on corticosteroids, immunomodulators, and infliximab in inflammatory bowel disease. Gastroenterology 2006 Mar;130(3):935-9.
19. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum. 1993; 36 (6): 729-740.
20. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of Ankylosing spondylitis. Ann Rheum Dis. 2011;70:896-904.
21. British Society for Rheumatology (BSR) Guideline for Prescribing TNF-alpha Blockers in Adults with Ankylosing Spondylitis. London: BSR; 2004 July:1-21.
22. Van der Heijde D, Kivitz A, Schiff MH, et al. Efficacy and safety of adalimumab in patients with ankylosing spondylitis: Results of a multicenter, randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2006; 54(7):2136-2146.
23. Tumor necrosis factor-alpha blockers (TNF blockers), Cimzia (certolizumab pegol), Enbrel (etanercept), Humira (adalimumab), and Remicade (infliximab). Available at: http://www.fda.gov/MedWatch/safety/2008/safety08.htm#TNF2. Accessed September 21, 2008.
24. Gottlieb A, Korman NJ, Gordon KB, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis section 2. Psoriatic arthritis: Overview and guidelines of care for treatment with an emphasis on the biologics. J Am Acad Dermatol. 2008;58:851-64.
25. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case based presentations and evidence-based conclusions. J Am Acad Dermatol. 2011;65(1):137-74.
26. Pariser DM, Bagel J, Gelfand JM, et al. National Psoriasis Foundation Clinical Consensus on Disease Severity. Arch Dermatol. 2007 Feb;143(2):239-42.
27. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis:

recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013;65(10):2499-2512.
28. Lichtenstein GR, Hanauer SB, Sandborn WJ, and The Practice Parameters Committee of the American College of Gastroenterology. Management of Crohnâ€™s disease in adults. Am J Gastroenterol. 2009;104:465-483.
29. Per clinical consult with rheumatologist, June 30, 2011.
30. van der Heijde, Sieper J, Maksymowych WP, et al. 2010 update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. Ann Rheum Dis. 2011;70:905-908.
31. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012;64(5):625-39.
32. Kornbluth A, Sachar DB, and The Practice Parameters Committee of the American College of Gastroenterology. Ulcerative Colitis Practice Guidelines in Adults. Am J Gastroenterology. 2010;105:501-523.
33. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011. Ann Rheum Dis. 2012;71(Supp II):i2â€“i45.
34. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011;63(4):465-82.
35. AbbVie. Efficacy and Safety Study of Adalimumab in the Treatment of Hidradenitis Suppurativa (PIONEER I). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2015. https://clinicaltrials.gov/ct2/show/NCT01468207. Accessed October 19, 2015.
36. AbbVie. Efficacy and Safety Study of Adalimumab in the Treatment of Hidradenitis Suppurativa (PIONEER II). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2015. Available at: https://clinicaltrials.gov/ct2/show/NCT01468233. Accessed October 19, 2015.

Prior Authorization Guideline

GL-30834 Hyaluronic Acid Derivatives

Formulary OptumRx SP

Formulary Note

Approval Date 8/24/2016

Revision Date 8/24/2016

Technician Note :

P&T Approval Date: 2/7/2006; P&T Revision Date: 8/18/2016 **Effective 9/15/2016**

1 . Indications

Drug Name: Euflexxa/Hyalgan/Supartz/Supartz FX/Gelsyn-3/Genvisc 850 (sodium hyaluronate), Gel-One (cross-linked hyaluronate), Monovisc/Orthovisc/Hymovis (hyaluronan), Synvisc/Synvisc-One (hylan)

Indications

Osteoarthritis (OA) of the knee Indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics (e.g., acetaminophen).

2 . Criteria

Product Name: Euflexxa, Synvisc

Approval Length	3 Week
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of osteoarthritis (OA) of the knee

AND

2 History of failure, contraindication, or intolerance to two of the following: [A]

- Acetaminophen
- Formulary non-steroidal antiinflammatory drugs (NSAIDs)
- Tramadol

AND

3 History of failure, contraindication, or intolerance to intra-articular steroid injection

Product Name: Euflexxa, Synvisc

Approval Length	3 Week
Therapy Stage	Reauthorization

Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of improvement in pain with previous course of treatment

AND

2 At least 6 months have elapsed since last injection of the prior treatment cycle [9]

Product Name: Synvisc-One

Approval Length	1 Time
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of OA of the knee

AND

2 History of failure, contraindication, or intolerance to two of the following: [A]

- Acetaminophen
- Formulary NSAIDs
- Tramadol

AND

3 History of failure, contraindication, or intolerance to intra-articular steroid injection [8]

Product Name: Synvisc-One

Approval Length	1 Time
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of improvement in pain with previous course of treatment

AND

2 At least 6 months have elapsed since last injection of the prior treatment cycle [9]

Product Name: Gel-One, Monovisc

Approval Length	1 Time
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of OA of the knee

AND

2 History of failure, contraindication, or intolerance to two of the following: [A]

- Acetaminophen
- Formulary NSAIDs
- Tramadol

AND

3 History of failure, contraindication, or intolerance to intra-articular steroid injection [8]

AND

4 History of failure or intolerance to one of the following hyaluronic acid derivatives:

- Euflexxa*
- Synvisc*
- Synvisc-One*

Notes	*These products may require Prior Authorization.

Product Name: Gel-One, Monovisc

Approval Length	1 Time
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of improvement in pain with previous course of treatment

AND

2 At least 6 months have elapsed since last injection of the prior treatment cycle [9]

Product Name: Genvisc 850, Hyalgan, Supartz, Supartz FX

Approval Length	5 Week
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of OA of the knee

AND

2 History of failure, contraindication, or intolerance to two of the following: [A]

- Acetaminophen
- Formulary NSAIDs
- Tramadol

AND

3 History of failure, contraindication, or intolerance to intra-articular steroid injection [8]

AND

4 History of failure or intolerance to one of the following hyaluronic acid derivatives:

- Euflexxa*
- Synvisc*
- Synvisc-One*

Notes	*These products may require Prior Authorization.

Product Name: Genvisc 850, Hyalgan, Supartz, Supartz FX

Approval Length	5 Week
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of improvement in pain with previous course of treatment

AND

2 At least 6 months have elapsed since last injection of the prior treatment cycle [9]

Product Name: Orthovisc*, Gelsyn-3**

Approval Length	3 or 4 weeks
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of OA of the knee

AND

2 History of failure, contraindication, or intolerance to two of the following: [A]

- Acetaminophen
- Formulary NSAIDs
- Tramadol

AND

3 History of failure, contraindication, or intolerance to intra-articular steroid injection [8]

AND

4 History of failure or intolerance to one of the following hyaluronic acid derivatives:

- Euflexxa^
- Synvisc^
- Synvisc-One^

Notes	*Authorizations will be issued for a 3 or 4-week course of therapy. **Authorizations will be issued for a 3-week course of therapy. ^These products may require Prior Authorization.

Product Name: Orthovisc*, Gelsyn-3**

Approval Length	3 or 4 weeks
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of improvement in pain with previous course of treatment

AND

2 At least 6 months have elapsed since last injection of the prior treatment cycle [9]

Notes	*Authorizations will be issued for a 3 or 4-week course of therapy. **Authorizations will be issued for a 3-week course of therapy.

Product Name: Hymovis

Approval Length	2 Week
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of OA of the knee

AND

2 History of failure, contraindication, or intolerance to two of the following: [8, 11, A]

- Acetaminophen
- Formulary NSAIDs
- Tramadol

AND

3 History of failure, contraindication, or intolerance to intra-articular steroid injection [8]

AND

4 History of failure or intolerance to one of the following hyaluronic acid derivatives:

- Euflexxa*
- Synvisc*
- Synvisc-One*

Notes	Authorizations will be issued for a 2 week course of therapy. *These products may require Prior Authorization.

Product Name: Hymovis

Approval Length	2 Week
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of improvement in pain with previous course of treatment

AND **2** At least 6 months have elapsed since last injection of the prior treatment cycle [9]	
Notes	Authorizations will be issued for a 2 week course of therapy

3 . Endnotes

A. The American College of Rheumatology (2012) conditionally recommends the following pharmacologic therapies for the initial management of knee osteoarthritis: acetaminophen, oral NSAIDs, topical NSAIDS, tramadol, and intraarticular corticosteroids. [8] The American Academy of Orthopaedic Surgeons (AAOS) (2013) recommends the following pharmacologic therapies for patients with symptomatic knee osteoarthritis: oral NSAIDs, topical NSAIDs, or Tramadol. AAOS is unable to recommend for or against the use of acetaminophen, opioids, or pain patches. However, AAOS also recognizes that many practitioners prefer to start with acetaminophen prior to NSAIDs due to the side effect profile of NSAIDs.[11]

4 . References

1. Euflexxa Prescribing Information. Ferring Pharmaceuticals Inc., September 2011.
2. Gel-One Prescribing Information. Seikagaku Corporation. May 2011.
3. Hyalgan Prescribing Information. Fidia Pharmaceutical, June 2011.
4. Orthovisc Prescribing Information. DePuy Mitek, June 2005.
5. Supartz Prescribing Information. Seikagaku Corporation. June 2012.
6. Synvisc Prescribing Information. Genzyme Corporation. March 2010.
7. Synvisc-One Prescribing Information. Genzyme Corporation. January 2010.
8. Hochberg et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res 2012;65(4):465-474.
9. Tascioglu F, Oner C. Efficacy of intra-articular sodium hyaluronate in the treatment of knee osteoarthritis. Clin Rheumatol 2003;22:112-117.
10. Huskisson EC, Donnelly S. Hyaluronic acid in the treatment of osteoarthritis of the knee. Rheumatology 1999;38:602-607.

11. Jevsevar DS, Brown GA, Jones DL, et al. The American Academy of Orthopaedic Surgeons evidence-based guideline on: treatment of osteoarthritis of the knee, 2nd edition. J. Bone Joint Surg Am. 2013;95(20):1885-6.
12. Monovisc Prescribing Information, Anika Therapeutics, Inc. December 2013.
13. Genvisc 850 Prescribing Information. OrthogenRx, Inc. October 2015.
14. Hymovis Prescribing Information. Fidia Pharma USA Inc. October 2015.
15. Gelsyn-3 Prescribing Information. Bioventus. July 2016.

Prior Authorization Guideline

GL-32053 Hydroxyprogesterone caproate injection products

Formulary OptumRx SP

Formulary Note

Approval Date 10/5/2016

Revision Date 10/5/2016

Technician Note :

P&T Approval Date: 5/17/2011 P&T Revision Date: 9/28/2016 **Effective date: 10/15/2016**

1 . Indications

Drug Name: Makena (hydroxyprogesterone caproate injection)

Indications

Reduce Risk of Preterm birth Is a progestin indicated to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. Limitation of use: While there are many risk factors for preterm birth, safety and efficacy of Makena has been demonstrated only in women with a prior spontaneous singleton preterm birth. It is not intended for use in women with multiple gestations or other risk factors for preterm birth.

Drug Name: hydroxyprogesterone caproate injection

Indications

Adenocarcinoma of uterine corpus, Stage III or IV Indicated in nonpregnant women for treatment of advanced (stage III or IV) adenocarcinoma of the uterine corpus.

Amenorrhea, due to hormonal imbalance in the absence of organic pathology Indicated in nonpregnant women for management of primary or secondary amenorrhea and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology (eg, submucous fibroids or uterine cancer).

Secretory endometrium, production and desquamation Indicated in nonpregnant women for production of secretory endometrium and desquamation.

Estrogen measurement, endogenous; diagnosis Indicated as a test for endogenous estrogen production in nonpregnant women.

2 . Criteria

Product Name: Makena

Diagnosis	Reduce Risk of Preterm birth
Approval Length	21 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Patient had a previous singleton (single offspring) spontaneous preterm birth

AND

2 Patient is having a singleton pregnancy

AND

3 Therapy will be started between 16 weeks, 0 days and 20 weeks, 6 days of gestation

AND

4 Therapy will be continued until week 37 (through 36 weeks, 6 days) of gestation or delivery, whichever occurs first

AND

5 Prescribed by or in consultation with one of the following:

- Gynecologist
- Obstetrician

Product Name: hydroxyprogesterone caproate injection

Diagnosis	Amenorrhea
Approval Length	4 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of primary or secondary amenorrhea

AND

2 Amenorrhea is due to hormonal imbalance in the absence of organic pathology (eg, submucous fibroids or uterine cancer)

AND

3 Patient is not pregnant

Notes	Note: This product and its criteria do NOT apply to brand Makena.

Product Name: hydroxyprogesterone caproate injection

Diagnosis	Production of secretory endometrium and desquamation
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Used for production of secretory endometrium and desquamation

AND

2 Patient is not pregnant

Notes	Note: This product and its criteria do NOT apply to brand Makena.

Product Name: hydroxyprogesterone caproate injection

Diagnosis	Test for endogenous estrogen production
Approval Length	2 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Used for the testing of endogenous estrogen production

AND

2 Patient is not pregnant

Notes	Note: This product and its criteria do NOT apply to brand Makena.

Product Name: hydroxyprogesterone caproate injection

Diagnosis	Adenocarcinoma of uterine corpus
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Stage III or IV adenocarcinoma of the uterine corpus

AND **2** Patient is not pregnant **AND** **3** Prescribed by or in consultation with an oncologist

Notes	Note: This product and its criteria do NOT apply to brand Makena.

Product Name: hydroxyprogesterone caproate injection

Diagnosis	Adenocarcinoma of uterine corpus
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria **1** Patient does not show evidence of progressive disease while on hydroxyprogesterone caproate injection therapy **AND** **2** Patient is not pregnant

Notes	Note: This product and its criteria do NOT apply to brand Makena.

3 . References

1. Makena Prescribing Information. Ther-Rx Corporation. St. Louis, MO. April 2014.
2. Bernstein, P, Berck D, Burgess T, et al. Preventing preterm birth: the role of 17 alpha hydroxyprogesterone caproate. Albany, NY: American College of Obstetricians and Gynecologists, District II: January 2009. Available at:http://mail.ny.acog.org/website/17PResourceGuide.pdf. Accessed June 17, 2014.
3. Meis PJ, Klebanoff M, Thom E, et al. Prevention of recurrent preterm delivery by 17 alphahydroxyprogesterone caproate. N Engl J Med. 2003;348:2379-2385.
4. Patel Y, Rumore M. Hydroxyprogesterone caproate injection (MAKENA) one year later to compound or not to compoundâ€"that is the question. P&T. 2012; 37:405-411.
5. Hydroxyprogesterone Caproate Injection Prescribing Information. ANI Pharmaceuticals, Inc. June 2016.

Prior Authorization Guideline

GL-15452 Ibrance (palbociclib)

Formulary OptumRx SP

Formulary Note

Approval Date 4/14/2015

Revision Date 5/2/2016

Technician Note :

P&T Approval Date: 4/14/2015; P&T Revision Date: 4/27/2016. **Effective 5-15-2016**

1 . Indications

Drug Name: Ibrance (palbociclib)

Indications

Breast Cancer

Indicated for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer in combination with: (1) letrozole as initial endocrine based therapy in postmenopausal women, or (2) fulvestrant in women with disease progression following endocrine therapy. The indication in combination with letrozole is approved under accelerated approval based on progression-free survival (PFS). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

2 . Criteria

Product Name: Ibrance

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of breast cancer

AND

2 Disease is one of the following: [2,3]

- Locally advanced
- Metastatic

AND

3 Disease is estrogen-receptor (ER)-positive [1,5]

AND

4 Disease is human epidermal growth factor receptor 2 (HER2)-negative

AND

5 One of the following:

5.1 Both of the following:

- Used in combination with Femara (letrozole)
- Patient is a postmenopausal woman

OR

5.2 All of the following:

5.2.1 Used in combination with Faslodex (fulvestrant)

AND

5.2.2 Disease has progressed following endocrine therapy

AND

5.2.3 One of the following: [1,4,5]

5.2.3.1 Patient is a postmenopausal woman

OR

5.2.3.2 Both of the following: [A,B]

- Patient is a premenopausal or perimenopausal woman
- Patient is receiving a luteinizing hormone-releasing hormone (LHRH) agonist [eg, Zoladex (goserelin)]

AND
6 Prescribed by or in consultation with an oncologist

Product Name: Ibrance

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Ibrance therapy

3 . Endnotes

A. Per NCCN, Ibrance is used in combination with fulvestrant for the treatment of recurrent or metastatic estrogen receptor-positive, human epidermal growth factor receptor 2-negative disease that has progressed on endocrine therapy for postmenopausal women or premenopausal women receiving ovarian suppression with a luteinizing hormone-releasing hormone (LHRH) agonist. [4,5]
B. In the PALOMA-3 study, premenopausal or perimenopausal patients received the LHRH agonist goserelin for the duration of study treatment, starting at least 4 weeks before randomization and continuing every 28 days. [1,3]

4 . References

1. Ibrance Prescribing Information. Pfizer, February 2016.

2. Finn RS, Crown JP, Lang I, et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. Lancet Oncol. 2015;16(1):25-35.
3. Turner NC, Ro J, Andre F, et al. Palbociclib in hormone-receptor-positive advanced breast cancer. NEJM. 2015;373(3):209-219.
4. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Breast Cancer v.1.2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed March 9, 2016.
5. National Comprehensive Cancer Network. Drugs & Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=418. Accessed March 9, 2016.

Prior Authorization Guideline

GL-16902 Iclusig (ponatinib)

Formulary OptumRx SP

Formulary Note

Approval Date 10/2/2014

Revision Date 5/24/2016

Technician Note :

P&T Approval Date: 2/19/2013; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Iclusig (ponatinib)

Indications

Chronic Myeloid Leukemia

Indicated for the treatment of adult patients with T315I-positive chronic myeloid leukemia (CML) (chronic phase, accelerated phase, or blast phase), and for adult patients with chronic phase, accelerated phase, or blast phase CML for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated. This indication is based upon response rate. There are no trials verifying an improvement in disease-related symptoms or increased survival with Iclusig.

Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia

Indicated for the treatment of adult patients with T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL), and for adult patients with Ph+ALL for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated. This indication is based upon response rate. There are no trials verifying an improvement in disease-related symptoms or increased survival with Iclusig.

2 . Criteria

Product Name: Iclusig

Diagnosis	Chronic Myelogenous Leukemia
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic myelogenous leukemia

AND

2 One of the following:

2.1 History of failure, contraindication, or intolerance to all of the following*:

- Bosulif (bosutinib)
- Gleevec (imatinib)

- Sprycel (dasatinib)
- Tasigna (nilotinib)

OR

2.2 Confirmed documentation of T315I mutation

AND

3 Prescribed by or in consultation with a hematologist or oncologist

Notes	* These products may require prior authorization

Product Name: Iclusig

Diagnosis	Chronic Myelogenous Leukemia
Approval Length	6 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Iclusig

Product Name: Iclusig

Diagnosis	Acute Lymphoblastic Leukemia
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Philadelphia chromosome-positive acute lymphoblastic leukemia

AND

2 One of the following:

2.1 History of failure, contraindication, or intolerance to all other FDA-approved tyrosine kinase inhibitors

OR

2.2 Confirmed documentation of T315I mutation

AND

3 Prescribed by or in consultation with a hematologist or oncologist

Product Name: Iclusig

Diagnosis	Acute Lymphoblastic Leukemia
Approval Length	6 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1	Patient does not show evidence of progressive disease while on Iclusig

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . References

1. Iclusig Prescribing Information. Ariad Pharmaceuticals, Inc. January 2014.

Prior Authorization Guideline

GL-17445 Idiopathic Pulmonary Fibrosis (IPF) Agents

Formulary OptumRx SP

Formulary Note

Approval Date 10/31/2014

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 11/4//2014; P&T Revision Date: 2/25/2016; ** Effective 7/1/2016 **

1 . Indications

Drug Name: Esbriet (pirfenidone) **Indications** **Idiopathic pulmonary fibrosis** Indicated for the treatment of idiopathic pulmonary fibrosis (IPF).
Drug Name: Ofev (nintedanib) **Indications**

Idiopathic pulmonary fibrosis

Indicated for the treatment of idiopathic pulmonary fibrosis (IPF)

2 . Criteria

Product Name: Esbriet, Ofev

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of idiopathic pulmonary fibrosis (IPF) as documented by both of the following: [3]

1.1 Exclusion of other known causes of interstitial lung disease (ILD) (eg, domestic and occupational environmental exposures, connective tissue disease, drug toxicity), as documented by one of the following:

- ICD-9 Code 516.31
- ICD-10 Code J84.112

AND

1.2 One of the following:

1.2.1 In patients not subjected to surgical lung biopsy, the presence of a usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) revealing IPF or probable IPF

OR

1.2.2 In patients subjected to a lung biopsy, both HRCT and surgical lung biopsy pattern revealing IPF or probable IPF

AND

2 Not being used in combination with Esbriet or Ofev

AND

3 Prescribed by or in consultation with a pulmonologist

Product Name: Esbriet, Ofev

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Esbriet or Ofev therapy

3 . References

1. Esbriet Prescribing Information. InterMune, Inc., October 2014.
2. Ofev Prescribing Information. Boehringer Ingelheim Pharmaceuticals, Inc., October 2014.
3. Raghu G, Collard HR, Egan JJ, et al. Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-based Guidelines for Diagnosis and Management. Am J of Respir Crit Care Med. 2011;183:788-824.

Prior Authorization Guideline

GL-16975 Ilaris (canakinumab injection)

Formulary OptumRx SP

Formulary Note

Approval Date 9/3/2013

Revision Date 5/24/2016

Technician Note :

P&T Approval Date: 11/17/2009; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Ilaris (canakinumab injection)

Indications

Cryopyrin-Associated Periodic Syndromes (CAPS)

Indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) in adults and children 4 years of age and older including:(1) Familial Cold Autoinflammatory Syndrome (FCAS) and (2) Muckle-Wells Syndrome (MWS).

Systemic Juvenile Idiopathic Arthritis (SJIA)

Indicated for the treatment of active Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older.

2 . Criteria

Product Name: Ilaris

Diagnosis	Cryopyrin-Associated Periodic Syndromes (CAPS)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) and/or Muckle-Wells Syndrome (MWS)

AND

2 Prescribed by or in consultation with an immunologist, allergist, dermatologist, rheumatologist, neurologist or other medical specialist

AND

3 Patient is 4 years of age or older

AND

4 The medication will not be used in combination with another biologic agent

Product Name: Ilaris

Diagnosis	Systemic Juvenile Idiopathic Arthritis (SJIA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active systemic juvenile idiopathic arthritis (SJIA)

AND

2 Patient is 2 years of age or older

AND

3 History of failure, contraindication, or intolerance to corticosteroids or methotrexate

AND

4 The medication will not be used in combination with another biologic

Product Name: Ilaris

Diagnosis	All diagnoses listed above
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has experienced disease stability or improvement in clinical symptoms while on therapy as evidenced by one of the following:

- Improvement in rash, fever, joint pain, headache, conjunctivitis
- Decreased number of disease flare days
- Normalization of inflammatory markers (CRP, ESR, SAA)
- Corticosteroid dose reduction
- Improvement in MD global score or active joint count

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Definitions

Definition	Description
Cryopyrin-Associated Periodic Syndromes (CAPS):	A group of rare, autosomal dominantly inherited auto-inflammatory conditions comprising of Familial-Cold Auto-inflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS), Neonatal-Onset Multisystem Inflammatory Disease (NOMID) or also known as Chronic Infantile Neurologic Cutaneous Articular Syndrome (CINCA), which are caused by the CIAS1 gene mutation and characterized by recurrent symptoms (urticaria-like skin lesions, fever chills, arthralgia, profuse sweating, sensorineural hearing/vision loss, and increased inflammation markers the blood). Approximately 300 people in the United States are affected by CAPS. [1,2,3]
Familial Cold Autoinflammatory Syndrome (FCAS):	The mildest form of CAPS, is characterized by cold-induced, daylong episodes of fever associated with rash, arthralgia, headaches and less frequently conjunctivitis, but without other signs of CNS inflammation. Symptoms usually begin during the first 6 months of life and are predominantly triggered by cold exposure. Duration of episodes usually is less than 24 hours. [3]
Muckle-Wells Syndrome (MWS):	A subtype of CAPS, which is characterized by episodic attacks of inflammation associated with a generalized urticaria-like rash, fever, malaise, arthralgia, and progressive hearing loss. Duration of symptoms usually lasts from 24-48 hours. [3]

5 . References

1. Ilaris Prescribing Information. Novartis Pharmaceuticals Corporation, October, 2014
2. Lachmann HJ, Kone-Paut I, Kuemmerle-Deschner JB, et al. Use of canakinumab in the cryopyrin-associated periodic syndrome. N Engl J Med. 2009;360(23):2416-2425.

3. Aksentijevich I, Putnam CD, Remmers EF, et al. Clinical continuum of cryopyrinopathies: novel CIAS1 mutations in North-American patients and a new cryopyrin model. Arthritis Rheum. 2007;56(4):1273-1285.
4. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011 Apr;63(4):465-82.

Prior Authorization Guideline

GL-30244 Imbruvica (ibrutinib)

Formulary OptumRx SP

Formulary Note

Approval Date 7/8/2016

Revision Date 7/8/2016

Technician Note :

P&T Approval Date: 2/18/2014; P&T Revision Date: 6/22/2016. **Effective 7/15/2016**

1 . Indications

Drug Name: Imbruvica (ibrutinib)

Indications

Mantle Cell Lymphoma (MCL) Indicated for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. Accelerated approval was granted for this indication based on overall response rate. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Indicated for the treatment of patients with chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma

(SLL)

Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) with 17p deletion Indicated for the treatment of patients with chronic lymphocytic leukemia (CLL)/small lymphocytic leukemia (SLL) with 17p deletion

WaldenstrÃ¶m's Macroglobulinemia/Lymphoplasmacytic Lymphoma Indicated for the treatment of patients with WaldenstrÃ¶mâ€™s macroglobulinemia (WM).

2 . Criteria

Product Name: Imbruvica

Diagnosis	Mantle Cell Lymphoma
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of mantle cell lymphoma (MCL)

and

2 Patient has received at least one prior therapy for MCL (e.g., Rituxan [rituximab]) [1, 2, 3]

and

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Imbruvica

Diagnosis	Mantle Cell Lymphoma
Approval Length	6 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Imbruvica therapy

Product Name: Imbruvica

Diagnosis	Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of one of the following:

- chronic lymphocytic leukemia
- small lymphocytic lymphoma

and

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Imbruvica

Diagnosis	Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma
Approval Length	6 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Imbruvica therapy

Product Name: Imbruvica

Diagnosis	Waldenstrom's Macroglobulinemia
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of WaldenstrÃ¶m's Macroglobulinemia

and

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Imbruvica

Diagnosis	Waldenstrom's Macroglobulinemia
Approval Length	6 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Imbruvica therapy

3 . Endnotes

A. The duration of approval will be for six months due to the high occurrence of disease progression leading to death in the clinical study.

4 . References

1. Imbruvica Prescribing Information. Pharmacyclics, Inc., March 2016.

Prior Authorization Guideline

GL-17427 Immune Globulins

Formulary OptumRx SP

Formulary Note

Approval Date 3/15/2013

Revision Date 6/2/2016

Technician Note :

P&T Approval Date: 9/5/2000; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Bivigam, Flebogamma 5% and 10 %, Flebogamma 5% and 10 % DIF, Hizentra, Octagam 5% (immune globulin [Human])

Indications

Primary Immunodeficiency Disorders

Indicated for the treatment of primary immunodeficiency disorders associated with defects in humoral immunity. These include, but are not limited to: congenital agammaglobulinemia, X-linked agammaglobulinemia, common variable immunodeficiency, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

Drug Name: Gamastan S/D (immune globulin [Human])

Indications

Hepatitis A

The prophylactic value of Gamastan S/D is greatest when given before or soon after exposure to hepatitis A. Not indicated in persons with clinical manifestations of hepatitis A or in those exposed more than 2 weeks previously.

Measles (Rubeola)

Should be given to prevent or modify measles in a susceptible person exposed fewer than 6 days previously. A susceptible person is one who has not been vaccinated and has not had measles previously. Gamastan S/D may be especially indicated for susceptible household contacts of measles patients, particularly contacts under 1 year of age, for whom the risk of complications is highest. Gamastan S/D and measles vaccine should not be given at the same time. If a child is older than 12 months and has received Gamastan S/D, he should be given measles vaccine about 3 months later when the measles antibody titer will have disappeared. If a susceptible child exposed to measles is immunocompromised, Gamastan S/D should be given immediately. Do not administer measles vaccine or any other live viral vaccine to children who are immunocompromised.

Varicella

Passive immunization against varicella in immunosuppressed patients is best accomplished by use of Varicella Zoster Immune globulin (Human) [VZIG]. If VZIG is unavailable, Gamastan S/D, promptly given, may also modify varicella.

Rubella

Some studies suggest that the use of Gamastan S/D in exposed, susceptible women can lessen the likelihood of infection and fetal damage; therefore, Gamastan S/D may benefit those women who will not consider a therapeutic abortion.

Drug Name: Carimune NF (immune globulin [Human])

Indications

Idiopathic Thrombocytopenic Purpura (ITP)

(1) Acute ITP: A controlled study was performed in children in which Carimune was compared

with steroids for the treatment of acute (defined as less than 6 months duration) ITP. In this study sequential platelet levels of 30,000, 100,000, and 150,000/?L were all achieved faster with Carimune than with steroids and without any of the side effects associated with steroids. However, it should be noted that many cases of acute ITP in childhood resolve spontaneously within weeks to months. Carimune has been used with good results in the treatment of acute ITP in adult patients. In a study involving 10 adults with ITP of less than 16 weeks duration, Carimune therapy raised the platelet count to the normal range after a 5 day course. This effect lasted a mean of over 173 days, ranging from 30 to 372 days. (2) Chronic ITP: Children and adults with chronic (defined as greater than 6 months duration) ITP have also shown an increase (sometimes temporary) in platelet counts upon administration of Carimune.Therefore, in situations that require a rapid rise in platelet count, for example prior to surgery or to control excessive bleeding, use of Carimune should be considered. In children with chronic ITP, Carimune therapy resulted in a mean rise in platelet count of 312,000/?L with a duration of increase ranging from 2 to 6 months. Carimune therapy may be considered as a means to defer or avoid splenectomy. In adults, Carimune therapy has been shown to be effective in maintaining the platelet count in an acceptable range with or without periodic booster therapy. The mean rise in platelet count was 93,000/?L and the average duration of the increase was 20–24 days. However, it should be noted that not all patients will respond. Even in those patients who do respond, this treatment should not be considered to be curative.

Primary Immunodeficiency Disorders

Indicated for the maintenance treatment of patients with primary immunodeficiencies (PID), e.g., common variable immunodeficiency, X-linked agammaglobulinemia, severe combined immunodeficiency. Carimune NF is preferable to intramuscular Immune Globulin (Human) preparations in treating patients who require an immediate and large increase in the intravascular immunoglobulin level, in patients with limited muscle mass, and in patients with bleeding tendencies for whom intramuscular injections are contraindicated. The infusions must be repeated at regular intervals.

Drug Name: Privigen (immune globulin [Human])

Indications

Idiopathic Thrombocytopenic Purpura (ITP)

Indicated for the treatment of patients with chronic ITP to raise platelet counts.

Primary Immunodeficiency Disorders

Indicated as replacement therapy for primary humoral immunodeficiency (PI). This includes, but is not limited to, the humoral immune defect in congenital agammaglobulinemia, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, Wiskott- Aldrich syndrome, and severe combined immunodeficiencies.

Drug Name: Gammagard S/D (immune globulin [Human])

Indications

Kawasaki Disease

Indicated for the prevention of coronary artery aneurysms associated with Kawasaki syndrome in pediatric patients.

B-cell Chronic Lymphocytic Leukemia (CLL)

Indicated for prevention of bacterial infections in hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell Chronic Lymphocytic Leukemia (CLL).

Idiopathic Thrombocytopenic Purpura (ITP)

Indicated for prevention and/or control of bleeding in adult chronic idiopathic thrombocytopenic Purpura (ITP) patients.

Primary Immunodeficiency Disorders

Indicated for treatment of primary immunodeficiency (PI) in adults and pediatric patients two years of age or older.

Drug Name: Gammaked, Gamunex-C (immune globulin [Human])

Indications

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Indicated for the treatment of CIDP to improve neuromuscular disability and impairment and for maintenance therapy to prevent relapse.

Idiopathic Thrombocytopenic Purpura (ITP)

Indicated for the treatment of patients with idiopathic thrombocytopenic purpura to raise platelet counts to prevent bleeding or to allow a patient with ITP to undergo surgery.

Primary Immunodeficiency Disorders

Indicated as replacement therapy of primary humoral immunodeficiency. This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

Drug Name: Immune globulin products (IVIG)

Off Label Uses

Bone Marrow Transplant (BMT) [8, 33-36]

Has been used to decrease the incidence of infections and graft versus host disease (GVHD) in patients 20 years of age and older who underwent bone marrow transplantation.

Dermatomyositis [8, 37-41]

In patients with treatment-resistant dermatomyositis, IVIG therapy resulted in improvements in muscle strength and neuromuscular symptoms.

Multifocal Motor Neuropathy (MMN) [8, 42-46]

In placebo-controlled trials, IVIG has been shown to improve strength and reduce disability and conduction block in patients with MMN.

Pediatric HIV [8, 47-49, 95]

Used to decrease the frequency of serious and minor bacterial infections; the frequency of hospitalization; and to increase the time free of serious bacterial infections in patients with HIV.

Guillain-Barre Syndrome [8, 50-52]

Considered to be equally effective as plasma exchange for the treatment of Guillain-Barre Syndrome.

Lambert-Eaton Myasthenic Syndrome [8, 53]

Shown to produce short-term improvement in strength in patients with Lambert-Eaton Myasthenic Syndrome.

Myasthenia Gravis [8, 89, 93]

A clinical study comparing IVIG with plasma exchange did not show a significant difference between the two treatments in patients with myasthenia gravis exacerbation. Several open studies support beneficial affects of IVIG in treating myasthenia gravis.

Relapsing Remitting Multiple Sclerosis [8, 62, 64]

Published studies indicate that IVIG may reduce the frequency of acute exacerbations and provide symptomatic relief in patients with relapsing-remitting forms of multiple sclerosis.

Stiff-Person Syndrome [8, 103-104]

The efficacy of IVIG for the treatment of stiff-person syndrome was demonstrated in a randomized, double-blind, placebo-controlled, crossover trial.

Polymyositis [75, 77]

Found to be effective in reversing chronic polymyositis previously unresponsive to immunosuppressive therapy.

Drug Name: Gammagard liquid (immune globulin [Human])

Indications

Primary immunodeficiency disorder

Indicated as replacement therapy for primary humoral immunodeficiency (PI) in adult and pediatric patients two years of age or older.

Multifocal Motor Neuropathy [MMN]

Indicated as a maintenance therapy to improve muscle strength and disability in adult patients with Multifocal Motor Neuropathy [MMN].

Drug Name: Gammaplex (immune globulin [Human])

Indications

Primary immunodeficiency disorder

Indicated for replacement therapy in adults with primary humoral immunodeficiency (PI). This includes, but is not limited to, the humoral immune defect in common variable immunodeficiency, X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

Chronic Immune Thrombocytopenic Purpura (ITP)

Indicated for the treatment of adults with chronic immune thrombocytopenic purpura (ITP) to raise platelet counts.

Drug Name: Octagam 10% (immune globulin [Human])

Indications

Chronic Immune Thrombocytopenic Purpura

Indicated in chronic immune thrombocytopenic purpura to rapidly raise platelet counts to control or prevent bleeding in adults.

Drug Name: Cytogam (human cytomegalovirus immune globulin liquid)

Indications

Cytomegalovirus Disease Prophylaxis

Indicated for the prophylaxis of cytomegalovirus disease associated with transplantation of kidney, lung, liver, pancreas and heart. In transplants of these organs other than kidney from CMV seropositive donors into seronegative recipients, prophylactic CMV-IGIV should be considered in combination with ganciclovir.

Drug Name: Varizig (varicella zoster immune globulin [human] liquid)

Indications

Post-exposure prophylaxis of varicella

Indicated for post-exposure prophylaxis of varicella in high risk individuals. High risk groups include: •immunocompromised children and adults, •newborns of mothers with varicella shortly before or after delivery, •premature infants, •neonates and infants less than one year of age, •adults without evidence of immunity, •pregnant women. Limitations of Use: There is no convincing evidence that Varizig reduces the incidence of chickenpox infection after exposure to VZV. There is no convincing evidence that established infections with VZV can be modified by Varizig administration. There is no indication for the prophylactic use of Varizig in immunodeficient children or adults when there is a past history of varicella, unless the patient is undergoing bone marrow transplantation.

2 . Criteria

Product Name: Intravenous or subcutaneous immune globulins (IVIG or SCIG)

Diagnosis	Primary Immunodeficiency Syndrome
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 For patients with a primary immunodeficiency syndrome [1-6, 69, 73-74, 78-84, 109, I, J]

AND

2 Clinically significant functional deficiency of humoral immunity as evidenced by one of the following: [90]

2.1 Documented failure to produce antibodies to specific antigens

OR

2.2 History of significant recurrent infections

Product Name: Intravenous immune globulins (IVIG)

Diagnosis	Idiopathic Thrombocytopenic Purpura (ITP)
Approval Length	6 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of idiopathic thrombocytopenic purpura (ITP) [3, 5, 74, 80-82, 109]

AND

2 Documented platelet count of less than 50 x 10^9 / L [105]

Product Name: Intravenous immune globulins (IVIG)

Diagnosis	Kawasaki Disease (KD) [5, 19-21]
Approval Length	1 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Kawasaki Disease [5]

Product Name: Intravenous immune globulins (IVIG)

Diagnosis	B-cell Chronic Lymphocytic Leukemia (CLL) [5 ,22-26]
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of B-cell chronic lymphocytic leukemia (CLL) [5]

AND

2 One of the following:

2.1 Documented hypogammaglobulinemia (IgG less than 500 mg/dL) [25, 26, 98, B]

OR

2.2 History of bacterial infection(s) associated with B-cell CLL [25-27, 98, A]

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [27-32, 67, 70, C, H]
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) as confirmed by all of the following [97, C]:

1.1 Progressive symptoms present for at least 2 months

AND

1.2 Symptomatic polyradiculoneuropathy as indicated by one of the following:

1.2.1 Progressive or relapsing motor impairment of more than one limb

OR

1.2.2 Progressive or relapsing sensory impairment of more than one limb

AND

1.3 Electrophysiologic findings when three of the following four criteria are present:

- Partial conduction block of 1 or more motor nerve
- Reduced conduction velocity of 2 or more motor nerves
- Prolonged distal latency of 2 or more motor nerves
- Prolonged F-wave latencies of 2 or more motor nerves or the absence of F waves

AND

1.4 Both of the following findings following lumbar puncture:

1.4.1 White blood cell count less than 10/mm^3

AND

1.4.2 Elevated CSF protein

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [27-32, 67, 70, C, H]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to therapy as measured by an objective scale [eg, Rankin, Modified Rankin, Medical Research Council (MRC) scale][97, H, P]:

AND

2 Documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect [P]

Product Name: Gamastan S/D

Diagnosis	Hepatitis A
Approval Length	1 Course of therapy
Guideline Type	Prior Authorization

Approval Criteria

1 For prophylaxis of Hepatitis A before or soon after exposure [69]

AND

2 Patient does not have clinical manifestations of hepatitis A[69]

AND

3 Patient does not have exposure to hepatitis A for more than 2 weeks previously [69]

Product Name: Gamastan S/D

Diagnosis	Measles (Rubeola)
Approval Length	1 Course of therapy
Guideline Type	Prior Authorization

Approval Criteria

1 For use in susceptible individuals exposed to measles fewer than 6 days previously [69]

AND

2 Patient is not receiving measles vaccine at the same time [69]

Product Name: Gamastan S/D

Diagnosis	Varicella
Approval Length	1 Course of therapy
Guideline Type	Prior Authorization

Approval Criteria

1 For passive immunization against varicella [69]

AND

2 Patient is immunosuppressed [69]

AND

3 Varicella Zoster Immune Globulin (Human) vaccine is not available

Product Name: Gamastan S/D

Diagnosis	Rubella
Approval Length	1 Course of therapy

Guideline Type	Prior Authorization

Approval Criteria

1 For pregnant women who are exposed or susceptible to Rubella [69]

AND

2 Patient will not consider a therapeutic abortion [69]

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Bone Marrow Transplantation (off-label) [33-36]
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Confirmed allogeneic bone marrow transplant within the last 100 days [33-35, D]

AND

2 Documented severe hypogammaglobulinemia (IgG less than 400 mg/dL) [33, D]

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	HIV(off-label) [47-79, 95]
Approval Length	12 Month

Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of HIV disease [47, 95, K]

AND

2 Patient is less than or equal to 13 years of age [95, 100]

AND

3 One of the following:

3.1 Documented hypogammaglobulinemia (IgG less than 400 mg/dL) [51, L]

OR

3.2 Functional antibody deficiency as demonstrated by one of the following: [99]

- Poor specific antibody titers
- Recurrent bacterial infections

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Multifocal Motor Neuropathy (off-label) [42-46]
Approval Length	12 Month
Therapy Stage	Initial Authorization

Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multifocal motor neuropathy (MMN) as confirmed by all of the following [96, 107, 108, N]:

1.1 Weakness with slowly progressive or stepwise progressive course over at least one month

AND

1.2 Asymmetric involvement of two or more nerves

AND

1.3 Absence of both of the following:

1.3.1 Motor neuron signs

AND

1.3.2 Bulbar signs

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Multifocal Motor Neuropathy (off-label) [42-46]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to therapy as measured by an objective scale [eg, Rankin, Modified Rankin, Medical Research Council (MRC) scale] [96,108]

AND

2 Documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Relapsing-Remitting Multiple Sclerosis (off-label) [62-64]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of relapsing remitting multiple sclerosis (RRMS) [62, 64, 75, 95, G]

AND

2 Documentation of an MS exacerbation or progression (worsening) of the patient's clinical status from the visit prior to the one prompting the decision to initiate immune globulin therapy. [62, 64, 75, 95, G, M, O]

AND

3 History of failure, contraindication, or intolerance to two of the following agents: [64, G, M,

O]

- Aubagio (teriflunomide)
- Avonex (interferon beta-1a)
- Betaseron (interferon beta-1b)
- Copaxone (glatiramer acetate)
- Extavia (interferon beta-1b)
- Gilenya (Fingolimod)
- Rebif (interferon beta-1a)
- Tecfidera (dimethyl fumarate)
- Tysabri (natalizumab)

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Relapsing-Remitting Multiple Sclerosis (off-label) [62-64]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 The prescriber maintains and provides chart documentation of the patient's evaluation, including both of the following [62, 64, 75, 95, O]:

1.1 Findings of interval examination including neurological deficits incurred

AND

1.2 Assessment of disability (eg, Expanded Disability Status Score [EDSS], Functional Systems Score [FSS], Multiple Sclerosis Functional Composie [MSFC], Disease Steps [DS])

AND

2 Stable or improved disability score (eg, EDSS, FSS, MSFC, DS)[62, 64, 75, 95]

AND

3 Documentation of decreased number of relapses since starting immune globulin therapy [62, 64, 75, 95]

AND

4 Diagnosis continues to be the relapsing-remitting form of MS (RRMS)

AND

5 Documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Myasthenia Gravis Exacerbation (off-label) [57-60]
Approval Length	3 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of generalized myasthenia gravis [57, 89, 93, F, R]

AND

2 Evidence of myasthenic exacerbation, defined by one of the following symptoms in the last month:[57, 89, 93, F, R]

2.1 Difficulty swallowing

OR

2.2 Acute respiratory failure

OR

2.3 Major functional disability responsible for the discontinuation of physical activity

AND

3 Concomitant immunomodulator therapy (eg, azathioprine, mycophenolate mofetil, cyclosporine), unless contraindicated, will be used for long-term management of myasthenia gravis [57, 89, 93, F, R]

AND

4 Prescribed by or in consultation with a neurologist

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Stiff Person Syndrome (off-label) [65]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of stiff-person syndrome [67, 103-104]

AND

2 History of failure, contraindication or intolerance to GABAergic medication (eg, baclofen, benzodiazepines)[67, 103-104]

AND

3 History of failure, contraindication or intolerance to immunosuppressive therapy (eg, azathioprine, corticosteroids) [67, 103-104]

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Stiff Person Syndrome (off-label) [65]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Dermatomyositis and Polymyositis (off-label) [37-41, 75, 77]

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following diagnoses [41]:

- Dermatomyositis
- Polymyositis

AND

2 History of failure, contraindication, or intolerance to immunosuppressive therapy (eg, azathioprine, corticosteroids, cyclophosphamide, methotrexate)[41, Q]

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Dermatomyositis and Polymyositis (off-label) [37-41, 75, 77]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Guillain-Barre Syndrome (off-label) [50-52]
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Guillain-Barre Syndrome

AND

2 Patients with severe disease requiring aid to walk [52, E]

AND

3 Onset of neuropathic symptoms within the last four weeks [52, E]

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Guillain-Barre Syndrome (off-label) [50-52]
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Lambert-Eaton Myasthenic Syndrome (off-label) [53]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Lambert-Eaton Myasthenic Syndrome (LEMS) [53]

AND

2 History of failure, contraindication, or intolerance to immunomodulator monotherapy (eg, azathioprine, corticosteroids) [101-102]

AND

3 Concomitant immunomodulator therapy (eg, azathioprine, corticosteroids), unless contraindicated, will be used for long-term management of LEMS [101-102]

Product Name: Intravenous immune globulin (IVIG)

Diagnosis	Lambert-Eaton Myasthenic Syndrome (off-label) [53]
Approval Length	12 Month

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect

Product Name: Cytogam

Diagnosis	Prophylaxis for CMV Infection
Approval Length	16 Week
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Both of the following:

1.1.1 Patient requires prophylaxis for CMV infection following kidney transplantation

AND

1.1.2 Patient is CMV- seronegative and organ donor is CMV-seropositive

OR

1.2 All of the following:

1.2.1 Patient requires prophylaxis for CMV infection following liver, heart, lung, or pancreas transplantation

AND

1.2.2 Patient is CMV- seronegative and organ donor is CMV-seropositive

AND

1.2.3 Used in combination with ganciclovir or valganciclovir unless the patient has a hypersensitivity to, is intolerant of, or therapy is deemed inappropriate

Product Name: Varizig

Diagnosis	Varicella
Approval Length	1 Dose
Guideline Type	Prior Authorization

Approval Criteria

1 For passive immunization or post exposure-prophylaxis of varicella

AND

2 Patient is considered a high risk individual (e.g., immune compromised, pregnant woman, newborn of mother with varicella, premature infant, and infant less than 1 year old)

AND

3 Prescribed immune globulin is being used intramuscularly

3 . Endnotes

A. Guidelines from the British Committee for Standards in Haematology [23] and the NCCN[26] state that IVIG therapy may be beneficial in patients with recurrent infections. Clinical studies show that IVIG reduces the number of bacterial infections, but not viral or fungal infections. [26]
B. Based on inclusion criteria from Molica et al. [26]
C. According to published data, there appears to be no difference in efficacy among IVIG, plasma exchange, and corticosteroids. [27, 29, 32]
D. A controlled trial indicated that treatment with IVIG beyond three months was associated with a delayed recovery of humoral immunity, and the rate of infections after two years of treatment was increased significantly in IVIG recipients. [37] Centers for Disease Control and Prevention, Infectious Disease Society of America, and American Society of Blood and Marrow Transplantation guidelines recommended routine IVIG use to prevent bacterial infections among BMT recipients with unrelated marrow grafts who experience severe hypogammaglobulinemia (e.g., IgG < 400 mg/dl) within the first 100 days after transplant. [33]
E. The American Academy of Neurology recommends that IVIG is for patients with GBS who require aid to walk within 2 weeks from the onset of neuropathic symptoms. [52]
F. The effectiveness of IVIG for moderate-to-severe but stable myasthenia gravis, or for moderate exacerbations of myasthenia gravis have not been demonstrated in adequately controlled trials. [60] IVIG may be as effective as plasma exchange for patients with acute exacerbations of myasthenia gravis [57]. The indications for the use of IVIG are the same as those for plasma exchange: to produce rapid improvement to help the patient through a difficult period of myasthenic weakness. It has the advantages of not requiring special equipment or large-bore vascular access. [71] The usual dose of immune globulin is 400 mg per kilogram per day for five successive days. The improvement rate after immune globulin treatment, calculated from eight published reports, was 73 percent, but this figure is likely to be biased by selective reporting of positive uncontrolled trials. In patients who respond, improvement begins within four to five days. The effect is temporary but may be sustained for weeks to months, allowing intermittent long-term therapy in patients with otherwise refractory disease.
G. Guidelines from the American Academy of Neurology [64] state that interferon Beta or glatirimer are appropriate treatments for patients who have relapsing-remitting multiple sclerosis. The guidelines state that it is only possible that IVIG reduces the attack rate in RRMS, and that current evidence suggests IVIG is of little benefit with regard to slowing disease progression.
H. Treatment for CIDP includes corticosteroids such as prednisone, which may be prescribed alone or in combination with immunosuppressant drugs. [70] Plasmapheresis and intravenous immunoglobulin (IVIG) therapy are effective. IVIG may be used even as

a first-line therapy. Physiotherapy may improve muscle strength, function and mobility, and minimize the shrinkage of muscles and tendons and distortions of the joints.

I. Subcutaneous formulations of immune globulin are available for the treatment of patients with primary immune deficiency. Subcutaneous infusions may be an alternative for patients with adverse effects to intravenous infusions of immune globulin or with poor venous access. Other advantages include decreased cost of administration, independence from scheduled home nursing visits, better maintenance of intravenous immune globulin trough levels, and a serum IgG profile (smaller variation in the peak and trough IgG concentrations compared to intravenous administration) that is similar to that in a normal population. Disadvantages include more frequent infusions and local reactions. [75]
J. There are good data to show that all immune globulins (IVIG/SCIG) are effective for primary immunodeficiency. There are no data for SCIG for indications other than PI. Efficacy is a class effect for all immune globulins products. It is appropriate to combine all IVIG/SCIG products as they are used interchangeably for PI; can combine all IVIG for other indications. Gamastan S/D (IMIG) has unique indications and should be available on the formulary. [94]
K. IVIG has been used in children with symptomatic human immunodeficiency virus (HIV) infection who are immunosuppressed in association with acquired immunodeficiency syndrome (AIDS) or AIDS-related complex (ARC) in an attempt to control or prevent infections and improve immunologic parameters. Results of studies in adults and children with symptomatic HIV infection indicate that IVIG, used in dosages similar to those used for replacement therapy in patients with primary immunodeficiencies, reduces the incidence of recurrent bacterial infections and sepsis, including upper respiratory tract infections. [95]
L. The ACIP, AAP, CDC, National Institutes of Health (NIH), HIV Medicine Association of the Infectious Diseases Society of America (IDSA), Pediatric Infectious Diseases Society, and other experts state that HIV-infected infants and children who have hypogammaglobulinemia (IgG less than 400 mg/dL) should receive IVIG (400 mg/kg once every 2–4 weeks) to prevent serious bacterial infections. [95]
M. Per expert consultant regarding MS: IVIG is only used in acute, severe MS. IVIG is used for bad relapses of MS with significant neurological dysfunction when a patient is breaking through their regular maintenance medications. It takes about 3 months to see if there is improvement in MS and one cannot say a patient has failed a medication if they have a breakthrough episode of MS within this 3 month period [106].
N. Per expert consultant regarding multifocal motor neuropathy: the EFNS guidelines [108] as outlined on page 344 and in the table are fairly reasonable: 1. Weakness with slowly progressive or stepwise progressive course 2. Asymmetric involvement of two or more nerves 3. Absence of upper motor neuron signs and bulbar signs [107].
O. Per expert consultant regarding MS:there is no data to support the initial length of ivig treatment in MS. I would suggest 3 months and then reevaluate. An appropriate length of time for reauthorization of ivig is 12 months. Patients who receive IVIG for RRMS should be in acute exacerbation, should have tried steroids, have documentation of inability to tolerate ohter disease modifying drugs, as well as show progression of disease. IVIG should be used 2nd or 3rd line if other injectable disease modifying drugs are not tolerated. Guidelines do not support IVIG as first line treatment for MS [107].
P. Per expert consultant regarding CIDP: It is important to reevaluate a patient after initial treatment. Some patients may need changes in dosing intervals due to wearing off of a dose within 2-3 weeks. Treatment can be lifelong for some patient [107].
Q. Per expert consultant regarding dermatomyositis: It is reasonable to ask a patient to try steroids prior to treatment with IVIG. [107].

R. Per expert consultant regarding MG: IVIG should be used in patients with moderate to severe myasthenia gravis with acute exacerbation. Most MDs favor plasma exchange for maintenance therapy in MG patients. Myasthenic exacerbation= myasthenic crisis. [107]

4 . References

1. Gammagard Liquid Prescribing Information. Baxter Healthcare Corporation September 2013.
2. Gamunex Prescribing Information. Telecris Biotherapeutics, Inc. June 2012.
3. Carimune NF Prescribing Information. CSL Behring LLC. September 2013.
4. Flebogamma Prescribing Information. Grifols Biologicals, Inc. September 2004.
5. Gammagard S/D Prescribing Information. Baxter Healthcare Corporation. September 2013.
6. Gammar-P I.V. Prescribing Information. ZLB Behring LLC. August 2004.
7. Medicare Part B versus Part D Coverage Issues. Centers for Medicare & Medicaid Services Web site. Available at: http://www.cms.hhs.gov/pdps/PartB_DdocRevised3-30-05.pdf. Accessed July 25, 2005
8. United States Pharmacopeia Drug Information: Drug Information for the Health Care Professional. 25th ed. Greenwood Village, CO: Thomson Micromedex; 2005:1652-1658.
9. Imbach P, Barandun S, d'Apuzzo V, et al. High-dose intravenous gammaglobulin for idiopathic thrombocytopenic purpura in childhood. Lancet. 1981 6;1:1228-31.
10. Newland AC, Treleaven JG, Minchinton RM, Waters AH. High-dose intravenous IgG in adults with autoimmune thrombocytopenia. Lancet. 1983;1:84-7.
11. Imbach P, Wagner HP, Berchtold W, Gaedicke G, Hirt A, Joller P, Mueller-Eckhardt C, Muller B, Rossi E, Barandun S. Intravenous immunoglobulin versus oral corticosteroids in acute immune thrombocytopenic purpura in childhood. Lancet. 1985;2:464-8.
12. Bussel JB, Goldman A, Imbach P, Schulman I, Hilgartner MW. Treatment of acute idiopathic thrombocytopenia of childhood with intravenous infusions of gammaglobulin. J Pediatr. 1985;106:886-90.
13. Godeau B, Lesage S, Divine M, Wirquin V, Farcet JP, Bierling P. Treatment of adult chronic autoimmune thrombocytopenic purpura with repeated high-dose intravenous immunoglobulin. Blood. 1993;82:1415-21
14. Kurlander R, Coleman RE, Moore J, Gockerman J, Rosse W, Siegal R. Comparison of the efficacy of a two-day and a five-day schedule for infusing intravenous gamma globulin in the treatment of immune thrombocytopenic purpura in adults. Am J Med. 1987;83(4A):17-24.
15. Jacobs P, Wood L, Novitzky N. Intravenous gammaglobulin has no advantages over oral corticosteroids as primary therapy for adults with immune thrombocytopenia: a prospective randomized clinical trial. Am J Med. 1994;97:55-9.
16. George JN, Woolf SH, Raskob GE, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood. 1996;88:3-40.
17. British Committee for Standards in Haematology General Haematology Task Force. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. Br J Haematol. 2003;120:574-96.
18. Bussel JB, Pham LC, Aledort L, Nachman R. Maintenance treatment of adults with chronic refractory immune thrombocytopenic purpura using repeated intravenous infusions of gammaglobulin. Blood. 1988;72:121-7.

19. Newburger JW, Takahashi M, Beiser AS, et al. A single intravenous infusion of gamma globulin as compared with four infusions in the treatment of acute Kawasaki syndrome. N Engl J Med. 1991;324:1633-9.
20. Newburger JW, Takahashi M, Burns JC, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. N Engl J Med. 1986;315:341-7.
21. Terai M, Shulman ST. Prevalence of coronary artery abnormalities in Kawasaki disease is highly dependent on gamma globulin dose but independent of salicylate dose. J Pediatr 1997;131:888–93.
22. Cooperative Group for the Study of Immunoglobulin in Chronic Lymphocytic Leukemia: Intravenous immunoglobulin for the prevention of infection in chronic lymphocytic leukemia: a randomized, controlled trial. N Engl J Med. 1988;319:902-907.
23. Oscier D, Fegan C, Hillmen P, et al. Guidelines on the diagnosis and management of chronic lymphocytic leukaemia. Br J Haematol. 2004;125:294-317.
24. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Non-Hodgkin's Lymphoma, version 1.2013. http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf. Accessed July 3, 2013.
25. Gamm H, Huber C, Chapel H, Lee M, Ries F, Dicato MA. Intravenous immune globulin in chronic lymphocytic leukaemia. Clin Exp Immunol. 1994;97 Suppl 1:17-20.
26. Molica S, Musto P, Chiurazzi F, et al. Prophylaxis against infections with low-dose intravenous immunoglobulins (IVIG) in chronic lymphocytic leukemia. Results of a cross-over study. Haematologica. 1996;81:121-126.
27. Koller H, Kieseier BC, Jander S, Hartung HP. Chronic inflammatory demyelinating polyneuropathy. N Engl J Med. 2005;352(13):1343-56.
28. Saperstein DS, Katz JS, Amato AA, Barohn RJ. Clinical spectrum of chronic acquired demyelinating polyneuropathies. Muscle Nerve. 2001;24:311-24.
29. Hughes R, Bensa S, Willison H, et al; Inflammatory Neuropathy Cause and Treatment (INCAT) Group. Randomized controlled trial of intravenous immunoglobulin versus oral prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy. Ann Neurol. 2001;50:195-201.
30. Mendell JR, Barohn RJ, Freimer ML, et al; Working Group on Peripheral Neuropathy. Randomized controlled trial of IVIg in untreated chronic inflammatory demyelinating polyradiculoneuropathy. Neurology. 2001;56:445-9.
31. Dyck PJ, Litchy WJ, Kratz KM, et al.. A plasma exchange versus immune globulin infusion trial in chronic inflammatory demyelinating polyradiculoneuropathy. Ann Neurol. 1994;36:838-45.
32. van Schaik IN, Winer JB, de Haan R, Vermeulen M. Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy: a systematic review. Lancet Neurol. 2002;1:491-8.
33. Centers for Disease Control and Prevention; Infectious Disease Society of America; American Society of Blood and Marrow Transplantation. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. MMWR Recomm Rep. 2000;49(RR-10):1-125.
34. Sullivan KM, Kopecky KJ, Jocom J, et al. Immunomodulatory and antimicrobial efficacy of intravenous immunoglobulin in bone marrow transplantation. N Engl J Med. 1990;323:705-12.
35. Sullivan KM, Storek J, Kopecky K, et al. A controlled trial of long-term administration of intravenous immunoglobulin to prevent late infection and chronic graft-vs.-host disease after marrow transplantation: clinical outcome and effect on subsequent immune recovery. Biol Blood Marrow Transplant. 1996;2:44-53.

36. Sokos DR, Berger M, Lazarus HM. Intravenous immunoglobulin: appropriate indications and uses in hematopoietic stem cell transplantation. Biol Blood Marrow Transplant. 2002;8:117-30.
37. Dalakas MC, Illa I, Dambrosia JM, et al. A controlled trial of high-dose intravenous immune globulin infusions as treatment for dermatomyositis. N Engl J Med. 1993;329:1993-2000.
38. Danieli M, Malcangi G, Palmieri C, et al. Cyclosporin A and Intravenous Immunoglobulin Treatment in Polymyositis/Dermatomyositis. Ann Rheum Dis. 2002;61;37-41.
39. Cherin P, Herson S, Wechsler B, et al. Efficacy of intravenous gammaglobulin therapy in chronic refractory polymyositis and dermatomyositis: an open study with 20 adult patients. Am J Med. 1991;91:162-8.
40. Lang BA, Laxer RM, Murphy G, Silverman ED, Roifman CM. Treatment of dermatomyositis with intravenous gammaglobulin. Am J Med. 1991;91:169–72.
41. Drake LA, Dinehart SM, Farmer ER, et al. Guidelines of care for dermatomyositis. American Academy of Dermatology. J Am Acad Dermatol. 1996;34:824-9.
42. van Schaik IN, van den Berg LH, de Haan R, Vermeulen M. Intravenous immunoglobulin for multifocal motor neuropathy. Cochrane Database Syst Rev. 2005;(2):CD004429.
43. Federico P, Zochodne DW, Hahn AF, Brown WF, Feasby TE. Multifocal motor neuropathy improved by IVIg: randomized, double-blind, placebo-controlled study. Neurology. 2000;55:1256-62.
44. Van den Berg LH, Franssen H, Wokke JH. The long-term effect of intravenous immunoglobulin treatment in multifocal motor neuropathy. Brain. 1998;121:421-8.
45. Leger JM, Chassande B, Musset L, Meininger V, Bouche P, Baumann N. Intravenous immunoglobulin therapy in multifocal motor neuropathy: a double-blind, placebo-controlled study. Brain. 2001;124:145-53.
46. Van den Berg LH, Kerkhoff H, Oey PL, et al. Treatment of multifocal motor neuropathy with high dose intravenous immunoglobulins: a double blind, placebo controlled study. J Neurol Neurosurg Psychiatry. 1995;59:248-52.
47. Mofenson LM, Moye J Jr, Bethel J, Hirschhorn R, Jordan C, Nugent R. Prophylactic intravenous immunoglobulin in HIV-infected children with CD4+ counts of 0.20 x 10(9)/L or more. Effect on viral, opportunistic, and bacterial infections. The National Institute of Child Health and Human Development Intravenous Immunoglobulin Clinical Trial Study Group. JAMA. 1992;268:483-8.
48. Mofenson LM, Moye J Jr, Korelitz J, Bethel J, Hirschhorn R, Nugent R. Crossover of placebo patients to intravenous immunoglobulin confirms efficacy for prophylaxis of bacterial infections and reduction of hospitalizations in human immunodeficiency virus-infected children. The National Institute of Child Health and Human Development Intravenous Immunoglobulin Clinical Trial Study Group. Pediatr Infect Dis J. 1994;13:477-84.
49. U.S. Public Health Service (USPHS) and Infectious Diseases Society of America (IDSA). 2001 USPHS/IDSA Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus. Available at: http://www.aidsinfo.nih.gov/ContentFiles/OIpreventionGL07012001042.pdf Accessed November 6, 2005.
50. Plasma Exchange/Sandoglobulin Guillain-Barre Syndrome Trial Group. Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barre syndrome. Lancet. 1997;349:225-30.
51. van der Meche FG, Schmitz PI. A randomized trial comparing intravenous immune globulin and plasma exchange in Guillain-Barre syndrome. Dutch Guillain-Barre Study Group. N Engl J Med. 1992;326:1123-9

52. Hughes RA, Wijdicks EF, Barohn R, et al.; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: immunotherapy for Guillain-Barre syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2003;61:736-40.
53. Bain PG, Motomura M, Newsom-Davis J, et al. Effects of intravenous immunoglobulin on muscle weakness and calcium-channel autoantibodies in the Lambert-Eaton myasthenic syndrome. Neurology. 1996;47:678-83.
54. Winston DJ, Antin JH, Wolff SN, et al. A multicenter, randomized, double-blind comparison of different doses of intravenous immunoglobulin for prevention of graft-versus-host disease and infection after allogeneic bone marrow transplantation. Bone Marrow Transplant. 2001;28:187-96.
55. Cordonnier C, Chevret S, Legrand M, et al.; GREFIG Study Group. Should immunoglobulin therapy be used in allogeneic stem-cell transplantation? A randomized, double-blind, dose effect, placebo-controlled, multicenter trial. Ann Intern Med. 2003 1;139:8-18.
56. Immune Globulin. In: McEvoy GK, ed. AHFS 2004 Drug Information. Bethesda, MD: American Society of Health-System Pharmacists; 2004:3154-3164.
57. Gajdos P, Chevret S, Clair B, Tranchant C, Chastang C. Clinical trial of plasma exchange and high-dose intravenous immunoglobulin in myasthenia gravis. Myasthenia Gravis Clinical Study Group. Ann Neurol. 1997;41:789-96.
58. Wegner B, Ahmed I. Intravenous immunoglobulin monotherapy in long-term treatment of myasthenia gravis. Clin Neurol Neurosurg. 2002;105:3-8.
59. Jongen JL, van Doorn PA, van der Meche FG. High-dose intravenous immunoglobulin therapy for myasthenia gravis. J Neurol. 1998;245:26-31.
60. Gajdos P, Chevret S, Toyka K. Intravenous immunoglobulin for myasthenia gravis. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD002277.
61. Sharshar T, Chevret S, Mazighi M, et al. Validity and reliability of two muscle strength scores commonly used as endpoints in assessing treatment of myasthenia gravis. J Neurol. 2000;247:286-90.
62. Fazekas F, Deisenhammer F, Strasser-Fuchs S, Nahler G, Mamoli B. Randomised placebo-controlled trial of monthly intravenous immunoglobulin therapy in relapsing-remitting multiple sclerosis. Austrian Immunoglobulin in Multiple Sclerosis Study Group. Lancet. 1997;349:589-93.
63. Achiron A, Gabbay U, Gilad R, et al. Intravenous immunoglobulin treatment in multiple sclerosis. Effect on relapses. Neurology. 1998;50:398-402.
64. Goodin DS, Frohman EM, Garmany GP Jr, Halper J, Likosky WH, Lublin FD, Silberberg DH, Stuart WH, van den Noort S. Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology 2002;58:169-78.
65. Dalakas MC, Fujii M, Li M, Lutfi B, Kyhos J, McElroy B. High-dose intravenous immune globulin for stiff-person syndrome. N Engl J Med. 2001;345:1870-6.
66. Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation. 2004;110:2747-71.
67. Hughes RA, Bouche P, Cornblath DR, Evers E, Hadden RD, Hahn A, Illa I, Koski CL, Leger JM, Nobile-Orazio E, Pollard J, Sommer C, Van den Bergh P, van Doorn PA, van Schaik IN. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating

polyradiculoneuropathy: report of a joint task force of the EFNS and PNS. Eur J Neurol 2006 Apr;13(4):326-32.
68. Vivaglobin Prescribing Information. CSL Behring LLC. April 2010.
69. Gamastan S/D Prescribing Information. Grifols. September 2013.
70. National Institute of Neurological Disorders and Stroke. Available at: http://www.ninds.nih.gov/disorders/cidp/cidp.htm. Accessed January 25, 2008.
71. Drachman DB. Myasthenia Gravis. N Engl J Med. 1994;1797-1810.
72. Intravenous immunoglobulins - licensed and unlicensed uses. Available at: http://www.nelm.nhs.uk/Record%20Viewing/viewRecord.aspx?id=560283 . Accessed June 4, 2008.
73. Hizentra Prescribing Information. CSL Behring LLC. January 2015.
74. Privigen Prescribing Information. CSL Behring LLC. November 2013.
75. DRUGDEX System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed July 23, 2013.
76. Polygam S/D Prescribing Information. Baxter Healthcare Corporation. August 2002.
77. Apostolski, ES, Doorn PV, Gilhus NE, et al. EFNS Task Force. EFNS guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases. European Journal of Neurology 2008; 15:893-908.
78. Flebogamma 5% DIF Prescribing Information. Instituto Grifols. August 2014.
79. Flebogamma 10% DIF Prescribing Information. Instituto Grifols. September 2013.
80. Gammaplex 5% Prescribing Information. Bio Products Laboratory. September 2015.
81. Gamunex-C 10% Prescribing Information. Talecris Biotherapeutics. July 2014.
82. Gammaked 10% Prescribing Information. Kedrion Biopharma, Inc. September 2013.
83. Bivigam Prescribing Information. Biotest Pharmaceuticals. June 2013.
84. Octagam 5% Prescribing Information. Octapharma USA Inc. September 2009.
85. A Message from CSL Behring to Current Vivaglobin Patients in the United States April 4, 2011. Available at: http://www.vivaglobin.com. Accessed January 11, 2013.
86. Baxter Healthcare Corporation.S Dear Healthcare Professional letter. August, 2006.
87. U.S. Department of Health and Human Services (DHHS). Analysis of Supply, Distribution, Demand, and Access Issues Associated with Immune Globulin Intravenous (IGIV). Executive Summary 2007. Available at: http://aspe.hhs.gov/sp/reports/2007/IGIV/execsum.htm. Accessed January 11, 2013.
88. American College of Allergy, Asthma and Immunology (ACAAI) Web Site: Eight Guiding Principles for Effective Use of IVIG for Patients with Primary Immunodeficiency. December 2011. http://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Resources/IVIG-guiding-principles.pdf. Accessed January 16, 2013.
89. Orange JS, Hossny EM, Weiler CR, et al. Use of intravenous immunoglobulin in human disease: a review of evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology. J Allergy Clin Immunol. 2006;117:S525-S553.
90. Bonilla FA, Bernstein L, Khan DA, et. al. Practice management for the diagnosis and management of primary immunodeficiency. Ann Allergy Asthma Immunol. 2005;94(suppl):S1-S63.
91. Neunert C, Lim W, Crowther M, et al. American Society of Hematology. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011 Apr 21;117(16):4190-207.
92. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010 Jan 14;115(2):168-86.

93. Patwa HS, Chaudhry V, Katzberg H, et al. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2012 Mar 27;78(13):1009-15.
94. Per clinical consult with an allergist/immunologist, January 29, 2013.
95. AHFS Drug information Lexicomp. Available at http://online.lexi.com/lco/action/doc/retrieve/docid/complete_ashp/413799. Accessed July 23, 2013.
96. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society--first revision. J Peripher Nerv Syst. 2010 Dec;15(4):295-301. doi: 10.1111/j.1529-8027.2010.00290.x.
97. Van den Bergh PY, Hadden RD, Bouche P, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies [trunc]. Eur J Neurol 2010 Mar?17(3):356-63.
98. Oscier D, Fegan C, Hillmen P, et al. Guidelines on the diagnosis and management of chronic lymphocytic leukaemia. Br J Haematol. 2004;125:294-317.
99. Centers for Disease Control and Prevention. Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children. MMWR 2009;58(No. RR-11):11-12.
100. Yap PL. Does intravenous immune globulin have a role in HIV-infected patients? Clin Exp Immunol. 1994 Jul;97 Suppl 1:59-67.
101. Maddison P. Treatment in Lambert-Eaton myasthenic syndrome. Ann N Y Acad Sci. 2012 Dec;1275:78-84. doi: 10.1111/j.1749-6632.2012.06769.x.
102. Sanders DB. Lambert-Eaton myasthenic syndrome: diagnosis and treatment. Ann N Y Acad Sci. 2003 Sep;998:500-8.
103. McKeon A, Robinson MT, McEvoy KM, et al. Stiff-man syndrome and variants: clinical course, treatments, and outcomes. Arch Neurol. 2012 Feb;69(2):230-8. doi: 10.1001/archneurol.2011.991.
104. Levy LM, Dalakas MC, Floeter MK. The stiff-person syndrome: an autoimmune disorder affecting neurotransmission of gamma-aminobutyric acid. Ann Intern Med. 1999 Oct 5;131(7):522-30.
105. Stasi R, Evangelista ML, Stipa E, et al. Idiopathic thrombocytopenic purpura: current concepts in pathophysiology and management. Thrombosis and Haemostasis 2008;99(1):4-13.
106. Per clinical consult with a neurologist, July 23, 2013.
107. Per clinical consult with a neurologist, August 15, 2013.
108. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society--first revision. J Peripher Nerv Syst. 2010 Dec;15(4):295-301. doi: 10.1111/j.1529-8027.2010.00290.x.
109. Octagam 10% Prescribing Information. Octapharma USA Inc. August 2014.
110. Cytogam Prescribing Information. CSL Behring. August 2012.
111. Varizig Prescribing Information. Cangene Biopharma. August 2015.

Prior Authorization Guideline

GL-17300 Increlex (mecasermin [rDNA origin])

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 4/4/2006; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Increlex (mecasermin [rDNA origin]) injection

Indications

Severe Primary IGF-1 deficiency (Primary IGFD)

Indicated for the treatment of growth failure in children with severe primary IGF-1 deficiency (Primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH. Severe Primary IGFD is defined by: height standard deviation score less than or equal to -3.0, basal IGF-1 standard deviation score less than or equal to -3.0, and normal or elevated GH. Severe Primary IGFD includes classical and other forms of GH insensitivity. Patients with Primary IGFD may have mutations in the GH receptor (GHR), post-GHR signaling

pathway including the IGF-1 gene. They are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment. Increlex is not intended for use in subjects with secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids. Thyroid and nutritional deficiencies should be corrected before initiating Increlex treatment. Limitations of use: Increlex is not a substitute to GH for approved GH indications.

2 . Criteria

Product Name: Increlex

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following: [3, A]

1.1 All of the following:

1.1.1 Diagnosis of severe primary IGF-1 deficiency

AND

1.1.2 Height standard deviation score less than or equal to -3.0

AND

1.1.3 Basal IGF-1 standard deviation score less than or equal to -3.0

AND

1.1.4 Normal or elevated growth hormone

AND

1.1.5 Documentation of open epiphyses on last bone radiograph

AND

1.1.6 The patient will not be treated with concurrent growth hormone therapy [A]

OR

1.2 All of the following:

1.2.1 Diagnosis of growth hormone (GH) gene deletion in patients who have developed neutralizing antibodies to GH

AND

1.2.2 Documentation of open epiphyses on last bone radiograph

AND

1.2.3 The patient will not be treated with concurrent growth hormone therapy [A]

Notes	NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal. Increlex is not a substitute for GH for approved GH indications.

Product Name: Increlex

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria	
1 Growth increase of at least 2 cm/year over the previous year of treatment as documented by both of the following: [2, B] • Previous height and date obtained • Current height and date obtained **AND** **2** Both of the following: • Expected adult height is not obtained • Documentation of expected adult height goal	
Notes	NOTE: Increlex is not a substitute for GH for approved GH indications.

3 . Endnotes

A. Growth Hormone Deficiency (GHD) and severe Primary IGF-1 Deficiency (IGFD) are two distinct hormone disorders. Patients with severe Primary IGFD are not GH deficient, and therefore, exogenous GH treatment cannot be expected to resolve the patient's growth deficiency. [3]
B. Typically near-adult height is defined as bone age of 16 years or more for males and 14 years or more for females and a growth rate less than 2 cm/year for 1 year. [2]

4 . References

1. Increlex Prescribing Information. Ipsen Biopharmaceuticals, Inc., May 2014.

2. Mauras N, Attie KM, Reiter EO, Saenger P, Baptista J. High dose recombinant human growth hormone (GH) treatment of GH-deficient patients in puberty increases near-final height: a randomized, multicenter trial. Genentech, Inc., Cooperative Study Group. J Clin Endocrinol Metab. 2000;85(10):3653-60.
3. Increlex Web site. http://www.increlex.com/hcp-igf1-deficiencies.asp. Accessed August 25, 2014.

Prior Authorization Guideline

GL-32275 Infliximab

Formulary OptumRx SP

Formulary Note

Approval Date 10/25/2016

Revision Date 10/25/2016

Technician Note :

P&T Approval Date: 12/15/2009; P&T Revision Date: 2/25/2016, 8/19/2016 **Effective date 10/31/2016**

1 . Indications

Drug Name: Remicade (infliximab), Inflectra (infliximab)

Indications

Crohn's Disease (CD) Indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult and pediatric patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. Indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn's disease.

Ulcerative Colitis (UC) Indicated for reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in patients with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy.

Rheumatoid Arthritis (RA) Indicated, in combination with methotrexate, for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis.

Ankylosing Spondylitis (AS) Indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

Psoriatic Arthritis (PsA) Indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis.

Plaque Psoriasis Indicated for the treatment of adult patients with chronic severe (ie, extensive and /or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

Off Label Uses

Sarcoidosis Has been used for the treatment of refractory sarcoidosis. [2, 13, 14]

2 . Criteria

Product Name: Remicade, Inflectra

Diagnosis	Crohn's Disease or Fistulizing Crohn's Disease [A]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization
Approval Criteria	

1 One of the following diagnoses:

- Moderately to severely active Crohn's disease [B]
- Fistulizing Crohn's disease

AND

2 Prescribed by or in consultation with a gastroenterologist

AND

3 History of failure, contraindication, or intolerance to one of the following conventional therapies: [4]

- 6-mercaptopurine (Purinethol)
- Azathioprine (Imuran)
- Corticosteroids (e.g., prednisone, methylprednisolone)
- Methotrexate (Rheumatrex, Trexall)

AND

4 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

5 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Crohn's Disease or Fistulizing Crohn's Disease [A]
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to infliximab therapy

AND

2 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

3 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Ulcerative Colitis
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active ulcerative colitis

AND

2 Prescribed by or in consultation with a gastroenterologist

AND

3 History of failure, contraindication, or intolerance to one of the following conventional therapies: [5]

- 6-mercaptopurine (Purinethol)
- Aminosalicylate [e.g., mesalamine (Asacol, Pentasa, Rowasa), olsalazine (Dipentum), sulfasalazine (Azulfidine, Sulfazine)]
- Azathioprine (Imuran)
- Corticosteroids (e.g., prednisone, methylprednisolone)

AND

4 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

5 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Ulcerative Colitis
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to infliximab therapy

AND

2 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

3 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active RA

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 One of the following:

3.1 Patient is receiving concurrent therapy with methotrexate (Rheumatrex, Trexall)

OR

3.2 History of failure, contraindication, or intolerance to methotrexate (Rheumatrex,Trexall)

AND

4 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

5 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz

(tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to infliximab therapy

AND

2 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

3 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Ankylosing Spondylitis (AS)
Approval Length	12 Month

Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active ankylosing spondylitis

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to two NSAIDs [3,7]

AND

4 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

5 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Ankylosing Spondylitis (AS)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to infliximab therapy

AND

2 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

3 Patient is not receiving inflixikmab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Psoriatic Arthritis (PsA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active PsA

AND

2 Prescribed by or in consultation with one of the following:

- Dermatologist
- Rheumatologist

AND

3 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

4 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Psoriatic Arthritis (PsA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to infliximab therapy

AND

2 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

3 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Plaque Psoriasis
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic severe (ie, extensive and/or disabling) plaque psoriasis

AND

2 Prescribed by or in consultation with a dermatologist

AND

3 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

4 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade, Inflectra

Diagnosis	Plaque Psoriasis
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to infliximab therapy

AND

2 Patient is not receiving infliximab in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

3 Patient is not receiving infliximab in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade

Diagnosis	Sarcoidosis [Off-label] [13,14]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of sarcoidosis [13,14]

AND

2 History of failure, contraindication, or intolerance to corticosteroids (e.g., prednisone)

AND

3 Prescribed by or in consultation with a pulmonologist

AND

4 History of failure, contraindication, or intolerance to one immunosuppressant [e.g., methotrexate (Rheumatrex, Trexall), Cytoxan (cyclophosphamide), or Imuran (azathioprine)]

AND

5 Patient is not receiving Remicade in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

6 Patient is not receiving Remicade in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

Product Name: Remicade

Diagnosis	Sarcoidosis [Off-label] [2, 13,14]
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Remicade therapy

AND

2 Patient is not receiving Remicade in combination with a biologic DMARD [e.g., Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

AND

3 Patient is not receiving Remicade in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

3 . Endnotes

A. Per expert consultant, it is acceptable to combine the Crohn's disease criteria with the fistulizing Crohn's disease criteria, and remove any age requirements in order to receive Remicade. Patients should still be seen by a gastroenterologist and only be required to fail one of four treatment options: corticosteroids, 5-ASA, immunomodulators, or antibiotics. Requiring failure to more than 1 drug would not be appropriate as this would cause treatment delay and disease progression.
B. In the Remicade clinical study, moderate to severely active Crohnâ€™s disease was defined as a Crohn's Disease Activity Index (CDAI), greater than or equal to 220 and less than or equal to 400, inclusive. [1]
C. Remicade has not been studied in children with Crohnâ€™s disease < 6 years of age. Long term (greater than one year) safety and efficacy of Remicade in pediatric Crohnâ€™s disease patients have not been established in clinical trials. [1]
D. Methotrexate is used by most rheumatologists as the first line disease-modifying antirheumatic drug for patients with RA. This choice rests on the good effectiveness and safety profile of the drug, its low cost, and the availability of long-term follow-up data on

RA patients given methotrexate. In addition, recent data indicate that methotrexate can produce substantial survival benefits by reducing cardiovascular mortality in patients with RA. The recommended starting dosage for MTX in patients with RA should not be less than 10 mg/week and increase at 6 weeks interval to a maximum of 20 mg/week based on disease severity, patient related factors, and tolerance. [15]

4 . References

1. Remicade Prescribing Information. Janssen Biotech, Inc., November 2013.
2. DRUGDEX System [Internet database]. Greenwood Village, Colo: Truven Health Analytics. Updated periodically. Accessed September 29, 2014.
3. Milliman Care Guidelines. Ambulatory Care 18th Edition. Infliximab. Available at http://careweb.careguidelines.com/ed18/index.html. Accessed on July 23, 2014.
4. Lichtenstein GR, Hanauer SB, Sandborn WJ, and The Practice Parameters Committee of the American College of Gastroenterology. Management of Crohnâ€™s disease in adults. Am J Gastroenterol. 2009;104:465-483.
5. Kornbluth A, Sachar DB, and The Practice Parameters Committee of the American College of Gastroenterology. Ulcerative Colitis Practice Guidelines in Adults. Am J Gastroenterology. 2010;105:501-523.
6. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012;64:625-39.
7. van der Heijde, Sieper J, Maksymowych WP, et al. 2010 update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. Ann Rheum Dis. 2011;70:905-908.
8. Gottlieb A, Korman NJ, Gordon KB, et al. American Academy of Dermatology Guidelines for the Care and Management of Psoriasis and Psoriatic Arthritis. Section 2: Psoriatic arthritis: Overview and guidelines of care for treatment with an emphasis on the biologics. J Am Acad Dermatol 2008;58:851-64.
9. Menter A, Korman NJ, Elmets CA, et al. American Academy of Dermatology Guidelines for the Care and Management of Psoriasis and Psoriatic Arthritis. Section 3: Overview of psoriasis and guidelines of care for the treatment of psoriasis with topical therapies. J Am Acad Dermatol 2009;60:643-59.
10. Menter A, Korman NJ, Elmets CA, et al. American Academy of Dermatology Guidelines for the Care and Management of Psoriasis and Psoriatic Arthritis. Section 4: Overview of psoriasis and guidelines of care for the treatment of psoriasis with traditional systemic agents. J Am Acad Dermatol 2009;61:451-85.
11. Menter A, Korman NJ, Elmets CA, et al. American Academy of Dermatology Guidelines for the Care and Management of Psoriasis and Psoriatic Arthritis. Section 5: Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy. J Am Acad Dermatol 2010;62:114-35.
12. Menter A, Korman NJ, Elmets CA, et al. American Academy of Dermatology Guidelines for the Care and Management of Psoriasis and Psoriatic Arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: Case-based presentations and evidence-based conclusions. J Am Acad Dermatol 2011;65:137-74.
13. Baughman RP, Drent M, Kavuru M, et al. Infliximab therapy in patients with chronic sarcoidosis and pulmonary involvement Am J Respir Crit Care Med. 2006 Oct 1;174(7):795-802.

14. Rossman M, Newman LS, Baughman RP, et al. A double-blind, randomized, placebo-controlled trial of infliximab in active pulmonary sarcoidosis. 8th Meeting of the World Association of Sarcoidosis and other Granulomatous Disorder. June 12-15, 2005. Denver, CO. Abstract T-12.
15. Pavy S, Constantin A, Pham T, et al. Methotrexate therapy for rheumatoid arthritis: clinical practice guidelines based on published evidence and expert opinion. Joint Bone Spine 2006;73:388-95.
16. Inflectra prescribing information. Hospira. Lake Forest, IL. April 2016.

Prior Authorization Guideline

GL-17145 Injectable Immunosuppressants

Formulary OptumRx SP

Formulary Note

Approval Date 4/10/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 4/5/2004; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Nulojix (belatacept)

Indications

Prophylaxis of organ rejection in organ transplant

Indicated for prophylaxis of organ rejection in adult patients receiving a kidney transplant. Nulojix is to be used in combination with basiliximab induction, mycophenolate mofetil, and corticosteroids. Nulojix should only be used in patients who are Epstein-Barr virus (EBV) seropositive. Use of Nulojix for the prophylaxis of organ rejection in transplanted organs other than kidney has not been established.

Drug Name: Simulect (basiliximab)

Indications

Prophylaxis of organ rejection in organ transplant

Indicated for the prophylaxis of acute organ rejection in patients receiving renal transplantation when used as part of an immunosuppressant regimen that includes cyclosporine, USP (modified) and corticosteroids. [4] The efficacy of Simulect for the prophylaxis of acute rejection in recipients of other solid organ allografts has not been demonstrated.

Off Label Uses

Prophylaxis of organ rejection in organ transplant

Used for the prophylaxis of rejection in transplanted liver allograft. [7]

2 . Criteria

Product Name: Nulojix

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is 18 years of age or older

AND

2 The medication is being used for prevention of kidney transplant organ rejection

AND

3 Patient is immune to the Epstein-Barr virus (i.e., EBV seropositive)

AND

4 Prescriber is experienced in immunosuppressive therapy and management of transplant patients

AND

5 Patient is prescribed concurrent therapy with mycophenolate and corticosteroids

Product Name: Simulect

Guideline Type	Non Formulary

Approval Criteria

1 For prophylaxis of acute organ rejection of one of the following transplanted allografts:

- Renal (kidney) [1]
- Hepatic (liver) [2, 3]

Notes	Authorization will be issued for length of therapy.

3 . References

1. Orthoclone OKT3 Prescribing Information, Ortho Biotech Products, L.P,. May 2011.
2. Ineke JM, Berge T, Parlevliet KJ, et al. Guidelines for the optimal use of muromonab CD3 in transplantation. Bio Drugs. 1999;11(4):277-284.
3. European Association of Urology. Guidelines on renal transplantation. Updated in March 2009. Available at: http://www.uroweb.org/gls/pdf/Renal%20Transplantation%202010.pdf. Accessed on February 25, 2013.
4. Simulect Prescribing Information. Novartis Pharmaceuticals Corporation, October 2009.
5. Ponticelli C, Yussim A, Cambi V, et al. A randomized, double-blind trial of basiliximab immunoprophylaxis plus triple therapy in kidney transplant recipients. Transplantation. 2001; 72:1261-7.
6. Kahan BD, Rajagopalan PR, Hall M. Reduction of the occurrence of acute cellular rejection among renal allograft recipients treated with basiliximab, a chimeric anti-interluekin-2-receptor monoclonal antibody. United States Simulect Renal Study Group. Transplantation. 1999;67(2):276-84.
7. DRUGDEX System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed October 10, 2013.
8. Nulojix Prescribing Information, Bristol-Myers Squibb Company; September, 2014.
9. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant. 2009;9(Suppl 3):S1-S155

Prior Authorization Guideline

GL-16130 Inlyta (axitinib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/23/2016

Technician Note :

P&T Approval Date: 8/21/2012; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Inlyta (axitinib)

Indications

Advanced Renal Cell Carcinoma

Indicated for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.

2 . Criteria

Product Name: Inlyta

Approval Length	12 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of renal cell cancer

AND

2 One of the following: [2,3]

2.1 Relapse following surgical excision

OR

2.2 Both of the following:

- Medically or surgically unresectable tumor
- Diagnosis of Stage IV disease

AND

3 One of the following: [2,3]

3.1 Patient with non-clear cell histology

OR

3.2 Both of the following:

3.2.1 Patient with predominantly clear cell histology

AND

3.2.2 History of failure, contraindication, or intolerance to one of the following: [A]

- Cytokine-based therapy [e.g., Interleukin (IL)-2]
- Kinase inhibitor therapy [e.g., Nexavar (sorafenib), Sutent (sunitinib), Votrient (pazopanib)]
- Avastin (bevacizumab) in combination with Interferon (IFN)-alfa therapy
- Mammalian target of rapamycin (mTOR) inhibitor therapy [e.g., Torisel (temsirolimus)]

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Inlyta

Approval Length	12 Months
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Inlyta therapy [C]

3 . Endnotes

A. In the axitinib pivotal trial, the inclusion criteria included patients with advanced RCC whose disease had progressed on or after treatment with 1 prior systemic therapy [ie, sunitinib-based therapy (54%), cytokine-based therapy (35%), bevacizumab-based therapy (8%), or temsirolimus-based therapy (3%)]. [1]
B. Mean progression-free survival in the pivotal study as described in the Inlyta prescribing information indicates a median progression-free survival of 6.7 months in axitinib-treated patients. [1]
C. Axitinib should be discontinued if patient experiences signs and symptoms of unacceptable toxicity [eg, severe hypertension (ie, persistent hypertension despite anti-hypertensive therapy and axitinib dose reduction), hypertensive crisis, reversible posterior leukoencephalopathy syndrome (RPLS)]. [1]

4 . References

1. Inlyta Prescribing Information. Pfizer Labs, September 2013.
2. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Kidney Cancer v.3.2014. Available at: http://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed July 9, 2014.
3. NCCN Drugs and Biologics Compendium: Axitinib. Available at: http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=379. Accessed July 9, 2014.

Prior Authorization Guideline

GL-16151 Istodax (romidepsin)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/23/2016

Technician Note :

P&T Approval Date: 5/18/2010; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Istodax (romidepsin)

Indications

Cutaneous T-cell lymphoma (CTCL)

Indicated for treatment of CTCL in patients who have received at least one prior systemic therapy.

Peripheral T-cell lymphoma (PTCL)

Indicated for the treatment of PTCL in patients who have received at least one prior therapy.

2 . Criteria

Product Name: Istodax

Diagnosis	Cutaneous T-cell lymphoma (CTCL)
Approval Length	12 months [7, A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cutaneous T-cell lymphoma (CTCL)

AND

2 History of failure, contraindication, or intolerance to at least one systemic therapy for the treatment of CTCL [B]

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Istodax

Diagnosis	Cutaneous T-cell lymphoma (CTCL)

Approval Length	12 months
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Istodax therapy

Product Name: Istodax

Diagnosis	Peripheral T-cell lymphoma (PTCL)
Approval Length	12 months [7, A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of peripheral T-cell lymphoma (PTCL)

AND

2 History of failure, contraindication, or intolerance to at least one therapy for the treatment of PTCL [C]

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Istodax

Diagnosis	Peripheral T-cell lymphoma (PTCL)
Approval Length	12 months
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Istodax therapy

3 . Endnotes

A. A 12-month length of authorization is an appropriate amount of time for approval as the minimum is 6 cycles (6 months) and there is no established maximum number of cycles for CTCL and PTCL. [7]
B. Examples of CTCL systemic therapies include: Campath (alemtuzumab), Cytoxan (cyclophosphamide), Doxil (liposomal doxorubicin), Extracorporeal photopheresis, Folotyn (pralatrexate), Gemzar (gemcitabine), Interferon-alpha , Leukeran (chlorambucil), Nipent (pentostatin), Ontak (denileukin diftitox), Targretin (bexarotene), Temodar (temozolamide), Toposar (etoposide), Trexall (methotrexate), Velcade (bortezomib).
C. Examples of PTCL therapies include: Adcetris (brentuximab vedotin), Campath (alemtuzumab), Cyclosporine, Folotyn (pralatrexate), Gemzar (gemcitabine), Ontak (denileukin difitox), Radiation therapy, Velcade (bortezumib), CHOP(cyclophosphamide, doxorubicin, vincristine, etoposide and prednisone), CHOP followed by ICE (ifosfamide, carboplatin, etoposide), CHOP followed by IVE (ifosfamide, etoposide, epirubicin) alternating with methotrexate, HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with methrotrexate and cytarabine, DHAP

(dexamethasone, cisplatin, cytarabine), ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin), GDP (gemcitabine, dexamethasone, cisplatin), GemOx (gemcitabine, oxaliplatin), ICE (ifosfamide, carboplatin, etoposide), MINE (mesna, ifosfamide, mitoxantrone, etoposide).

4 . References

1. Istodax Prescribing Information. Celgene, June 2011.
2. Piekarz RL, Frye R, Turner M, et al. Phase II multi-institutional trial of the histone deacetylase inhibitor romidepsin as monotherapy for patients with cutaneous T-cell lymphoma. J Clin Oncol. 2009;27(32):5410-5417.
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology™ Non-Hodgkin's Lymphomas (Version 1.2010). Available at: http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf. Accessed April 10, 2010.
4. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed April 10, 2010.
5. American Joint Committee on Cancer. Lymphoid neoplasms. In: AJCC Cancer Staging Manual. 6th ed. New York, NY: Springer, 2002:393-406.
6. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology™ Non-Hodgkin's Lymphomas (Version 4.2011). Available at: http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf. Accessed September 6, 2011.
7. Per clinical consult with oncologist, September 7, 2011.

Prior Authorization Guideline

GL-17488 Jakafi (ruxolitinib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 6/1/2016

Technician Note :

P&T Approval Date: 2/21/2012; P&T Revision Date: 2/25/2016; ** Effective 7/1/2016 **

1 . Indications

Drug Name: Jakafi (ruxolitinib)

Indications

Myelofibrosis

Indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis.

Polycythemia Vera

Indicated for treatment of patients with polycythemia vera who have had an inadequate response to or are intolerant of hydroxyurea.

2 . Criteria

Product Name: Jakafi

Diagnosis	Myelofibrosis
Approval Length	6 Months [1, A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following diagnoses: [1]

- Primary myelofibrosis
- Post-polycythemia vera myelofibrosis
- Post-essential thrombocythemia myelofibrosis

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Jakafi

Diagnosis	Polycythemia Vera
Approval Length	8 Months [1, B]

Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of polycythemia vera [1]

AND

2 History of failure, contraindication, or intolerance to hydroxyurea [1]

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Jakafi

Diagnosis	All indications listed above
Approval Length	6 Month
Therapy Stage	Reauthorization (for patients with clinical response)
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Jakafi therapy (e.g., spleen volume reduction, symptom improvement, hematocrit control)

Product Name: Jakafi

Diagnosis	All indications listed above
Approval Length	2 Month*
Therapy Stage	Reauthorization (for patients with no clinical response)
Guideline Type	Prior Authorization
Approval Criteria **1** Documentation does not provide evidence of positive clinical response while on Jakafi therapy (e.g., spleen volume reduction, symptom improvement, hematocrit control)	
Notes	*Authorization will be issued to allow for gradual dose tapering for therapy discontinuation. [1]

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to a standard quantity limit. The quantity limit may vary from the standard limit based upon the plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. Jakafi should be discontinued after 6 months if there is no spleen size reduction or symptom improvement since initiation of therapy. [1]
B. The initial authorization duration of 8 months is based on clinical trials (primary endpoint of hematocrit control and spleen volume reduction was evaluated at 32 weeks). [1]

5 . References

1. Jakafi Prescribing Information. Incyte Corp., December 2014.
2. Barbui T, Barosi G, Birgegard G, et al. Philadelphia-negative classical myeloproliferative neoplasms: critical concepts and management recommendations from European LeukemiaNet. J Clin Oncol. 2011;29(6):761-70.

Prior Authorization Guideline

GL-16595 Jevtana (cabazitaxel)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval: 2/15/2011; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Jevtana (cabazitaxel)

Indications

Hormone-refractory metastatic prostate cancer (mHRPC) (also referred to as metastatic castration-resistant prostate cancer (mCRPC))

In combination with prednisone, indicated for the treatment of patients with hormone-refractory metastatic prostate cancer (mHRPC) previously treated with a docetaxel-containing treatment regimen.

2 . Criteria

Product Name: Jevtana

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 All of the following: [2,3]

1.1 Diagnosis of metastatic hormone-refractory or castration-resistant prostate cancer [3, 4, A]

AND

1.2 Used in combination with prednisone

AND

1.3 Documented disease progression after previous treatment with docetaxel-based chemotherapy

Product Name: Jevtana

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease [3]

3 . Endnotes

A. Several different terms have been used to denote patients who progress on ADT in the face of castrate levels of testosterone: castration-resistant or castrate-resistant prostate cancer (CRPC), castration-recurrent prostate cancer (CRPC), hormone-refractory prostate cancer (HRPC), and androgen-independent prostate cancer (AIPC). [3, 4]

4 . References

1. Jevtana Prescribing Information. Sanofi-Aventis, June 2010.
2. deBono JS, Oudard S, Ozguroglu M, et al. for the TROPIC Investigators. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomized open-label trial. Lancet. 2010;376:1147-54.
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Prostate Cancer. v.3.2011.Available at: http://www.nccn.org/professionals/physician_gls/PDF/prostate.pdf. Accessed May 19, 2011.
4. Dawson NA. Overview of treatment for advanced prostate cancer. UpToDate. Available at www.uptodate.com. Accessed June 1, 2011.

Prior Authorization Guideline

GL-16607 Juxtapid (lomitapide)

Formulary OptumRx SP

Formulary Note

Approval Date 10/14/2015

Revision Date 4/4/2016

Technician Note :

P&T Approval Date: 2/19/2013; P&T Revision Date: 2/25/2016 **Effective: 7/1/2016**

1 . Indications

Drug Name: Juxtapid (lomitapide)

Indications

Homozygous familial hypercholesterolemia (HoFH)

Indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH). Limitations of Use: (1) The safety and effectiveness of lomitapide have not been established in patients with hypercholesterolemia who do not have HoFH. (2) The effect of lomitapide on cardiovascular

morbidity and mortality has not been determined.

2 . Criteria

Product Name: Juxtapid

Approval Length	6 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (eg, chart notes, laboratory values) documenting diagnosis of homozygous familial hypercholesterolemia as confirmed by one of the following: [1-3]

1.1 Genetic confirmation of 2 mutations in the LDL receptor, ApoB, PCSK9, or LDL receptor adaptor protein 1 (ie, LDLRAP1 or ARH)

OR

1.2 Both of the following:

1.2.1 One of the following:

- Untreated LDL-C > 500 mg/dL
- Treated LDL-C > 300 mg/dL

AND

1.2.2 One of the following:

- Xanthoma before 10 years of age

- Evidence of heterozygous familial hypercholesterolemia in both parents

AND

2 One of the following: [2-4, A]

2.1 Patient has been receiving at least 12 consecutive weeks of high-intensity statin therapy and will continue to receive a HIGH-INTENSITY statin [ie, atorvastatin 40-80 mg, Crestor (rosuvastatin) 20-40 mg] at maximally tolerated dose

OR

2.2 Both of the following:

2.2.1 Patient is unable to tolerate high-intensity statin as evidenced by one of the following intolerable and persistent (ie, more than 2 weeks) symptoms:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times ULN)

AND

2.2.2 Patient has been receiving at least 12 consecutive weeks of moderate-intensity statin therapy and will continue to receive a MODERATE-INTENSITY statin [ie, atorvastatin 10-20 mg, Crestor (rosuvastatin) 5-10 mg, simvastatin 20-40 mg, pravastatin 40-80 mg, lovastatin 40 mg, Lescol XL (fluvastatin XL) 80 mg, fluvastatin 40 mg twice daily, or Livalo (pitavastatin) 2-4 mg] at maximally tolerated dose

OR

2.3 Both of the following:

2.3.1 Patient is unable to tolerate moderate- and high-intensity statins as evidenced by one of the following intolerable and persistent (ie, more than 2 weeks) symptoms for both moderate- and high-intensity statins:

- Myalgia (muscle symptoms without CK elevations)

- Myositis (muscle symptoms with CK elevations < 10 times ULN)

AND

2.3.2 Patient has been receiving at least 12 consecutive weeks of low-intensity statin therapy and will continue to receive a LOW-INTENSITY statin [ie, simvastatin 10 mg, pravastatin 10-20 mg, lovastatin 20 mg, fluvastatin 20-40 mg, Livalo (pitavastatin) 1 mg] at maximally tolerated dose

OR

2.4 Both of the following:

2.4.1 Patient is unable to tolerate low-, moderate-, and high-intensity statins as evidenced by one of the following intolerable and persistent (ie, more than 2 weeks) symptoms for low-, moderate-, and high-intensity statins:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times ULN)

AND

2.4.2 Patient has undergone a trial of statin rechallenge with pravastatin 10-40 mg or Crestor (rosuvastatin) 5 mg with documented reappearance of muscle symptoms

OR

2.5 Patient has a labeled contraindication to all statins as documented in medical records

OR

2.6 Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations > 10 times ULN

AND

3 One of the following: [5, 6, B]

3.1 Patient has been receiving at least 12 consecutive weeks of and will continue to receive one of the following as adjunct to maximally tolerated statin therapy:

- Ezetimibe
- Bile acid sequestrant [eg, Welchol (colesevelam), cholestyramine]

OR

3.2 History of contraindication or intolerance to both of the following:

- Ezetimibe
- Bile acid sequestrant [eg, Welchol (colesevelam), cholestyramine]

AND

4 One of the following LDL-C values while on maximally tolerated lipid-lowering regimen within the last 30 days: [7, 8]

- LDL-C greater than or equal to 100 mg/dL with ASCVD
- LDL-C greater than or equal to 130 mg/dL without ASCVD

AND

5 Used as adjunct to a low-fat diet and exercise regimen [1]

AND

6 Prescribed by one of the following:

- Cardiologist
- Endocrinologist
- Lipid specialist [C]

AND

7 One of the following:

7.1 History of failure after 12 consecutive weeks to Repatha (evolocumab) therapy

OR

7.2 History of intolerance to Repatha (evolocumab)

AND

8 Not used in combination with Kynamro (mipomersen)

AND

9 Not used in combination with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

AND

10 Patient is not pregnant

AND

11 Patient does not have moderate or severe hepatic impairment (ie, Child-Pugh category B

or C) or active liver disease including unexplained persistent abnormal liver function tests

AND

12 Patient is not concomitantly on moderate or strong CYP 3A4 inhibitors (eg, clarithromycin)

Product Name: Juxtapid

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient continues to receive statin at the maximally tolerated dose (unless patient has documented inability to take statins)

AND

2 Patient continues to receive ezetimibe or bile acid sequestrant therapy as an adjunct to maximally tolerated statin therapy (unless patient has documented inability to take ezetimibe AND bile acid sequestrant therapy)

AND

3 Patient has been adherent to Juxtapid therapy

AND

4 Patient is continuing a low-fat diet and exercise regimen

AND

5 Prescribed by one of the following:

- Cardiologist
- Endocrinologist
- Lipid specialist [C]

AND

6 Submission of medical records (eg, laboratory values) documenting a sustained LDL-C reduction from pre-treatment baseline (ie, prior Juxtapid therapy) while on Juxtapid therapy

AND

7 Not used in combination with Kynamro (mipomersen)

AND

8 Not used in combination with a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

AND

9 Patient is not pregnant

AND

10 Patient does not have moderate or severe hepatic impairment (ie, Child-Pugh category B or C) or active liver disease including unexplained persistent abnormal liver function tests

AND

11 Patient is not concomitantly on moderate or strong CYP 3A4 inhibitors (eg, clarithromycin)

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product may be subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. Per the 2013 ACC/AHA national treatment guidelines, it is reasonable to use the following as indicators of anticipated therapeutic response to the recommended intensity of statin therapy. Focus is on the intensity of the statin therapy. As an aid to monitoring: a) High-intensity statin therapy generally results in an average LDL-C reduction of ? 50% from the untreated baseline; b) Moderate-intensity statin therapy generally results in an average LDL-C reduction of 30 to < 50% from the untreated baseline. [4]
B. To date, IMPROVE-IT is the only randomized controlled trial (RCT) to demonstrate significant ASCVD event reduction with non-statin lipid-lowering therapy. IMPROVE-IT was a prospective RCT evaluating the addition of ezetimibe to simvastatin 40 mg in a high-risk patient population for secondary prevention over 7 years. The addition of ezetimibe significantly reduced ASCVD events, albeit very modestly (HR 0.936; 95% CI 0.887, 0.988; p = 0.016; number needed to treat [NNT] = 50). [5] The effect of lomitapide on cardiovascular morbidity and mortality has not been determined. [1]
C. Lipid specialists are physicians certified by the American Board of Clinical Lipidology (ABCL) or the Accreditation Council for Clinical Lipidology (ACCL). [9, 10]

5 . References

1. Juxtapid Prescribing Information. Aegerion Pharmaceuticals, Inc. March 2016..
2. Raal FJ, Santos RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. Atherosclerosis. 2012;223:262-8.
3. Cuchel M, Bruckert E, Ginsberg HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. Eur Heart J. 2014;35:2146-57.
4. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2889-934.
5. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med. 2015a; DOI: 10.1056/NEJMoa1410489 [Epub ahead of print].
6. The Lipid Research Clinics Coronary Primary Prevention Trial results. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA. 1984;251:365-74.
7. ATP III Final Report PDF. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. Circulation. 2002;106:3143-3421.
8. Per clinical drug consult with cardiologist. August 3, 2015.
9. American Board of Clinical Lipidology website. www.lipidboard.org. Accessed September 23, 2015.
10. Accreditation Council for Clinical Lipidology website. www.lipidspecialist.org. Accessed September 23, 2015.

Prior Authorization Guideline

GL-17305 Kadcyla (ado-trastuzumab emtansine)

Formulary OptumRx SP

Formulary Note

Approval Date 5/22/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 5/21/2013; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Kadcyla (ado-trastuzumab emtansine)

Indications

Metastatic breast cancer

Indicated for the treatment of patients with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: •Received prior therapy for metastatic disease, or •Developed disease recurrence during or within six months of completing adjuvant therapy.

2 . Criteria

Product Name: Kadcyla

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of recurrent or metastatic breast cancer

AND

2 Patient has human epidermal growth factor receptor 2 (HER2)-positive disease

AND

3 Patient has been previously treated with trastuzumab and a taxane

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Kadcyla

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease

3 . References

1. Kadcyla [package insert], South San Francisco, CA: Genentech Inc.; February 2013.
2. Breast Cancer, National Comprehensive Cancer Network.http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed March 22, 2013.
3. Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. N Engl J Med. 2012; 367:1783-91.
4. Pazdur, Richard. FDA/CDER resources page. Food and Drug Administration Website http://www.fda.gov/drugs/developmentapprovalprocess/druginnovation/default.htm. Accessed March 22, 2013.
5. Breast Cancer. National Cancer Institute at the National Institutes of Health Web site: http://www.cancer.gov/cancertopics/types/breast. Accessed March 22, 2013.
6. Hayes, Daniel F. Systemic treatment for metastatic breast cancer: Molecular targeted therapy. UpToDate. http://www.uptodate.com/contents/systemic-treatment-for-metastatic-breast-cancer-molecular-targeted-therapy?source=search_result&search=kadcyla&selectedTitle=4%7E12. Accessed March 23, 2013.

Prior Authorization Guideline

GL-16814 Kalydeco (ivacaftor)

Formulary OptumRx SP

Formulary Note

Approval Date 1/3/2013

Revision Date 6/3/2016

Technician Note :

P&T Approval Date: 2/21/2012; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Kalydeco (ivacaftor)

Indications

Cystic fibrosis

Indicated for the treatment of cystic fibrosis (CF) in patients age 2 years and older who have one of the following mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R. Indicated for the treatment of CF in patients age 2 years and older who have an R117H mutation in the CFTR gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test

instructions for use. Limitations of Use: Kalydeco Is not effective in patients with CF who are homozygous for the F508del mutation in the CFTR gene.

2 . Criteria

Product Name: Kalydeco

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cystic fibrosis

AND

2 Patient has one of the following mutations on at least one allele in the cystic fibrosis transmembrane conductance regulator gene:

- G551D
- G1244E
- G1349D
- G178R
- G551S
- R117H
- S1251N
- S1255P
- S549N
- S549R

AND

3 The presence of a mutation was documented by an FDA-cleared cystic fibrosis mutation test and followed by verification with bi-directional sequencing when recommended by the mutation test instructions

AND

4 Patient is 2 years of age or older

AND

5 Prescribed by or in consultation with a cystic fibrosis specialist

Product Name: Kalydeco

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response (e.g., improvement in lung function [forced expiratory volume in one second {FEV1}], decreased number of pulmonary exacerbations) to Kalydeco therapy [A]

3 . Endnotes

A. The primary efficacy endpoint in both Kalydeco pivotal trials was improvement in lung function as determined by the mean absolute change from baseline in percent predicted pre-dose FEV1 through 24 weeks of treatment. [1-2]

4 . References

1. Kalydeco Prescribing Information. Vertex Pharmaceuticals, March 2015.
2. Ramsey BW, Davies J, McElvaney G, et al. A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. N Engl J Med. 2011;365:1663-1672.
3. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. Am J Respir Crit Care Med. 2013;187(7):680-9.

Prior Authorization Guideline

GL-14637 Kanuma (sebelipase alfa)

Formulary OptumRx SP

Formulary Note

Approval Date 3/18/2016

Revision Date 3/18/2016

Technician Note :

P&T Approval Date: 2/25/2016

1 . Indications

Drug Name: Kanuma (sebelipase alfa)

Indications

Lysosomal Acid Lipase (LAL) deficiency

Indicated for the treatment of patients with a diagnosis of Lysosomal Acid Lipase (LAL) deficiency.

2 . Criteria

Product Name: Kanuma

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of lysosomal acid lipase deficiency (LAL-D)

AND

2 Diagnosis was confirmed by an enzymatic blood (e.g., dried blood spot test) or genetic test [3,7,A]

AND

3 Prescribed by or in consultation with a specialist experienced in the treatment of inborn errors of metabolism

3 . Endnotes

A. Due to similar clinical presentations, LAL-D is often misdiagnosed as familial defective apolipoprotein B (ApoB) deficiency, heterozygous familial hypercholesterolemia (HeFH), familial combined hyperlipidemia (FCH), or polygenic hypercholesterolaemia [3,7]. A diagnosis of LAL-D can be confirmed by identification of a LIPA mutation or a deficient LAL enzyme in peripheral blood leukocytes, fibroblasts, or dried blood spots. A biopsy and/or radiographic findings may help support a LAL-D diagnosis, however these are not considered diagnostic.

4 . References

1. Burton BK, Balwani M, Feillet F, et al. A Phase 3 Trial of Sebelipase Alfa in Lysosomal Acid Lipase Deficiency. N Engl J Med. 2015;373(11):1010-20.
2. FDA News Release. December 8, 2015. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm476013.htm. Accessed January 19, 2016.
3. Hoffman EP, Barr ML, Giovanni MA, et al. Lysosomal Acid Lipase Deficiency. 2015 Jul 30. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Accessed 1/7/16. Available at: http://www.ncbi.nlm.nih.gov/books/NBK305870/
4. Jones SA, Valayannopoulos V, Schneider E, et al. Impact of sebelipase alfa on survival and liver function in infants with rapidly progressive lysosomal acid lipase deficiency [poster]. Presented at SSIEM 2015. Poster P-627.
5. Kanuma prescribing information, Alexion Pharmaceuticals. Cheshire, CT.October 2015.
6. Porto AF. Lysosomal acid lipase deficiency: diagnosis and treatment of Wolman and Cholesteryl Ester Storage Diseases. Pediatr Endocrinol Rev. 2014;12(1):125-32.
7. Reiner, Guardamagna, Nair, et al. Lysosomal acid lipase deficiency - an under-recognized cause of dyslipidaemia and liver dysfunction. Atherosclerosis. 2014;235(1): 21-30. Accessed 1/7/16. Available at: http://www.atherosclerosis-journal.com/article/S0021-9150(14)00202-0/abstract

Prior Authorization Guideline

GL-16347 Keveyis (dichlorphenamide)

Formulary OptumRx SP

Formulary Note

Approval Date 11/19/2015

Revision Date 3/25/2016

Technician Note :

P&T Approval Date: 11/18/2015; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Keveyis (dichlorphenamide)

Indications

Primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.

Indicated for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.

2 . Criteria

Product Name: Keveyis

Approval Length	3 Months [A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of one of the following:

- Primary hyperkalemic periodic paralysis [1, B]
- Primary hypokalemic periodic paralysis [1, B]
- Paramyotonia Congenita with periodic paralysis [2, B]

AND

2 Patient does not have hepatic insufficiency (e.g., Child-Pugh class A) [1]

AND

3 Patient does not have severe pulmonary disease (e.g., severe chronic obstructive pulmonary disease (COPD)) [1,3]

AND

4 Patient is not concomitantly on high dose aspirin (i.e., greater than 100 mg per day) [1]

AND

5 Prescribed by or in consultation with a neurologist

Product Name: Keveyis

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Keveyis therapy

AND

2 Patient does not have hepatic insufficiency (e.g., Child-Pugh class A) [1]

AND

3 Patient does not have severe pulmonary disease (e.g., severe chronic obstructive pulmonary disease (COPD)) [1,3]

AND

4	Patient is not concomitantly on high dose aspirin (i.e., greater than 100 mg per day) [1]

3 . Endnotes

A. Prescribers should evaluate the patient's response to Keveyis after 2 months of treatment to decide whether treatment should be continued [1]. An additional month is added to the initial authorization duration to allow patient follow-up with the provider.
B. The efficacy of Keveyis was evaluated in two clinical studies, Study 1 and Study 2. Study 1 was a 9-week, double blind, placebo-controlled multi-center study. Study 1 consisted of two substudies: a substudy in patients with hypokalemic periodic paralysis (n=44), and a substudy in patients with hyperkalemic periodic paralysis (n=21). The primary efficacy endpoint in both substudies was the average number of self-reported attacks of muscle weakness per week over the final 8 weeks of the trial. Study 2 was a 35-week, double blind, placebo-controlled, multi-center, two-period crossover study. Study 2 also consisted of two substudies: a substudy in a substudy in patients with hypokalemic periodic paralysis (n=42), and a substudy in patients with hyperkalemic periodic paralysis (n=31), including patients with Paramyotonia Congenita. The primary endpoint in the hypokalemic periodic paralysis substudy was the incidence of acute intolerable worsening (based on attack frequency or severity) necessitating withdrawal. The primary endpoint in the hyperkalemic periodic paralysis substudy was the average number of self-reported attacks of muscle weakness per week. Dosing was determined similarly to Study 1 [1, 2].

4 . References

1. Keveyis Prescribing Information. Taro Pharmaceuticals. 2015.
2. Tawil R, McDermott MP, Brown R Jr, et al. Randomized trials of dichlorphenamide in the periodic paralyses. Working Group on Periodic Paralysis. Ann Neurol. 2000;47(1):46-53.
3. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: Revised 2015. Global Initiative for Chronic Obstructive Lung Disease (GOLD). www.goldcopd.org. Accessed on October 12, 2015.

Prior Authorization Guideline

GL-16833 Kineret (anakinra)

Formulary OptumRx SP

Formulary Note

Approval Date 2/18/2015

Revision Date 4/15/2016

Technician Note :

P&T Approval Date: 1/28/2002; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Kineret (anakinra)

Indications

Rheumatoid Arthritis

Indicated for the reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis, in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs). Kineret can be used alone or in combination with DMARDs other than Tumor Necrosis Factor (TNF) blocking agents.

Cryopyrin-associated periodic syndromes (CAPS): Neonatal-Onset Multisystem Inflammatory Disease (NOMID) [C]

Indicated for the treatment of Neonatal-Onset Multisystem Inflammatory Disease (NOMID).

Off Label Uses

Systemic Juvenile Idiopathic Arthritis

Has been used for the treatment of systemic juvenile idiopathic arthritis. [9, 10]

2 . Criteria

Product Name: Kineret

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active RA

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to one nonbiologic disease modifying anti-rheumatic drug (DMARD) [e.g., methotrexate (Rheumatrex/Trexall), Arava (leflunomide), Azulfidine (sulfasalazine)] [5, 12]

AND

4 One of the following:

4.1 History of failure, contraindication, or intolerance to two of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Simponi (golimumab) or Simponi Aria (golimumab IV)

OR

4.2 For continuation of prior Kineret therapy

AND

5 Patient is not receiving Kineret in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,15,A,B]

AND

6 Patient is not receiving Kineret in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,15,A,B]

Product Name: Kineret

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Kineret therapy

AND

2 Patient is not receiving Kineret in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,15,A,B]

AND

3 Patient is not receiving Kineret in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,15,A,B]

Product Name: Kineret

Diagnosis	Neonatal-Onset Multisystem Inflammatory Disease (NOMID) [1, C]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of neonatal-onset multisystem inflammatory disease (NOMID)

AND

2 Diagnosis of NOMID has been confirmed by one of the following: [C]

2.1 NLRP-3 (nucleotide-binding domain, leucine rich family (NLR), pyrin domain containing 3] gene (also known as Cold- Induced Auto-inflammatory Syndrome-1 [CIAS1]) mutation

OR

2.2 Evidence of active inflammation which includes both of the following:

- Clinical symptoms (e.g., rash, fever, arthralgia)
- Elevated acute phase reactants (e.g., ESR, CRP)

AND

3 Prescribed by or in consultation with one of the following

- Allergist/Immunologist
- Rheumatologist

AND

4 Patient is not receiving Kineret in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,15,A,B]

AND

5 Patient is not receiving Kineret in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,15,A,B]

Product Name: Kineret

Diagnosis	Neonatal-Onset Multisystem Inflammatory Disease (NOMID) [1, C]
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Kineret therapy

AND

2 Patient is not receiving Kineret in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,15,A,B]

AND

3 Patient is not receiving Kineret in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,15,A,B]

Product Name: Kineret

Diagnosis	Systemic Juvenile Idiopathic Arthritis (SJIA) (off-label)

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active systemic juvenile idiopathic arthritis

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to one of the following:

- Non-steroidal anti-inflammatory drug (NSAID) [e.g., Motrin (ibuprofen), Naprosyn (naproxen)]
- Systemic glucocorticoid (e.g., prednisone)

AND

4 Patient is not receiving Kineret in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,15,A,B]

AND

5 Patient is not receiving Kineret in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,15,A,B]

Product Name: Kineret

Diagnosis	Systemic Juvenile Idiopathic Arthritis (SJIA) (off-label)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Kineret therapy

AND

2 Patient is not receiving Kineret in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,15,A,B]

AND

3 Patient is not receiving Kineret in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,15,A,B]

3 . Endnotes

A. Use of Kineret in combination with TNF blocking agents is not recommended. In a 24-week study of concurrent Kineret and etanercept therapy in RA patients, the rate of serious infections in the combination arm (7%) was higher than with etanercept alone (0%). The combination of Kineret and etanercept did not result in higher ACR response rates compared to etanercept alone. [1]
B. Use of Xeljanz in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended. [15]
C. Three clinically overlapping, interleukin-1-associated, autoinflammatory disorders are known collectively as the cryopyrin-associated periodic syndromes (CAPS) or cryopyrinopathies: familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal onset multisystem inflammatory disorder (NOMID, also known as chronic infantile neurological cutaneous and articular [CINCA] syndrome). [14] In addition to clinical symptoms, a diagnosis should be made using a combination of procedures including laboratory assessments, skin biopsy, and genetic testing. [16]

4 . References

1. Kineret Prescribing Information. Swedish Orphan Biovitrum. October 2013.
2. Bresnihan B, et al. Treatment of rheumatoid arthritis with recombinant human interleukin-1 receptor antagonist. Arthritis Rheum.1998;41(12):2196-2204.
3. Jiang Y, et al. A multicenter, double-blind, dose-ranging, randomized, placebo-controlled study of recombinant human interleukin-1 receptor antagonist in patients with rheumatoid arthritis: radiologic progression and correlation of Genant and Larsen scores. Arthritis Rheum.2000;43(5):1001-1009.
4. Schiff MH, et al. Safety of combination therapy with anakinra and etanercept in patients with rheumatoid arthritis. Arthritis Rheum.2001;44:S79.
5. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care & Research. 2012;64(5):625-639.
6. Pavy S. Constantin A, Pham T, et al. Methotrexate therapy for rheumatoid arthritis: clinical practice guidelines based on published evidence and expert opinions. Joint Bone Spine 2006;73(4):388-95.
7. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995; 38(6):727-735.
8. Felson D, Anderson JJ, Boers M, et al. The American College of Rheumatology preliminary core sets of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum. 1993;36(6): 729-740.
9. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic

arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013;65(10):2499-2512.
10. Quartier P, Allantaz, Cimaz R, et al. A multicentre, randomised, double-blind, placebo-controlled trial with the interleukin-1 receptor antagonist anakinra in patients with systemic-onset juvenile idiopathic arthritis (ANAJIS trial). Ann Rheum Dis. 2011 May;70(5):747-54.
11. Per clinical consult with pediatric rheumatologist, August 2, 2011.
12. Per clinical consult with rheumatologist, June 30, 2011.
13. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011. Ann Rheum Dis. 2012 ;71(Suppl II):i2- i45 .
14. Nigrovic PA. Cryopyrin-associated periodic syndromes and related disorders. UpToDate Web Site. Updated November 25, 2014. http:www.uptodate.com. Accessed January 5, 2015.
15. Xeljanz Prescribing Information. Pfizer. March 2014.
16. Yu JR and Leslie KS. Cryopyrin-associated periodic syndrome: an update on diagnosis and treatment response. Curr Allergy Asthma Rep. 2011;11(1):12-20

Prior Authorization Guideline

GL-17417 Krystexxa (pegloticase)

Formulary OptumRx SP

Formulary Note

Approval Date 4/22/2014

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 2/15/2011; P&T Revision date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Krystexxa (pegloticase)

Indications

Refractory gout

Indicated for the treatment of chronic gout in adult patients refractory to conventional therapy. Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated. Important Limitations of Use: Krystexxa is not recommended for the treatment of asymptomatic hyperuricemia.

2 . Criteria

Product Name: Krystexxa

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of severe chronic gout

AND

2 Patient has one of the following symptoms of treatment failure gout: [A]

- Greater than or equal to 3 flares in previous 18 months
- Greater than or equal to 1 gout tophus
- Gouty arthritis

AND

3 History of failure to maximum recommended doses or intolerance to both of the following conventional therapies: [B]

- Xanthine oxidase inhibitor (i.e., allopurinol, febuxostat)
- Uricosuric agent (e.g., probenecid)

Product Name: Krystexxa

Approval Length	12 Months [C]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Krystexxa therapy demonstrated by both of the following:

- Serum urate level has decreased since initiating therapy
- Clinical improvement in the signs and symptoms of gout (e.g., decrease in tophi size or frequency of gouty flares per year from baseline or improvement in chronic arthropathy or quality of life)

3 . Endnotes

A. The inclusion criteria for the pivotal trial for Krystexxa were as follows: Patients were 18 years or older and met the following criteria for refractory gout: a baseline serum uric acid of 8.0 mg/dL or greater (to convert to micromol/L, multiply by 59.485) and at least 1 of the following: 3 or more self-reported gout flares during the previous 18 months; 1 or more tophi; and gouty arthropathy, defined clinically or radiographically as joint damage due to gout. [2]
B. Additional inclusion criteria in pivotal trials were as follows: Contraindication to treatment with allopurinol or history of failure to normalize serum uric acid despite 3 or more months of treatment with the maximum medically appropriate allopurinol dose (determined by the treating physician) [2]. Febuxostat is another first-line pharmacologic agent for the treatment of gout [3]

C. The efficacy and safety profile of long-term pegloticase treatment (mean follow-up of 2.5 years) has been shown to be consistent with that observed in the 6 month pivotal trials. [4]

4 . References

1. Krystexxa Prescribing Information. Savient Pharmaceutical, Inc. September 2012.
2. Sundy JS, Baraf HS, Yood RA, et al. Efficacy and tolerability of pegloticase for the treatment of chronic gout in patients refractory to conventional treatment: two randomized controlled trials. JAMA. 2011;306(7):711-20.
3. Khanna K, Fitzgerald JD, Khanna PP, et al. 2012 American College of RheumatologyGuidelines for Management of Gout. Part 1: Systematic Nonpharmacologic and Pharmacologic Therapeutic Approaches to Hyperuricemia. Arthritis Care Res (Hoboken). 2012 Oct;64(10):1447-61.
4. Becker MA, Baraf HS, Yood RA. Long-term safety of pegloticase in chronic gout refractory to conventional treatment. Ann Rheum Dis. 2013;72(9):1469-74.

Prior Authorization Guideline

GL-16256 Kuvan (sapropterin dihydrochloride)

Formulary OptumRx SP

Formulary Note

Approval Date 4/23/2016

Revision Date 4/23/2016

Technician Note :

P&T Approval Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Kuvan (sapropterin dihydrochloride)

Indications

Phenylketonuria

Indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet.

2 . Criteria

Product Name: Kuvan

Approval Length	2 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of phenylketonuria (PKU)

AND

2 Used in conjunction with a phenylalanine (Phe)-restricted diet

AND

3 Patient will have Phe blood levels measured after 1 week of therapy and periodically for up to 2 months of therapy to determine response [B]

Product Name: Kuvan

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has had an objective response to therapy, defined as a 30% or greater reduction in phenylalanine (Phe) blood levels from baseline [A]

AND

2 Used in conjunction with a phenylalanine (Phe)-restricted diet

AND

3 Patient will continue to have blood Phe levels measured periodically during therapy

3 . Endnotes

A. In clinical trials, response to therapy was defined as greater than or equal to 30% decrease in blood Phe from baseline [6]
B. Sapropterin was evaluated in a phase III, randomized, placebo-controlled trial to determine its efficacy in reducing blood Phe concentration [3]. The primary endpoint was mean change from baseline in concentration of Phe in blood after 6 weeks. The mean age was 20 years. Results showed that after 6 weeks of therapy, patients who received sapropterin (n=41) had a decrease in mean blood Phe of 236 micromol/L, compared with a 3 micromol/L increase in the placebo group (n=47; p less than 0.0001).

4 . References

1. Kuvan Prescribing information. BioMarin Pharmaceutical Inc. Novato, CA April, 2014
2. Burton B, Nowacka M, Hennermann J, Lipson M, Grange D, Chakrapani A, et al. Safety of extended treatment with sapropterin dihydrochloride in patients with phenylketonuria: results of a phase 3b study. Mol Genet Metab. 2011 Aug;103(4):315-22.
3. Levy HL, Milanowski A, Chakrapani A, Cleary M, Lee P, Trefz FK, et al. Efficacy of sapropterin dihydrochloride (tetrahydrobiopterin, 6R-BH4) for reduction of phenylalanine concentration in patients with phenylketonuria: a phase III randomised placebo-controlled study. Lancet. 2007;370(9586):504-10.
4. Lindegren M, Krishnaswami S, Reimschisel T, Fonnesbeck C, Sathe N, McPheeters M. A Systematic Review of BH4 (Sapropterin) for the Adjuvant Treatment of Phenylketonuria. JIMD Rep. 2013;8:109-19
5. Trefz F, Burton B, Longo N, Casanova M, Gruskin D, Dorenbaum A, et al. Efficacy of sapropterin dihydrochloride in increasing phenylalanine tolerance in children with phenylketonuria: a phase III, randomized, double-blind, placebo-controlled study. J Pediatr. 2009 May;154(5):700-7.
6. Vockley J, Andersson HC, Antshel KM, Braverman NE, Burton BK, Frazier DM, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. Genet Med. 2014 Feb;16(2):188-200

Prior Authorization Guideline

GL-17066 Kyprolis (carfilzomib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/24/2016

Technician Note :

P&T Approval Date: 11/13/2012; P&T Revision Date: 5/19/2016 **Effective 6/15/2016**

1 . Indications

Drug Name: Kyprolis (carfilzomib)

Indications

Multiple myeloma - combination therapy

Indicated in combination with lenalidomide and dexamethasone for the treatment of patients with relapsed multiple myeloma who have received one to three prior lines of therapy.

Multiple myeloma - monotherapy

Indicated as a single agent for the treatment of patients with relapsed or refractory multiple

myeloma who have received one or more lines of therapy.

2 . Criteria

Product Name: Kyprolis

Approval Length	12 months [E]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple myeloma [1-5]

AND

2 Disease is relapsed or refractory [1, A]

AND

3 Patient has received at least one prior therapy for MM [1, C]

AND

4 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Kyprolis

Approval Length	12 months [D]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Kyprolis therapy [E]

3 . Endnotes

A. Relapsed multiple myeloma is defined as progressive disease following a complete response, whereas refractory multiple myeloma refers to disease that is either unresponsive to current therapy or progresses within 60 days of the last treatment. Relapsed and refractory multiple myeloma describes patients with a previous achievement of at least a minimal response, but who experience progressive disease while on salvage therapy, or progress within 60 days of the last treatment. [7]
B. The FDA approval of Kyprolis was supported by a single-arm pivotal phase 2 trial which required eligible patients to have received at least 2 prior regimens for relapsed disease, including bortezomib, thalidomide or lenalidomide, an alkylating agent, or an anthracycline. [2] Based on this study, Kyprolis is indicated “for the treatment of patients with multiple myeloma who have received at least two prior therapies including bortezomib and an immunomodulatory agent and have demonstrated disease progression on or within 60 days of completion of the last therapy”. [1]
C. The NCCN Panel has included single agent carfilzomib as a preferred salvage therapy option in patients who have received at least one prior therapy for MM. (category 2A). [5]
D. In open-label, single-arm, phase-2 clinical trials, the duration of response observed with carfilzomib ranged from 7.8 to 13.1 months in heavily pretreated relapsed/refractory multiple myeloma patients. [2, 3, 4]

E. Treatment with Kyprolis should be continued until disease progression or until unacceptable toxicity occurs [e.g., Grade 3 or 4 neutropenia, Grade 4 thrombocytopenia, cardiac toxicity, pulmonary hypertension, Grade 3 or 4 pulmonary complications, Grade 3 or 4 hepatic toxicity, renal toxicity, Grade 3 or 4 peripheral neuropathy]. [1]
F. In addition to the labeled indication for relapsed multiple myeloma in patients who have received one to three prior lines of therapy, the NCCN Myeloma panel has included the carfilzomib, lenalidomide and dexamethasone regimen as a category 2A option for primary treatment of transplant-eligible patients with multiple myeloma. [5]

4 . References

1. Kyprolis Prescribing Information. Onyx Pharmaceuticals, Inc. January 2016.
2. Siegel DS, Martin T, Wang M, et al. A phase 2 study of single-agent carfilzomib (PX-171-003-A1) in patients with relapsed and refractory multiple myeloma. Blood. 2012;120:2817-25.
3. Vij R, Wang M, Kaufman JL, et al. An open-label, single-arm, phase 2 (PX-171-004) study of single agent carfilzomib in bortezomib-naive patients with relapsed and/or refractory multiple myeloma. Blood. 2012;119(24):5661-70.
4. Vij R, Siegel DS, Jagannath S, et al. An open-label, single-arm, phase 2 study of single-agent carfilzomib in patients with relapsed and/or refractory multiple myeloma who have been previously treated with bortezomib. Br J Haematol. 2012;[Epub ahead of print].
5. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Multiple Myeloma-Version 3.2016. Available at: http://www.nccn.org/professionals/physician_gls/PDF/myeloma.pdf. Accessed April 15, 2016
6. Per clinical consultation with hematologist/oncologist, September 6, 2012.
7. Lonial S, Mitsiades CS, Richardson RG. Treatment options for relapsed and refractory multiple myeloma. Clin Cancer Res. 2011;17(6):1264-77.
8. Stewart AK, Rajkumar SV, Dimopoulos MA, et al. Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. N Engl J Med. 2015;372:142-52.

Prior Authorization Guideline

GL-30247 Lenvima (lenvatinib)

Formulary OptumRx SP

Formulary Note

Approval Date 7/8/2016

Revision Date 7/8/2016

Technician Note :

P&T Approval Date: 4/14/2015; P&T Revision Date: 6/22/2016 **Effective 7/15/2016**

1 . Indications

Drug Name: Lenvima (lenvatinib)

Indications

Differentiated Thyroid Carcinoma Indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).

Renal Cell Carcinoma (RCC) Indicated in combination with everolimus for the treatment of patients with advanced RCC following one prior anti-angiogenic therapy.

2 . Criteria

Product Name: Lenvima

Diagnosis	Differentiated thyroid cancer (DTC)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of differentiated thyroid cancer (DTC) [2,A]

and

2 One of the following: [1,2]

- Locally recurrent disease
- Metastatic disease

and

3 One of the following: [2]

- Patient has symptomatic disease [2,B]
- Patient has progressive disease

and

4 Disease is refractory to radioactive iodine treatment

and

5 Prescribed by or in consultation with an oncologist

Product Name: Lenvima

Diagnosis	Renal Cell Carcinoma (RCC)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced renal cell carcinoma (RCC) [1, 3, C]

and

2 History of failure, contraindication, or intolerance to at least one prior anti-angiogenic therapy [eg, Inlyta (axitinib), Votrient (pazopanib), Nexavar (sorafenib), Sutent (sunitinib)] [1, 3, C]

and

3 Used in combination with Afinitor (everolimus) [1, 3, C]

and

4 Prescribed by or in consultation with an oncologist

Product Name: Lenvima

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Lenvima therapy

3 . Endnotes

A. Differentiated thyroid carcinoma includes papillary carcinoma, follicular carcinoma, Hurthle cell carcinoma, and poorly differentiated carcinoma. [2]
B. Commercially available small molecular kinase inhibitors can be considered for progressive and/or symptomatic disease if clinical trials or other systemic therapies are not available or appropriate. Kinase inhibitors include sorafenib, sunitinib, axitinib, vandetanib, pazopanib, and lenvatinib. [2]

C. C. NCCN recognizes use for subsequent therapy in combination with everolimus for relapse or for surgically unresectable stage IV disease with predominant clear cell histology that progressed on prior antiangiogenic therapy. [3]

4 . References

1. Lenvima Prescribing Information. Eisai Inc., May 2016.
2. National Comprehensive Cancer Network. Practice Guidelines in Oncology. Thyroid Carcinoma v.2.2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed June 8, 2016.
3. National Comprehensive Cancer Network. Practice Guidelines in Oncology. Kidney Cancer v.3.2016. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed June 8, 2016.

Prior Authorization Guideline

GL-17424 Lonsurf (trifluridine and tipiracil)

Formulary OptumRx SP

Formulary Note

Approval Date 11/19/2015

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 11/18/2015; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Lonsurf (trifluridine and tipiracil)

Indications

Metastatic Colorectal Cancer (mCRC)

Indicated for the treatment of patients with mCRC who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and, if RAS wild type, an anti-EGFR therapy.

2 . Criteria

Product Name: Lonsurf

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of metastatic colorectal cancer (mCRC)

AND

2 History of failure, contraindication or intolerance to fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy (e.g., FOLFOX, FOLFIRI, FOLFOXIRI)

AND

3 History of failure, contraindication or intolerance to an anti-VEGF therapy (e.g., Avastin [bevacizumab], Zaltrap [ziv-aflibercept])

AND

4 One of the following:

4.1 Patient has KRAS mutant tumors

OR

4.2 Both of the following:

4.2.1 Patient has KRAS wild-type tumors

AND

4.2.2 History of failure, contraindication or intolerance to an anti-EGFR therapy (e.g., Vectibix [panitumumab], Erbitux [cetuximab])

AND

5 Prescribed by or in consultation with an oncologist

Product Name: Lonsurf

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Lonsurf therapy

AND

2 Prescribed by or in consultation with an oncologist

3 . Background

Benefit/Coverage/Program Information **Quantity Limit** This product is subject to a standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . References

1. Lonsurf Prescribing Information. Taiho Oncology, Inc., September 2015.

Prior Authorization Guideline

GL-16398 Lumizyme, Myozyme (alglucosidase alfa)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 3/31/2016

Technician Note :

P&T Approval Date: 12/5/2006; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Lumizyme (alglucosidase alfa) **Indications** **Pompe Disease** Indicated for patients with Pompe disease [acid alpha-glucosidase (GAA) deficiency].
Drug Name: Myozyme (alglucosidase alfa) **Indications**

Pompe Disease

Indicated for use in patients with Pompe disease (GAA deficiency). Myozyme has been shown to improve ventilator-free survival in patients with infantile-onset Pompe disease as compared to an untreated historical control, whereas use of Myozyme in patients with other forms of Pompe disease has not been adequately studied to assure safety and efficacy.

2 . Criteria

Product Name: Lumizyme, Myozyme

Approval Length	5 Year
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Pompe disease (GAA deficiency) [1, 2, A]

3 . Endnotes

A. There are different tests available for diagnosis of Pompe disease. [3] The clinical diagnosis is traditionally confirmed by the virtual absence (infantile-onset) or markedly reduced (late onset) GAA activity in tissues such as cultured fibroblasts from skin biopsy, muscle biopsy, purified lymphocytes, mononuclear cells and lymphoid cell lines. Historically, GAA enzyme measurement is most reliably performed in cultured fibroblasts or muscle due to the possibility of alternate isoenzyme activities making disease in white cell assays. New methods have now been developed that assay GAA activity in dried

blood spot (DBS) extracts. DBS can be conveniently collected by the heel-or finger-stick method and shipped from locations remote from the analytical center. [4] Diagnosis of Pompe disease should be confirmed by ordering one of the following tests to measure acid alpha-glucosidase (GAA) enzyme activity: [5] (1) Dried blood spot (blood draw, heel prick, or finger stick): turnaround time for results: 2-10 days (2) Lymphocytes (blood draw): turnaround time for results: 7-10 days (3) Mixed lymphocytes (blood draw): turnaround time for results: 7-10 days (4) Fibroblasts (skin biopsy): turnaround time for results: 4-6 weeks (5) Muscle tissue (muscle biopsy): turnaround time for results: 1-4 weeks

4 . References

1. Myozyme Prescribing Information. Genzyme Corporation, May 2014.
2. Lumizyme Prescribing Information. Genzyme Corporation, August 2014.
3. Per clinical consultation with geneticist, November 10, 2010.
4. Kishani PS, Steiner RD, Bali, D. ACMG Practice Guideline. Pompe disease diagnosis and management guideline. Genet Med. 2006;8(5):267-88.
5. Diagnosing Pompe Disease (also known as Acid Maltase Deficiency). Available at: http://www.pompe.com/~/media/Pompe/Files/en/PDF/POMPUSP141_LabList.pdf. Accessed August 10, 2014.

Prior Authorization Guideline

GL-17355 Lynparza (olaparib)

Formulary OptumRx SP

Formulary Note

Approval Date 2/19/2015

Revision Date 5/31/2016

Technician Note :

P&T Approval Date: 2/18/2015; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Lynparza (olaparib)

Indications

gBRCA-mutated advanced ovarian cancer

Indicated as monotherapy in patients with deleterious or suspected deleterious germline BRCA mutated (as detected by an FDA-approved test) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. The indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

2 . Criteria

Product Name: Lynparza

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced ovarian cancer

AND

2 Presence of deleterious or suspected deleterious germline BRCA-mutations as detected by an FDA-approved test or Clinical Laboratory Improvement Amendments-approved facility [A, B]

AND

3 History of failure, contraindication, or intolerance to three or more prior lines of chemotherapy (e.g., paclitaxel with cisplatin)

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Lynparza

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Lynparza therapy

3 . Endnotes

A. The BRCA1 and BRCA2 alleles have been identified as markers for an increased incidence of Hereditary Breast and Ovarian Syndrome (HBOC). Subsequently, an FDA-approved test is available to detect the presence of germline BRCA-mutations and assess if the identified mutations are deleterious or not. *Please note that the presence of a BRCA mutation is not automatically considered to be deleterious or suspected deleterious. This designation will need to be corroborated by genetic testing and/or attestation by the prescriber [2].
B. BRACAnalysis CDx is a product of Myriad Genetic Laboratories and is currently the only Food and Drug Administration(FDA) approved laboratory developed test that indicates whether or not a patient with ovarian cancer is positive for a deleterious or suspected deleterious BRCA mutation. BRACAnalysis CDx test results are provided to the requesting healthcare professional and should clearly state “positive for a deleterious mutation” which indicates that Lynparza therapy is appropriate. *Please note that other FDA approved genetic tests which assess BRCA mutation status may become available. This information is current as of 6/12/2015 [2].

4 . References

1. Lynparza Prescribing Information. AstraZeneca Pharmaceuticals LP, Inc, December 2014.
2. Lynparza FDA Medical Review. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/206162Orig1s000MedR.pdf. Accessed on June 12, 2015.

Prior Authorization Guideline

GL-15715 Mekinist (trametinib)

Formulary OptumRx SP

Formulary Note

Approval Date 7/11/2013

Revision Date 3/30/2016

Technician Note :

P&T Approval Date: 7/9/2013 P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Mekinist (trametinib)

Indications

Unresectable or metastatic melanoma

Indicated as a single agent and in combination with dabrafenib for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test. Mekinist, in combination with dabrafenib, is indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test. This indication is based on the demonstration of durable response rate. Improvement in disease-related symptoms or overall survival has not been

demonstrated for Mekinist in combination with dabrafenib. Limitation of use: Mekinist as a single agent is not indicated for treatment of patients who have received prior BRAF-inhibitor therapy.

2 . Criteria

Product Name: Mekinist

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following diagnoses: [1]

- Unresectable melanoma
- Metastatic melanoma

AND

2 Cancer is BRAFV600 mutant type (MT) as detected by an FDA-approved test (THxID-BRAF Kit) or performed at a facility approved by Clinical Laboratory Improvement Amendments (CLIA) [2]

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Mekinist

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Mekinist therapy

3 . References

1. Mekinist Prescribing Information. GlaxoSmithKline, January 2014.
2. National Comprehensive Cancer Network. Clinical practice guidelines in oncology: melanoma. v.3.2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf. Accessed May 12, 2015.

Prior Authorization Guideline

GL-30934 Mitoxantrone

Formulary OptumRx SP

Formulary Note

Approval Date 8/24/2016

Revision Date 8/24/2016

Technician Note :

P&T Approval Date: 5/18/2001; P&T Revision Date: 8/18/2016 **Effective 10/1/2016**

1 . Indications

Drug Name: Mitoxantrone

Indications

Multiple Sclerosis Indicated for reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening relapsing-remitting multiple sclerosis (i.e., patients whose neurologic status is significantly abnormal between relapses). Is not indicated in the treatment of patients with primary progressive multiple sclerosis.

Prostate Cancer In combination with corticosteroids is indicated as initial chemotherapy for the

treatment of patients with pain related to advanced hormone-refractory prostate cancer.

Acute Non-Lymphocytic Leukemia (ANLL) In combination with other approved drug(s) is indicated in the initial therapy of ANLL in adults. This category includes myelogenous, promyelocytic, monocytic, and erythroid acute leukemias.

2 . Criteria

Product Name: Mitoxantrone

Diagnosis	Multiple Sclerosis
Approval Length	6 Months [5-6, A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of one of the following:

1.1 Secondary progressive multiple sclerosis: gradually worsening disability with or without superimposed relapses [2]

OR

1.2 Progressive relapsing multiple sclerosis: progression of disability from the onset with superimposed relapses [2]

OR

1.3 Worsening relapsing-remitting multiple sclerosis: neurological status remains significantly abnormal in between multiple sclerosis relapses [3]

AND

2 Disease progression despite one of the following therapies: [3]

- Aubagio (teriflunomide)*
- Avonex (interferon beta-1a)*
- Betaseron (interferon beta-1b)*
- Copaxone (glatiramer acetate)*
- Extavia (interferon beta-1b)*
- Gilenya (fingolimod)*
- Glatopa (glatiramer acetate)*
- Lemtrada (alemtuzumab)*
- Plegridy (peginterferon beta-1a)*
- Rebif (interferon beta-1a)*
- Tecfidera (dimethyl fumarate)*
- Tysabri (natalizumab)*
- Zinbryta (daclizumab)*

AND

3 Left ventricular ejection fraction (LVEF) greater than or equal to 50%

AND

4 Neutrophil count greater than or equal to 1,500 cell/mm^3

Notes	*These products may require Prior Authorization.

Product Name: Mitoxantrone

Diagnosis	Multiple Sclerosis
Approval Length	6 Months [5-6, A]

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to mitoxantrone therapy

AND

2 Left ventricular ejection fraction (LVEF) greater than or equal to 50% [2, 5-6]

AND

3 A lifetime cumulative dose less than 140mg/m^2

Product Name: Mitoxantrone

Diagnosis	Prostate Cancer
Approval Length	6 Months [5-6, A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced hormone-refractory (castration-resistant) prostate cancer

AND

2 Used in combination with corticosteroids (e.g., prednisone, methylprednisolone) [12]

AND

3 Left ventricular ejection fraction (LVEF) greater than or equal to 50% [2, 5-6]

AND

4 Neutrophil count greater than or equal to 1,500 cell/mm^3

Product Name: Mitoxantrone

Diagnosis	Prostate Cancer
Approval Length	6 Months [5-6, A]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on mitoxantrone therapy

AND

2 Left ventricular ejection fraction (LVEF) greater than or equal to 50% [2, 5-6]

AND

3 A lifetime cumulative dose less than 140mg/m^2 [1]

Product Name: Mitoxantrone

Diagnosis	Acute Non-Lymphocytic Leukemia (ANLL)
Approval Length	6 Months [5-6, A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of acute non-lymphocytic leukemia (ANLL) (e.g., myelogenous, promyelocytic, monocytic, and erythroid)

AND

2 Used in combination with other medications used for the treatment of ANLL

AND

3 Left ventricular ejection fraction (LVEF) greater than or equal to 50% [2, 5-6]

Product Name: Mitoxantrone

Diagnosis	Acute Non-Lymphocytic Leukemia (ANLL)
Approval Length	6 Months [5-6, A]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on mitoxantrone therapy

AND

2 Left ventricular ejection fraction (LVEF) greater than or equal to 50% [2, 5-6]

AND

3 A lifetime cumulative dose less than 140mg/m^2

3 . Endnotes

A. All patients should be carefully assessed for cardiac signs and symptoms by history and physical examination prior to start of Novantrone therapy. Left ventricular ejection

fraction (LVEF) should be evaluated prior to administration of the initial dose of mitoxantrone and all subsequent doses. Mitoxantrone is recommended to be dosed once every three months. Additional doses of mitoxantrone should not be administered to multiple sclerosis patients who have experienced either a drop in LVEF to below 50% or a clinically significant reduction in LVEF during mitoxantrone therapy. [1]

4 . References

1. Mitoxantrone Prescribing Information. Fresenius Kabi USA, LLC. June 2015.
2. Hartung HP, Gonsette R, Konig N, et al. Mitoxantrone in progressive multiple sclerosis: a placebo-controlled, double-blind, randomized, mulitcentre trial. Lancet 2002;360:2018-25.
3. Marriott JJ, Miyasaki JM, Gronseth G, Oâ€™Connor PW. Evidence Report: The efficacy and safety of mitoxantrone (Novantrone) in the treatment of multiple sclerosis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2010;74:1463-70.
4. Avasarala JR, Cross AH, Clifford DB, Singer BA, Siegal BA, Abbey EE. Rapid onset mitoxantrone-induced cardiotoxicity in secondary progressive multiple sclerosis. Mult Scler. 2003;9:59-62.
5. Ghalie RG, Edan G, Laurent M, et al. Cardiac adverse effects associated with mitoxantrone (Novantrone) therapy in patients with MS. Neurology. 2002;59:909-13.
6. Bastianello S, Pozzilli C, Dâ€™Andrea F, et al. A controlled trial of mitoxantrone in multiple sclerosis: serial MRI evaluation at one year. Can J Neurol Sci. 1994;21:266-70.
7. Petrylak DP, Tangen CM, Hussain MH, et al. Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. N Engl J Med. 2004;351:1513-20.
8. Tannock IF, de Wit R, Berry WR, et al. Investigators. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. N Engl J Med. 2004;351:1502-12.
9. Anderson JE, Kopecky KJ, Willman CL, et al. Outcome after induction chemotherapy for older patients with acute myeloid leukemia is not improved with mitoxantrone and etoposide compared to cytarabine and daunorubicin: a Southwest Oncology Group study. Blood. 2002;100:3869-76. Epub 2002 Aug 1.
10. NCCN Clinical Practice Guidelines in Oncology. Acute Myeloid Leukemia v. 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf Accessed July 25, 2016.
11. NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer v. 3.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed July 25, 2016.

Prior Authorization Guideline

GL-17079 Mozobil (plerixafor injection)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/25/2016

Technician Note :

P&T Approval Date: 5/19/2009; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Mozobil (plerixafor injection)

Indications

Hematopoietic Stem Cell Mobilization

Indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells (HSCs) to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma (NHL) and multiple myeloma (MM).

2 . Criteria

Product Name: Mozobil

Approval Length	1 course of therapy (up to four days of therapy). [2, 3, 4, 5, A]
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

- Patients with NHL who will be undergoing autologous HSC transplantation
- Patients with MM who will be undergoing autologous HSC transplantation

AND

2 Used in combination with granulocyte-colony stimulating factor (G-CSF) [e.g., Neupogen (filgrastim), Zarxio (filgrastim)]

AND

3 Prescribed by or in consultation with a hematologist/oncologist

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. The duration of treatment for Mozobil in both the pivotal studies and compassionate use data was limited to one course of therapy. [2, 3, 4]

5 . References

1. Mozobil Prescribing Information. Genzyme Corporation, June 2013.
2. DiPersio JF, Micallef I, Stiff P, et al. Months report from the phase 3 study of plerixafor + G-CSF vs. placebo + G-CSF for mobilization of hematopoietic stem cell for autologous transplant in patients with NHL. [abstract]. Blood. 2008;112:Abstract 1136.
3. DiPersio JF, Stadtmauer E, Nademanee A, et al. Months report from a phase 3 study of plerixafor + G-CSF vs. placebo + G-CSF for mobilization of hematopoietic stem cell for autologous transplant in patients with multiple myeloma. [abstract]. Blood. 2008;112:Abstract 3312.
4. Calandra G, McCarty J, McGuirk J, et al. AMD3100 plus G-CSF can successfully mobilize CD34+ cells from non-hodgkin's lymphoma, hodgkin's disease and multiple myeloma patients previously failing mobilization with chemotherapy and/or cytokine treatment: compassionate use data. Bone Marrow Transplant. 2008;41:331-38.
5. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Myeloid Growth Factors v.1.2014. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloid_growth.pdf. Accessed March 4, 2014.

Prior Authorization Guideline

GL-30907 Multiple Sclerosis (MS) Agents

Formulary OptumRx SP

Formulary Note

Approval Date 8/24/2016

Revision Date 8/24/2016

Technician Note :

P&T Approval Date: 11/20/2000; P&T Revision Date: 8/18/2016 **Effective 9/15/2016**

1 . Indications

Drug Name: Avonex (interferon beta-1a)

Indications

Relapsing forms of multiple sclerosis (MS) Indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations. Patients with MS in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with MS.

Drug Name: Betaseron (interferon beta-1b)

Indications

Relapsing forms of MS Indicated for the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations. Patients with MS in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with MS.

Drug Name: Copaxone (glatiramer acetate), Glatopa (glatiramer acetate)

Indications

Relapsing-remitting MS Indicated for the treatment of patients with relapsing forms of MS.

Drug Name: Extavia (interferon beta-1b)

Indications

Relapsing forms of MS Indicated for the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations. Patients with MS in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with MS.

Drug Name: Rebif (interferon beta-1a)

Indications

Relapsing forms of MS Indicated for the treatment of patients with relapsing forms of MS to decrease the frequency of clinical exacerbations and delay the accumulation of physical disability.

Drug Name: Plegridy (peginterferon beta-1a)

Indications

Relapsing forms of MS Indicated for the treatment of patients with relapsing forms of MS.

Drug Name: Aubagio (teriflunomide)

Indications

Relapsing forms of MS Indicated for the treatment of patients with relapsing forms of MS.

Drug Name: Gilenya (fingolimod)

Indications

Relapsing forms of MS Indicated for the treatment of patients with relapsing forms of MS to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability.

Drug Name: Tecfidera (dimethyl fumarate)

Indications

Relapsing forms of MS Indicated for the treatment of patients with relapsing forms of MS.

Drug Name: Lemtrada (alemtuzumab)

Indications

Relapsing forms of MS Indicated for treatment of patients with relapsing forms of MS. Becuase of its safety profile, the use of Lemtrada should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

2 . Criteria

Product Name: Avonex, Copaxone, Glatopa, Plegridy, or Tecfidera

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of a relapsing form of multiple sclerosis (MS) (e.g., relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS with relapses) [A-D]

Product Name: Aubagio, Betaseron*, Extavia*, Rebif*

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of a relapsing form of MS (e.g., relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS with relapses) [A]

AND

2 One of the following:

2.1 For continuation of therapy

OR

2.2 History of failure following a trial for at least 4 weeks or history of intolerance or contraindication to at least two of the following disease-modifying therapies for MS:

- Avonex (interferon beta-1a)**
- Copaxone (glatiramer acetate)**
- Plegridy (peginterferon beta-1a)**
- Tecfidera (dimethyl fumarate)**

Notes	*Product may be excluded depending on the plan. **These products may require Prior Authorization.

Product Name: Gilenya

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of a relapsing form of multiple sclerosis (MS) (e.g., relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS with relapses) [A]

AND

2 One of the following:

2.1 For continuation of therapy

OR

2.2 History of failure following a trial for at least 4 weeks or history of intolerance or contraindication to one of the following disease-modifying therapies for MS:

- Avonex (interferon beta-1a)*
- Copaxone (glatiramer acetate)*
- Plegridy (peginterferon beta-1a)*
- Tecfidera (dimethyl fumarate)*

Notes	*These products may require Prior Authorization.

Product Name: Lemtrada

Approval Length	1 Time [E]
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of a relapsing form of multiple sclerosis (MS) (e.g., relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS with relapses) [A]

AND

2 One of the following:

2.1 All of the following:

2.1.1 Patient has not been previously treated with alemtuzumab

AND

2.1.2 Patient has history of failure following a trial for at least 4 weeks or history of intolerance or contraindication to Tysabri (natalizumab)* [F]

AND

2.1.3 Patient has history of failure following a trial for at least 4 weeks or history of intolerance or contraindication to one of the following disease-modifying therapies for MS:

- Gilenya (fingolimod)*
- Tecfidera (dimethyl fumarate)*

OR

2.2 All of the following: [E]

2.2.1 Patient has previously received treatment with alemtuzumab

AND

2.2.2 At least 12 months have or will have elapsed since the first treatment with alemtuzumab

AND **2.2.3** Patient has not already received the FDA-recommended lifetime limit of two (2) treatment courses of alemtuzumab **AND** **3** Patient is not receiving alemtuzumab in combination with another disease modifying agent (e.g., interferon beta preparations, glatiramer acetate, natalizumab, fingolimod, or teriflunomide)	
Notes	*These products may require Prior Authorization.

3 . Endnotes

A. According to the National MS Society, of the four disease courses that have been identified in MS, one (relapsing-remitting) is characterized primarily by relapses, and two (progressive-relapsing and secondary-progressive) have both relapsing and progressive characteristics. These three constitute â€œrelapsing forms of MSâ€ if they describ disease course that is characterized by the occurrence of relapses. [12] The effectiveness of IFNÃŸ in SPMS patients without relapses is uncertain. [9, 10]
B. Initiation of treatment with an interferon beta medication or glatiramer acetate should be considered as soon as possible following a definite diagnosis of MS with active, relapsing disease, and may also be considered for selected patients with a first attack who are at high risk of MS. [11]
C. Based on several years of experience with glatiramer acetate and interferon beta 1a and 1b, it is the consensus of researchers and clinicians with expertise in MS that these agents are likely to reduce future disease activity and improve quality of life for many individuals with relapsing forms of MS, including those with secondary progressive disease who continue to have relapses. For those who are appropriate candidates for one of these drugs, treatment must be sustained for years. Cessation of treatment may result in a resumption of pre-treatment disease activity. [11]

D. MS specialists will use Copaxone in relapsing forms of disease, including SPMS with relapses. While there have been no trials of Copaxone in SPMS (so we have no evidenced-based data upon which to make decisions or recommendations), it's clear that where there are relapses, the injectable therapies are partially effective â€“ they reduce relapses and new lesions on MRI. In SPMS, the trials suggest that the interferons work better in earlier, more inflammatory (i.e. those with relapses prior to the trial and with gadolinium-enhancing lesions, which is the MRI equivalent of active inflammation). Since Copaxone and the interferons appear to have rather similar efficacy in the head-to-head trials, most assume that Copaxone has a similar efficacy in SPMS: where there are relapses or active inflammation on MRI, it will likely have some benefit. Thus, most MS specialists will use Copaxone in patients with SPMS who have persistent relapses. [13]
E. Not to exceed the FDA-recommended dosage of 2 treatment courses (with the second course administered 12 months following the first course). According to Prescribing Information, the recommended dosage of Lemtrada is 12 mg/day administered by intravenous infusion for 2 treatment courses (first treatment course: 12 mg/day on 5 consecutive days; second treatment course: 12 mg/day on 3 consecutive days administered 12 months after the first treatment course). [18]
F. Although not included in the Prescribing Information as a true contraindication, any factors that may increase the risk of PML while on Tysabri therapy should be considered an acceptable contraindication to Tysabri, allowing for the bypass of this embedded step through Tysabri. These risk factors include, but are not limited to, longer treatment duration with Tysabri (especially beyond 2 years), prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil), or the presence of anti-John Cunningham Virus (JCV) antibodies. [18]

4 . References

1. Avonex Prescribing Information, Biogen Idec Inc. August 2014.
2. Betaseron Prescribing Information, Bayer, July 2016.
3. Copaxone Prescribing Information, Teva Pharmaceuticals. May 2016.
4. Extavia Prescribing Information, Novartis, May 2016.
5. Rebif Prescribing Information, Serono Inc., January 2016.
6. European study group on interferon Î²-1b in secondary progressive MS. Placebo controlled multicentre randomised trial of interferon Î²-1b in treatment of secondary progressive multiple sclerosis. Lancet 1998;352(7):1491-97.
7. Panitch H, Miller A, Paty D, Weinshenker B; North American Study Group on Interferon beta-1b in Secondary Progressive MS. Neurology 2004;63:1788-95.
8. Secondary Progressive Efficacy Clinical Trial of Recombinant Interferon-beta-1a in MS (SPECTRIM) Study Group. Randomized controlled trial of interferon-beta-1a in secondary progressive MS. Neurology 2001;56:1496-1504.
9. Goodin DS, Frohman EM, Garmany, Jr. GP, et al. Disease modifying therapies in multiple sclerosis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for clinical practice guidelines. Neurology 2002; 58:169-78. (Reaffirmed 7/19/2008)
10. McEvoy, GK. American Society of Health-System Pharmacists (ASHP). Bethesda, MD: ASHP Inc.; 2004.
11. National Clinical Advisory Board of the National Multiple Sclerosis Society. MS Disease Management Consensus Statement. 2008. Modified February 2, 2010. Available at:

http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/ExpOp_Consensus.pdf. Accessed July 25, 2016.
12. National Multiple Sclerosis Society. About MS: Relapsing MS. Available at: http://www.nationalmssociety.org/What-is-MS/Types-of-MS/Relapsing-remitting-MS. Accessed July 25, 2016.
13. Per clinical consultation with MS specialist, December 29, 2010.
14. Plegridy Prescribing Information, Biogen Idec Inc. October 2015.
15. Aubagio Prescribing Information. Genzyme Corporation, June 2016.
16. Gilenya Prescribing Information. Novartis, February 2016.
17. Tecfidera Prescribing Information. Biogen Idec Inc., February 2016.
18. Lemtrada Prescribing Information, Genzyme Corporation. November 2014.
19. Glatopa Prescribing Information, Sandoz Inc. January 2016.

Prior Authorization Guideline

GL-16876 Myalept (metreleptin for injection)

Formulary OptumRx SP

Formulary Note

Approval Date 5/21/2014

Revision Date 5/25/2016

Technician Note :

P&T Approval Date: 5/21/2014; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Myalept (metreleptin for injection)

Indications

Congenital or acquired generalized lipodystrophy

Indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy

2 . Criteria

Product Name: Myalept

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of congenital or acquired generalized lipodystrophy

AND

2 Patient is refractory to current standards of care for lipid and diabetic management

AND

3 Prescribed by or in consultation with an endocrinologist

AND

4 Documentation demonstrates that patient has at least one of the following metabolic abnormalities:

- Insulin resistance (defined as requiring more than 200 units per day)
- Hypertriglyceridemia
- Diabetes

Product Name: Myalept

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Myalept therapy, such as one of the following:

- Sustained reduction in hemoglobin A1c level from baseline
- Sustained reduction in triglyceride levels from baseline

3 . References

1. Myalept Prescribing Information. Aegerion Pharmaceuticals, Inc., March 2015.

Prior Authorization Guideline

GL-15491 Myobloc (rimabotulinumtoxin B)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/7/2016

Technician Note :

P&T Approval Date: 4/20/2001; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Myobloc (rimabotulinumtoxin B)

Indications

Cervical Dystonia (CD)

Indicated for the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.

2 . Criteria

Product Name: Myobloc

Diagnosis	Cervical Dystonia (also known as spasmodic torticollis)
Approval Length	3 Months for a single dose (up to 10,000 units) [1]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cervical dystonia (also known as spasmodic torticollis)

Product Name: Myobloc

Diagnosis	Cervical Dystonia (also known as spasmodic torticollis)
Approval Length	3 Months for a single dose (up to 10,000 units) [1]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Myobloc therapy

AND

2 At least 3 months have elapsed since the last treatment with Myobloc

3 . Dosing

Drug Name	Description
Myobloc - Recommended Initial Dose:	2500 - 5000 U IM divided among affected muscles. Patients without a prior history of tolerating botulinum toxin injections should receive a lower initial dose. Subsequent dosing should be optimized according to the patient's individual response. Myobloc should be administered by physicians familiar and experienced in the assessment and management of patients with CD. The duration of effect in patients responding to Myobloc treatment has been observed in studies to be between 12 and 16 weeks at doses of 5000 U or 10,000 U.

4 . References

1. Myobloc Prescribing Information. Solstice Neurosciences, Inc., May 2010.
2. Brashear A, et al. Safety and efficacy of NeuroBloc (botulinum toxin type B) in type-A responsive cervical dystonia. Neurology 1999;53(7):1439-1446.
3. Brin MF, et al. Safety and efficacy of NeuroBloc (botulinum toxin type B) in type A-resistant cervical dystonia. Neurology 1999;53(7):1431-1438.
4. Lew MF, et al. Botulinum toxin type B: a double-blind, placebo-controlled,safety and efficacy study in cervical dystonia. Neurology 1997;49(3):701-707.
5. Simpson DM, Blitzer A, Brashear A, et al. Assessment: otulinum neurotoxin for the treatment of movement disorders (an evidence-based review). Neurology 2008;70:1699-1706.

Prior Authorization Guideline

GL-17081 Naglazyme (galsulfase injection)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/25/2016

Technician Note :

P&T Approval Date: 8/1/2006; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Naglazyme (galsulfase injection)

Indications

Mucopolysaccharidosis (MPS VI)

Indicated for patients with Mucopolysaccharidosis VI (MPS VI). Naglazyme has been shown to improve walking and stair-climbing capacity.

2 . Criteria

Product Name: Naglazyme

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Mucopolysaccharidosis VI (MPS VI, Maroteaux-Lamy Syndrome)

3 . References

1. Naglazyme Prescribing Information. BioMarin Pharmaceutical Inc. June 2005.
2. Harmatz P, Giugliani R, Schwartz I, et al. Enzyme replacement therapy for Mucopolysaccharidosis VI: A phase 3, randomized, double-blind, placebo-controlled, multinational study of recombinant human n-acetylgalactosamine 4-sulfate (recombinant human arylsulfatase B or rhASB) and follow-on, open label extension study. The J of Pediatr 2006;148:533-539.
3. [No authors listed]. Galsulfatase b, BM 102, recombinant arylsulfatase B, recombinant n-acetylgalactosamine-4-sulfatase, rhASB. Drugs R D 2005;6:312-5.
4. Maroteaux-Lamy syndrome website. Available at: http://www.maroteaux-lamy.com/English/HCP/Glossary.aspx Assessed March 9, 2009.
5. Harmatz P, Giugliani R, Schwartz IV et al. Long-term follow-up of endurance and safety outcomes during enzyme replacement therapy for mucopolysaccharidosis VI: Final results of three clinical studies of recombinant human N-acetylgalactosamine 4-sulfatase. Mol Genet Metab. 2008;94(4):469-75.
6. Giugliani R, Harmatz P, Wraith JE. . Management Guidelines for Mucopolysaccharidosis VI. Pediatrics 2007;120;405-418

Prior Authorization Guideline

GL-17080 Neumega (oprelvekin)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/29/2016

Technician Note :

P&T Approval Date: 3/17/2000; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Neumega (oprelvekin)

Indications

Severe thrombocytopenia

Indicated for the prevention of severe thrombocytopenia and the reduction of the need for platelet transfusions following myelosuppressive chemotherapy in adult patients with nonmyeloid malignancies who are at high risk of severe thrombocytopenia. Efficacy was demonstrated in patients who had experienced severe thrombocytopenia following the previous chemotherapy cycle. Is not indicated following myeloablative chemotherapy. The safety and efficacy of Neumega have not been established in pediatric patients In clinical studies,

Neumega was shown to be effective in patients with a variety of non-myeloid malignancies, which included myelosuppressed breast cancer patients on various chemotherapy regimens.

2 . Criteria

Product Name: Neumega

Approval Length	3 week intervals for up to six cycles post-chemotherapy [C]
Guideline Type	Prior Authorization

Approval Criteria

1 Verification that the cancer is a non-myeloid malignancy

AND

2 Platelet count less than 50,000 cells/microliter [A]

AND

3 Patients with one or more of the following risk factors:

- Patients who have had extensive prior cytotoxic chemotherapy [B]
- Patients with prior severe chemotherapy-induced thrombocytopenia
- Patients receiving chemotherapy regimens associated with high risk for thrombocytopenia (e.g., dose-intensive chemotherapy) [B]

AND

4 Prescribed by or in consultation with an oncologist and/or hematologist	
Notes	Will not be authorized in patients following myeloablative chemotherapy. [1]

3 . Definitions

Definition	Description
Thrombocytopenia:	Generally, thrombocytopenia is defined as a reduction in platelet count below 100,000 cells per microliter or a 50% reduction in platelet count from baseline. Currently, there is no accepted definition of the terms mild, moderate, or severe thrombocytopenia. The National Cancer Institute classifies thrombocytopenia into four gradations, based on quantitative measurements. These are: [5, 6, A] Grade 1: 75,000 to 150,000 cells/microliter; Grade 2: 50,000 to < 75,000 cells/microliter; Grade 3: 25,000 to < 50,000 cells/microliter; Grade 4: < 25,000 cells/microliter

4 . Endnotes

A. While there is no accepted definition of mild, moderate, or severe thrombocytopenia, the National Cancer Institute has categorized thrombocytopenia into severity grades (see Definitions sections). In the studies conducted, severe thrombocytopenia was defined as platelet count less than or equal to 20,000 cells per microliter. Platelet count should be monitored during the time of the expected nadir and until recovery has occurred (post-nadir counts greater than or equal to 50,000/microL). Dosing should be continued until the post-nadir platelet count is greater than or equal to 50,000/microL. [1]

B. Dosing of Neumega should begin 6 to 24 hours following the completion of chemotherapy dosing. The safety and efficacy of Neumega given immediately prior to or concurrently with cytotoxic chemotherapy or initiated at the time of expected nadir have not been established. [1]
C. In controlled clinical trials, doses were administered in courses of 10 to 21 days. Dosing beyond 21 days per treatment course is not recommended. Neumega has been administered safely using the recommended dosage schedule for up to six cycles following chemotherapy. The safety and efficacy of chronic administration of Neumega have not been established. [1]

5 . References

1. Neumega Prescribing Information. Wyeth Pharmaceuticals, Inc., January 2011.
2. Isaacs C, Robert NJ, Bailey FA, Schuster MW, Overmoyer B, Graham M, et al. Randomized, placebo-controlled study of recombinant human interleukin-11 to prevent chemotherapy-induced thrombocytopenia in patients with breast cancer receiving dose-intensive cyclophosphamide and doxorubicin. J Clin Oncol. 1997;15:3368-3377.
3. Tepler I, Elias L, Smith JW, Hussein M, Rosen G, Chang AYC, et al. A randomized placebo-controlled trial of recombinant human interleukin-11 in cancer patients with severe thrombocytopenia due to chemotherapy. Blood. 1996:87;3607-3614.
4. Gordon MS, McCaskill-Stevens WJ, Battiato LA, Loewy J, Loesch D, Breeden D, et al. A phase I trial of recombinant human interleukin-11 (NeumegaÒ rhIL-11 growth factor) in women with breast cancer receiving chemotherapy. Blood. 1996;87:3615-3624.
5. Sekhon SS, Roy V. Thrombocytopenia in adults: a practical approach to evaluation and management. South Med J. 2006 May;99(5):491-8
6. National Cancer Institute. CTC v2.0 to CTCAE v3.0 grade mapping. Available at: http://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcaev3.pdf. Accessed July 3, 2012

Prior Authorization Guideline

GL-17350 Nexavar (sorafenib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/23/2016

Technician Note :

P&T Approval Date: 4/4/2006; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Nexavar (sorafenib)

Indications

Renal Cell Carcinoma

Indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

Hepatocellular Carcinoma

Indicated for the treatment of patients with unresectable hepatocellular carcinoma (HCC).

Differentiated Thyroid Carcinoma

Indicated for the treatment of patients with locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) that is refractory to radioactive iodine treatment.

Off Label Uses

Medullary Thyroid Carcinoma

Used for treatment of disseminated symptomatic disease if: (1) clinical trials, vandetanib, or cabozantinib are not available or appropriate, or (2) there is progression on vandetanib or cabozantinib. [8]

2 . Criteria

Product Name: Nexavar

Diagnosis	Renal cell carcinoma
Approval Length	12 Months [B]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of renal cell carcinoma [4, A]

AND

2 One of the following: [4,8]

2.1 Relapse following surgical excision

OR

2.2 Both of the following:

- Medically or surgically unresectable tumor
- Diagnosis of Stage IV disease

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Nexavar

Diagnosis	Renal cell carcinoma
Approval Length	12 Months [B]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Nexavar therapy

Product Name: Nexavar

Diagnosis	Hepatocellular carcinoma
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of hepatocellular carcinoma [5]

AND

2 One of the following: [5,8]

2.1 Patient has metastatic disease

OR

2.2 Patient has extensive liver tumor burden

OR

2.3 Patient is inoperable by performance status or comorbidity (local disease or local disease with minimal extrahepatic disease only)

OR

2.4 Both of the following:

- Patient is not a transplant candidate
- Disease is unresectable

AND

3 Prescribed by or in consultation with one of the following:

- Oncologist
- Hepatologist

- Gastroenterologist

Product Name: Nexavar

Diagnosis	Hepatocellular carcinoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Nexavar therapy

Product Name: Nexavar

Diagnosis	Thyroid Carcinoma
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 All of the following:

1.1.1 Diagnosis of differentiated thyroid carcinoma (i.e., follicular, Hurthle, or papillary carcinoma) [8]

AND

1.1.2 One of the following: [6]

- Locally recurrent disease
- Metastatic disease

AND

1.1.3 One of the following: [6]

- Patient has symptomatic disease
- Patient has progressive disease

AND

1.1.4 Disease is refractory to radioactive iodine (RAI) treatment

OR

1.2 All of the following: [8]

1.2.1 Diagnosis of disseminated medullary thyroid carcinoma (off-label)

AND

1.2.2 Patient has symptomatic disease

AND

1.2.3 History of failure, contraindication, or intolerance to one of the following:

- Caprelsa (vandetanib)
- Cometriq (cabozantinib)

AND

2 Prescribed by or in consultation with an oncologist

Product Name: Nexavar

Diagnosis	Thyroid Carcinoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Nexavar therapy

3 . Endnotes

A. Renal cell carcinoma is highly resistant to systemic chemotherapy, and no agent should be considered standard in the treatment of metastatic disease. [2, 3]
B. Treatment should continue until the patient is no longer clinically benefiting from therapy or until unacceptable toxicity occurs. Mean progression-free survival in Study 1 as described in the Nexavar prescribing information indicates a median progression-free survival of 167 days in Nexavar-treated patients with renal cell carcinoma. [1]
C. Mean progression-free survival in patients with differentiated thyroid carcinoma as described in the Nexavar prescribing information indicates a median progression-free survival of 10.8 months in Nexavar-treated patients [1]
D. Differentiated thyroid carcinoma includes papillary carcinoma, follicular carcinoma, Hurthle cell carcinoma, and poorly differentiated carcinoma. [7]

4 . References

1. Nexavar Prescribing Information. Bayer HealthCare Pharmaceuticals Inc., November 2013.
2. Amato RJ. Chemotherapy for renal cell carcinoma. Semin Oncol. 2000;27:177-86.
3. Vogelzang NJ, Stadler WM. Kidney cancer. Lancet. 1998;352:1691-6.

4. National Comprehensive Cancer Network. Practice Guidelines in Oncology. Kidney Cancer v.3.2014. Available at: http://www.nccn.org/professionals/physician_gls/PDF/kidney.pdf. Accessed July 11, 2014.
5. National Comprehensive Cancer Network. Practice Guidelines in Oncology. Hepatobiliary Cancers v.2.2014. Available at: http://www.nccn.org/professionals/physician_gls/PDF/hepatobiliary.pdf. Accessed July 11, 2014.
6. National Comprehensive Cancer Network. Practice Guidelines in Oncology. Thyroid Carcinoma v.2.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed July 11, 2014.
7. Brose MS, Nutting CM, Sherman SI, et al. Rationale and design of DECISION: a doubleblind, randomized, placebo-controlled phase III trial evaluating the efficacy and safety of sorafenib in patients with locally advanced or metastatic radioactive iodine (RAI)-refractory, differentiated thyroid cancer. BMC Cancer. 2011;349.
8. NCCN Drugs and Biologics Compendium: Sorafenib. Available at: http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=134. Accessed July 11, 2014.

Prior Authorization Guideline

GL-17075 Ninlaro (ixazomib citrate)

Formulary OptumRx SP

Formulary Note

Approval Date 2/15/2016

Revision Date 4/15/2016

Technician Note :

P&T Approval Date: 1/27/2016; P&T Revision Date: 5/19/2016 **Effective 6/15/2016**

1 . Indications

Drug Name: Ninlaro (ixazomib citrate)

Indications

Multiple Myeloma

Indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy.

2 . Criteria

Product Name: Ninlaro**

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple myeloma [1]

AND

2 Patient has received at least one prior therapy for multiple myeloma [eg, Revlimid (lenalidomide), Thalomid (thalidomide), Velcade (bortezomib)]

AND

3 Used in combination with both of the following: [1]

- Revlimid (lenalidomide)*
- dexamethasone

AND

4 Prescribed by or in consultation with a hematologist/oncologist

Notes	*These products may require Prior Authorization. **Product may be

	excluded depending on the plan.

Product Name: Ninlaro*

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Patient does not show evidence of progressive disease while on Ninlaro therapy	
Notes	*Product may be excluded depending on the plan.

3 . Endnotes

A. According to Ninlaro Prescribing Information, Ninlaro therapy should be discontinued when patients experience Grade 4 rash or Grade 4 peripheral neuropathy. [1]

4 . References

1. Ninlaro Prescribing Information. Takeda Pharmaceutical Company Limited. Cambridge, MA. November 2015.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Multiple Myeloma-Version 2.2016. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed December 9, 2015.

Prior Authorization Guideline

GL-17386 Nplate (romiplostim)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 6/1/2016

Technician Note :

P&T Approval Date: 4/7/2009; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Nplate (romiplostim)

Indications

Chronic Idiopathic Thrombocytopenic Purpura (ITP)

Indicated for the treatment of thrombocytopenia in patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Nplate is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than chronic ITP. Nplate should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding. Nplate should not be used in an attempt to

normalize platelet counts.

2 . Criteria

Product Name: Nplate

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of relapsed/refractory chronic immune (idiopathic) thrombocytopenic purpura (ITP) for greater than 6 months

AND

2 Patient's baseline platelet count is less than 50,000/mcL

AND

3 History of failure, contraindication, or intolerance to at least one of the following: [2]

- Corticosteroids
- Immunoglobulins
- Splenectomy

AND

4 Patient's degree of thrombocytopenia and clinical condition increase the risk of bleeding

AND

5 Prescribed by or in consultation with a hematologist or oncologist

Product Name: Nplate

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient's platelet count has increased to a level sufficient to avoid clinically important bleeding

3 . References

1. Nplate Prescribing Information. Amgen, February 2014.

2. Kuter DJ, Bussel JB, Lyons RM, et al. Efficacy of romiplostim in patients with chronic immume thrombocytopenic purpura: a double-blind randomised controlled trial. Lancet. 2008;371:395-403.
3. 2011 Clinical Practice Guideline on the evaluation and management of immune thrombocytopenia (ITP). Available at: http://www.hematology.org/Clinicieans/Guidelines-Quality/Guidelines.aspx. Accessed May 22, 2014.

Prior Authorization Guideline

GL-16862 Nucala (mepolizumab)

Formulary OptumRx SP

Formulary Note

Approval Date 11/20/2015

Revision Date 4/7/2016

Technician Note :

P&T Approval Date: 11/17/2015 P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Nucala

Indications

Severe eosinophilic asthma

Indicated for the add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype. Limitations of Use: Nucala is not indicated for treatment of other eosinophilic conditions. Nucala is not indicated for the relief of acute bronchospasm or status asthmaticus.

2 . Criteria

Product Name: Nucala

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of severe asthma [1, A]

AND

2 Asthma is an eosinophilic phenotype as defined by one of the following [1, 3, B]:

- Baseline peripheral blood eosinophil levels are greater than or equal to 150 cells/microliter
- Peripheral blood eosinophil levels were greater than or equal to 300 cells/microliter within the past 12 months

AND

3 One of the following:

3.1 Patient has had at least two or more asthma exacerbations requiring systemic corticosteroids within the past 12 months [2-4]

OR

3.2 Any prior intubation for an asthma exacerbation

OR

3.3 Prior asthma-related hospitalization within the past 12 months

AND

4 Patient is currently being treated with one of the following [2-4]:

4.1 Both of the following:

- High-dose inhaled corticosteroid (ICS) [eg, greater than or equal to 880 mcg fluticasone propionate equivalent/day]
- Additional asthma controller medication [eg, leukotriene receptor antagonist, long-acting beta-2 agonist (LABA), theophylline]

OR

4.2 One maximally-dosed combination ICS/LABA product [eg, Advair (fluticasone propionate/salmeterol), Dulera (mometasone/formoterol), Symbicort (budesonide/formoterol)]

AND

5 Age greater than or equal to 12 years [1]

AND

6 Prescribed by or in consultation with one of the following:

- pulmonologist
- allergy/immunology specialist

Product Name: Nucala

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response (eg, reduction in exacerbations) [C]

AND

2 Patient is currently being treated with one of the following [2-4]:

2.1 Both of the following:

- High-dose inhaled corticosteroid (ICS) [eg, greater than or equal to 880 mcg fluticasone propionate equivalent/day]
- Additional asthma controller medication [eg, leukotriene receptor antagonist, long-acting beta-2 agonist (LABA), theophylline]

OR

2.2 One maximally-dosed combination ICS/LABA product [eg, Advair (fluticasone propionate/salmeterol), Dulera (mometasone/formoterol), Symbicort (budesonide/formoterol)]

AND

3 Prescribed by or in consultation with one of the following:

- pulmonologist
- allergy/immunology specialist

3 . Endnotes

A. Patients included across the 3 pivotal studies (DREAM, MENSA, and SIRIUS) [2-4] were characterized with clinical features of severe refractory asthma per American Thoracic Society (ATS) criteria [5]. Per the ATS: "Severe asthma is defined as ‘‘asthma which requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller (and/or systemic corticosteroids) to prevent it from becoming ‘uncontrolled’ or which remains ‘uncontrolled’ despite this therapy.’’ This definition includes patients who received an adequate trial of these therapies in whom treatment was stopped due to lack of response. In patients greater than 6 years of age, ‘‘Gold Standard/International Guidelines treatment’’ is high dose ICS plus a longacting b2-agonist (LABA), leukotriene modifier or theophylline and/or continuous or near continuous systemic corticosteroids as background therapy."
B. Inclusion criteria was modified from the DREAM study to the MENSA study to be limited to patients with eosinophils greater than or equal to 150 cells/mcL in the peripheral blood at screening or greater than or equal to 300 cells/mcL at some time during the previous year [3].
C. The primary endpoint for the DREAM and MENSA studies was the annual rate of clinically significant asthma exacerbations as a composite of the required use of systemic corticosteroids for at least 3 days, admission, or ED visit. Both studies showed mepolizumab-treated patients experienced a significant improvement in exacerbation rates compared with baseline and compared with placebo. [2,3]

4 . References

1. Nucala Prescribing Information. GlaxoSmithKline, November 2015.
2. Pavord ID, Korn S, Howarth P, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. Lancet. 2012; 380: 651-59.

3. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. N Engl J Med. 2014;371(13):1198-1207.
4. Bel EH, Wenzel SE, Thompson PJ, et al. Oral Glucocorticoid-Sparing Effect of Mepolizumab in Eosinophilic Asthma. N Engl J Med. 2014; 371:1189-1197.
5. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J. 2014; 43:343-373.

Prior Authorization Guideline

GL-16836 Orencia (abatacept)

Formulary OptumRx SP

Formulary Note

Approval Date 10/14/2014

Revision Date 4/15/2016

Technician Note :

P&T Approval Date: 1/28/2002; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Orencia (abatacept)

Indications

Adult Rheumatoid Arthritis (RA)

Indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. Orencia may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists. Orencia should not be administered concomitantly with TNF antagonists. Orencia is not recommended for use concomitantly with other biologic rheumatoid

arthritis (RA) therapy, such as anakinra.

Juvenile Idiopathic Arthritis

Indicated for reducing signs and symptoms in pediatric patients 6 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis. Orencia may be used as monotherapy or concomitantly with methotrexate (MTX).

2 . Criteria

Product Name: Orencia SC or Orencia IV

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active RA

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to one nonbiologic disease modifying anti-

rheumatic drug (DMARD) [e.g., methotrexate (Rheumatrex/Trexall), Arava (leflunomide), Azulfidine (sulfasalazine)] [6,11]

AND

4 One of the following:

4.1 History of failure, contraindication, or intolerance to two of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Simponi (golimumab) or Simponi Aria (golimumab IV)

OR

4.2 For continuation of prior Orencia therapy

AND

5 Patient is not receiving Orencia in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,12,A,B]

AND

6 Patient is not receiving Orencia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,12,A,B]

Product Name: Orencia SC or Orencia IV

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	24 Month

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Orencia therapy

AND

2 Patient is not receiving Orencia in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,12,A,B]

AND

3 Patient is not receiving Orencia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,12,A,B]

Product Name: Orencia IV

Diagnosis	Juvenile Idiopathic Arthritis (JIA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active polyarticular JIA

AND

2 Prescribed by or in consultation with a rheumatologist

AND

3 History of failure, contraindication, or intolerance to one of the following nonbiologic disease modifying anti-rheumatic drugs (DMARDs): [10, 15]

- Arava (leflunomide)
- methotrexate (Rheumatrex/Trexall)

AND

4 Patient is not receiving Orencia in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,12,A,B]

AND

5 Patient is not receiving Orencia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,12,A,B]

Product Name: Orencia IV

Diagnosis	Juvenile Idiopathic Arthritis (JIA)
Approval Length	24 Month

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Orencia therapy

AND

2 Patient is not receiving Orencia in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] [1,12,A,B]

AND

3 Patient is not receiving Orencia in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,12,A,B]

3 . Endnotes

A. Patients should be informed that they should not receive Orencia treatment concomitantly with a TNF antagonist, such as adalimumab, etanercept, and infliximab because such combination therapy may increase their risk for infections, and that they should not receive Orencia concomitantly with other biologic RA therapy, such as

anakinra because there is not enough information to assess the safety and efficacy of such combination therapy. [1]

B. Xeljanz should not be used in combination with biologic DMARDs. [12]

4 . References

1. Orencia Prescribing Information. Bristol-Myers Squibb Company, December 2013.
2. Genovese MC, Becker JC, Schiff M, et al. Abatacept for Rheumatoid Arthritis Refractory to Tumor Necrosis Factor Inhibition. N Engl J Med. 2005. 353 (11):1114-1123.
3. Kremer JM, Dougados M, Emery P, et al. Treatment of rheumatoid arthritis with the selective costimulation modulator abatacept: twelve-month results of a phase IIb, double-blind, randomized, placebo-controlled trial. Arthritis Rheum. 2005. 52(8):2263-71.
4. Kremer JM, Genant HK, Moreland LW, et al. Effects of abatacept in patients with methotrexate-resistant active rheumatoid arthritis: a randomized trial. Ann Intern Med. 2006 Jun 20;144(12):865-76.
5. The Canadian Coordinating Office for Health Technology Assessment (CCOHTA)Abatacept as add-on therapy for rheumatoid arthritis. . September 2005. Issue #71 Available at: https://www.ccohta.ca/entry_e.html Accessed February 10, 2005.
6. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012;64(5):625-639.
7. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995; 38(6):727-735.
8. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum. 1993; 36 (6): 729-740.
9. Kremer JM, Genant HK, Moreland LW, et al. Results of a two-year follow-up study of patients with rheumatoid arthritis who received a combination of abatacept and methotrexate. Arthritis Rheum. 2008 Apr;58(4):953-63.
10. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011 Apr;63(4):465-82.
11. Per clinical consult with rheumatologist, June 30, 2011.
12. Xeljanz Prescribing Information. Pfizer Inc., November 2013.
13. Silverman E, Mouy R, Spiegel L, et al. Leflunomide or methotrexate for juvenile rheumatoid arthritis. N Engl J Med. 2005; 352 (16):1655-1666.
14. DRUGDEX System [Internet database]. Thomson Micromedex. Updated periodically. Accessed January 9, 2014.
15. Milliman Care Guidelines. Ambulatory Care 18th Edition. Abatacept. Avaialble at: http://cgi.careguidelines.com/login-careweb.htm. Accessed September 25, 2014.

Prior Authorization Guideline

GL-30450 PCSK9 Inhibitors

Formulary OptumRx SP

Formulary Note

Approval Date 7/14/2016

Revision Date 7/14/2016

Technician Note :

P&T Approval Date: 5/20/2015; P&T Revision Date: 8/18/2016 **Effective 7/15/2016**

1 . Indications

Drug Name: Praluent (alirocumab)

Indications

Primary Hyperlipidemia Indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C. Limitations of use: The effect of alirocumab on cardiovascular morbidity and mortality has not been determined.

Drug Name: Repatha (evolocumab)

Indications

Primary Hyperlipidemia Indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C. Limitations of use: The effect of evolocumab on cardiovascular morbidity and mortality has not been determined.

Homozygous Familial Hypercholesterolemia Indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C. Limitations of use: The effect of evolocumab on cardiovascular morbidity and mortality has not been determined.

2 . Criteria

Product Name: Praluent

Diagnosis	Primary Hyperlipidemia
Approval Length	6 Months [A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (e.g., chart notes, laboratory values) documenting one of the following diagnoses:

1.1 Heterozygous familial hypercholesterolemia (HeFH) as confirmed by one of the following: [1-2, B]

1.1.1 Documented assessment of patient using Dutch Lipid Clinic Network diagnostic criteria with a cumulative score greater than or equal to 9 points (i.e., definite FH) [3]

OR

1.1.2 Both of the following: [4]

- Presence of tendinous xanthomas in patient, first degree relative, or second degree relative
- Untreated/pre-treatment LDL-cholesterol (LDL-C) > 190 mg/dL in an adult or > 155 mg/dL in a child less than 16 years of age

OR

1.1.3 Genetic confirmation of a mutation in the LDL receptor, ApoB, or PCSK9 [3-4]

OR

1.2 Atherosclerotic cardiovascular disease (ASCVD) as confirmed by one of the following: [1, 2, 5]

- Acute coronary syndromes
- History of myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization
- Stroke
- Transient ischemic attack
- Peripheral arterial disease presumed to be of atherosclerotic origin

and

2 One of the following: [1, 2, 5]

2.1 Patient has been receiving at least 12 consecutive weeks of high-intensity statin therapy and will continue to receive a HIGH-INTENSITY statin [i.e., atorvastatin 40-80 mg, Crestor (rosuvastatin) 20-40 mg] at maximally tolerated dose

OR

2.2 Both of the following:

2.2.1 Patient is unable to tolerate high-intensity statin as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

and

2.2.2 Patient has been receiving at least 12 consecutive weeks of moderate-intensity statin therapy and will continue to receive a MODERATE-INTENSITY statin [i.e., atorvastatin 10-20 mg, Crestor (rosuvastatin) 5-10 mg, simvastatin 20-40 mg, pravastatin 40-80 mg, lovastatin 40 mg, Lescol XL (fluvastatin XL) 80 mg, fluvastatin 40 mg twice daily, or Livalo (pitavastatin) 2-4 mg] at maximally tolerated dose

OR

2.3 Both of the following:

2.3.1 Patient is unable to tolerate moderate- and high-intensity statins as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms for both moderate- and high-intensity statins:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times ULN)

and

2.3.2 Patient has been receiving at least 12 consecutive weeks of low-intensity statin therapy and will continue to receive a LOW-INTENSITY statin [i.e., simvastatin 10 mg, pravastatin 10-20 mg, lovastatin 20 mg, fluvastatin 20-40 mg, Livalo (pitavastatin) 1 mg] at maximally tolerated dose

OR

2.4 Both of the following:

2.4.1 Patient is unable to tolerate low-, moderate-, and high-intensity statins as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms for low-, moderate-, and high-intensity statins:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times ULN)

and

2.4.2 Patient has undergone a trial of a statin rechallenge with pravastatin 10-40 mg or rosuvastatin 5 mg with documented reappearance of muscle symptoms

OR

2.5 Patient has a labeled contraindication to all statins as documented in medical records

OR

2.6 Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations > 10 times ULN

and

3 One of the following: [5-7, C]

3.1 Patient has been receiving at least 12 consecutive weeks of and will continue to receive one of the following as adjunct to maximally tolerated statin therapy:

- Ezetimibe
- Bile acid sequestrant [e.g., Welchol (colesevelam), cholestyramine]

OR

3.2 History of contraindication or intolerance to both of the following:

- Ezetimibe
- Bile acid sequestrant [e.g., Welchol (colesevelam), cholestyramine]

and

4 One of the following LDL-C values while on maximally tolerated lipid-lowering regimen within the last 30 days: [8, 9]

- LDL-C greater than or equal to 100 mg/dL with ASCVD
- LDL-C greater than or equal to 130 mg/dL without ASCVD

and

5 Used as adjunct to a low-fat diet and exercise regimen [1, 2]

and

6 Prescribed by one of the following:

- Cardiologist
- Endocrinologist
- Lipid specialist [D]

and

7 Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

Product Name: Repatha

Diagnosis	Primary Hyperlipidemia
Approval Length	6 Months [A]
Therapy Stage	Initial Authorization

Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (e.g., chart notes, laboratory values) documenting one of the following diagnoses:

1.1 Heterozygous familial hypercholesterolemia (HeFH) as confirmed by one of the following: [1-2, B]

1.1.1 Documented assessment of patient using Dutch Lipid Clinic Network diagnostic criteria with a cumulative score greater than or equal to 9 points (i.e., definite FH) [3]

OR

1.1.2 Both of the following: [4]

- Presence of tendinous xanthomas in patient, first degree relative, or second degree relative
- Untreated/pre-treatment LDL-cholesterol (LDL-C) > 190 mg/dL in an adult or > 155 mg/dL in a child less than 16 years of age

OR

1.1.3 Genetic confirmation of a mutation in the LDL receptor, ApoB, or PCSK9 [3-4]

OR

1.2 Atherosclerotic cardiovascular disease (ASCVD) as confirmed by one of the following: [1, 2, 5]

- Acute coronary syndromes
- History of myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization
- Stroke
- Transient ischemic attack
- Peripheral arterial disease presumed to be of atherosclerotic origin

and

2 One of the following: [1, 2, 5]

2.1 Patient has been receiving at least 12 consecutive weeks of high-intensity statin therapy and will continue to receive a HIGH-INTENSITY statin [i.e., atorvastatin 40-80 mg, Crestor (rosuvastatin) 20-40 mg] at maximally tolerated dose

OR

2.2 Both of the following:

2.2.1 Patient is unable to tolerate high-intensity statin as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times upper limit of normal [ULN])

and

2.2.2 Patient has been receiving at least 12 consecutive weeks of moderate-intensity statin therapy and will continue to receive a MODERATE-INTENSITY statin [i.e., atorvastatin 10-20 mg, Crestor (rosuvastatin) 5-10 mg, simvastatin 20-40 mg, pravastatin 40-80 mg, lovastatin 40 mg, Lescol XL (fluvastatin XL) 80 mg, fluvastatin 40 mg twice daily, or Livalo (pitavastatin) 2-4 mg] at maximally tolerated dose

OR

2.3 Both of the following:

2.3.1 Patient is unable to tolerate moderate- and high-intensity statins as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms for both moderate- and high-intensity statins:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times ULN)

and

2.3.2 Patient has been receiving at least 12 consecutive weeks of low-intensity statin therapy and will continue to receive a LOW-INTENSITY statin [i.e., simvastatin 10 mg, pravastatin 10-20 mg, lovastatin 20 mg, fluvastatin 20-40 mg, Livalo (pitavastatin) 1 mg] at maximally tolerated dose

OR

2.4 Both of the following:

2.4.1 Patient is unable to tolerate low-, moderate-, and high-intensity statins as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms for low-, moderate-, and high-intensity statins:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times ULN)

and

2.4.2 Patient has undergone a trial of a statin rechallenge with pravastatin 10-40 mg or rosuvastatin 5 mg with documented reappearance of muscle symptoms

OR

2.5 Patient has a labeled contraindication to all statins as documented in medical records

OR

2.6 Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations > 10 times ULN

and

3 One of the following: [5-7, C]

3.1 Patient has been receiving at least 12 consecutive weeks of and will continue to receive one of the following as adjunct to maximally tolerated statin therapy:

- Ezetimibe
- Bile acid sequestrant [e.g., Welchol (colesevelam), cholestyramine]

OR

3.2 History of contraindication or intolerance to both of the following:

- Ezetimibe
- Bile acid sequestrant [e.g., Welchol (colesevelam), cholestyramine]

and

4 One of the following:

- History of failure after 12 consecutive weeks of Praluent 150 mg therapy
- History of intolerance to Praluent therapy

and

5 One of the following LDL-C values while on maximally tolerated lipid-lowering regimen within the last 30 days: [8, 9]

- LDL-C greater than or equal to 100 mg/dL with ASCVD
- LDL-C greater than or equal to 130 mg/dL without ASCVD

and

6 Used as adjunct to a low-fat diet and exercise regimen [1, 2]

and

7 Prescribed by one of the following:

- Cardiologist
- Endocrinologist
- Lipid specialist [D]

and

8 Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

Product Name: Praluent, Repatha

Diagnosis	Primary Hyperlipidemia
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient continues to receive statin at the maximally tolerated dose (unless patient has documented inability to take statins)

and

2 Patient continues to receive ezetimibe or bile acid sequestrant therapy as an adjunct to maximally tolerated statin therapy (unless patient has documented inability to take ezetimibe AND bile acid sequestrant therapy)

and

3 Patient has been adherent to Praluent or Repatha therapy

and

4 Patient is continuing a low-fat diet and exercise regimen

and

5 Prescribed by one of the following:

- Cardiologist
- Endocrinologist
- Lipid specialist [D]

and

6 Submission of medical records (e.g., laboratory values) documenting a sustained >30% reduction in LDL-C levels from pretreatment baseline (i.e., prior PCSK9 therapy) while on PCSK9 therapy

and

7 Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

Product Name: Repatha

Diagnosis	Homozygous Familial Hypercholesterolemia
Approval Length	3 Months [A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (e.g., chart notes, laboratory values) documenting diagnosis of homozygous familial hypercholesterolemia as confirmed by one of the following: [11-13]

1.1 Genetic confirmation of 2 mutations in the LDL receptor, ApoB, PCSK9, or LDL receptor adaptor protein 1 (i.e., LDLRAP1 or ARH)

OR

1.2 Both of the following:

1.2.1 One of the following:

- Untreated/pre-treatment LDL-C > 500 mg/dL
- Treated LDL-C > 300 mg/dL

and

1.2.2 One of the following:

- Xanthoma before 10 years of age
- Evidence of heterozygous familial hypercholesterolemia in both parents

and

2 One of the following: [1, 2, 5]

2.1 Patient has been receiving at least 12 consecutive weeks of high-intensity statin therapy and will continue to receive a HIGH-INTENSITY statin [i.e., atorvastatin 40-80 mg, Crestor (rosuvastatin) 20-40 mg] at maximally tolerated dose

OR

2.2 Both of the following

2.2.1 Patient is unable to tolerate high-intensity statin as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times ULN)

and

2.2.2 Patient has been receiving at least 12 consecutive weeks of moderate-intensity statin therapy and will continue to receive a MODERATE-INTENSITY statin [i.e., atorvastatin 10-20 mg, Crestor (rosuvastatin) 5-10 mg, simvastatin 20-40 mg, pravastatin 40-80 mg, lovastatin 40 mg, Lescol XL (fluvastatin XL) 80 mg, fluvastatin 40 mg twice daily, or Livalo (pitavastatin) 2-4 mg] at maximally tolerated dose

OR

2.3 Both of the following:

2.3.1 Patient is unable to tolerate moderate- and high-intensity statins as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms for both moderate- and high-intensity statins:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times ULN)

and

2.3.2 Patient has been receiving at least 12 consecutive weeks of low-intensity statin therapy and will continue to receive a LOW-INTENSITY statin [i.e., simvastatin 10 mg, pravastatin 10-20 mg, lovastatin 20 mg, fluvastatin 20-40 mg, Livalo (pitavastatin) 1 mg] at maximally tolerated dose

OR

2.4 Both of the following:

2.4.1 Patient is unable to tolerate low-, moderate-, and high-intensity statins as evidenced by one of the following intolerable and persistent (i.e., more than 2 weeks) symptoms for low-, moderate-, and high-intensity statins:

- Myalgia (muscle symptoms without CK elevations)
- Myositis (muscle symptoms with CK elevations < 10 times ULN)

and

2.4.2 Patient has undergone a trial of statin rechallenge with pravastatin 10-40 mg or Crestor (rosuvastatin) 5 mg with documented reappearance of muscle symptoms

OR

2.5 Patient has a labeled contraindication to all statins as documented in medical records

OR

2.6 Patient has experienced rhabdomyolysis or muscle symptoms with statin treatment with CK elevations > 10 times ULN

and

3 One of the following: [5-7, C]

3.1 Patient has been receiving at least 12 consecutive weeks of and will continue to receive one of the following as adjunct to maximally tolerated statin therapy:

- Ezetimibe
- Bile acid sequestrant [e.g., Welchol (colesevelam), cholestyramine]

OR

3.2 History of contraindication or intolerance to both of the following

- Ezetimibe
- Bile acid sequestrant [e.g., Welchol (colesevelam), cholestyramine]

and

4 One of the following LDL-C values while on maximally tolerated lipid-lowering regimen within the last 30 days:

- LDL-C greater than or equal to 100 mg/dL with ASCVD
- LDL-C greater than or equal to 130 mg/dL without ASCVD

and

5 Used as adjunct to a low-fat diet and exercise regimen [2]

and

6 Prescribed by one of the following:

- Cardiologist
- Endocrinologist
- Lipid specialist [D]

and

7 Not used in combination with Juxtapid (lomitapide)

and

8 Not used in combination with Kynamro (mipomersen)

and

9 Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

Product Name: Repatha

Diagnosis	Homozygous Familial Hypercholesterolemia
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient continues to receive statin at the maximally tolerated dose (unless patient has documented inability to take statins)

and

2 Patient continues to receive ezetimibe or bile acid sequestrant therapy as an adjunct to maximally tolerated statin therapy (unless patient has documented inability to take ezetimibe AND bile acid sequestrant therapy)

and

3 Patient has been adherent to Repatha therapy

and

4 Patient is continuing a low-fat diet and exercise regimen

and

5 Submission of medical records (e.g., laboratory values) documenting a sustained LDL-C reduction from pre-treatment baseline (i.e., prior Repatha therapy) while on Repatha therapy

and

6 Prescribed by one of the following:

- Cardiologist
- Endocrinologist
- Lipid specialist [D]

and

7 Not used in combination with Juxtapid (lomitapide)

and

8 Not used in combination with Kynamro (mipomersen)

and

9 Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor

3 . Background

Clinical Practice Guidelines

Dutch Lipid Clinic Network Criteria for Heterozygous Familial Hypercholesterolemia (HeFH) [4]

Scoring

Definite FH: > 8

Probable FH: 6-8

Possible FH: 3-5

Unlikely FH: 0-2

i. Group 1: Family History

- First-degree relative with premature CHD (male < 55 years of age; female < 60 years of age) (score: 1)
- First-degree relative with LDL-C > 95th percentile by age (score: 1)

Age, years	First-degree relative LDL-C
18-19	â‰¥ 155
20-29	â‰¥ 170
30-39	â‰¥ 190
â‰¥ 40	â‰¥ 205

- ℜ• First-degree relative with tendon xanthoma and/or corneal arcus (score: 2)
- ℜ• Children aged < 18 years with LDL-C â‰¥ 155 mg/dL (score: 2)

ii. Group 2: Personal clinical history

- ℜ• Premature CHD (male < 55 years of age; female < 60 years of age) (score: 2)
- ℜ• Premature cerebrovascular or peripheral vascular disease (male < 55 years of age; female < 60 years of age) (score: 1)

iii. Group 3: Physical exam

- ℜ• Tendon xanthoma (score: 6)
- ℜ• Corneal arcus in subject manifesting before 45 years of age (score: 4)

iv. Group 4: LDL-C level

- ℜ• > 325 mg/dL (> 8.5 mmol/L) (score: 8)
- ℜ• 251-325 mg/dL (6.5-8.4 mmol/L) (score: 5)
- ℜ• 191-250 mg/dL (5.0-6.4 mmol/L) (score: 3)
- ℜ• 155-190 mg/dL (4.0-4.9 mmol/L) (score: 1)

v. Group 5: Genetic testing

- ℜ• Causative mutation in LDLR, ApoB, or PCSK9 genes (score: 8)

Benefit/Coverage/Program Information

Quantity Limit

These products may be subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. Per the 2013 ACC/AHA national treatment guidelines, adherence, response to therapy, and adverse effects within 4â€“12 weeks following statin initiation or change in therapy. The same logic has been applied to other lipid-lowering therapies. [5]
B. In the Praluent and Repatha pivotal trials that enrolled patients with HeFH, the diagnosis of HeFH was made either by genotyping or clinical criteria ("definite FH" using either the Simon Broome or WHO/Dutch Lipid Network criteria). [1-4]
C. To date, IMPROVE-IT is the only randomized controlled trial (RCT) to demonstrate significant ASCVD event reduction with non-statin lipid-lowering therapy. IMPROVE-IT was a prospective RCT evaluating the addition of ezetimibe to simvastatin 40 mg in a high-risk patient population for secondary prevention over 7 years. The addition of ezetimibe significantly reduced ASCVD events, albeit very modestly (HR 0.936; 95% CI

0.887, 0.988; p = 0.016; number needed to treat [NNT] = 50). [6] At present, only LDL-C reductions have been demonstrated with Praluent. Outcomes trials evaluating the efficacy of Praluent are currently underway. Completed trial results will not be available until 2017-2018. [14]

D. Lipid specialists are physicians certified by the American Board of Clinical Lipidology (ABCL) or the Accreditation Council for Clinical Lipidology (ACCL). [15, 16]
E. Per the 2013 ACC/AHA national treatment guidelines, it is reasonable to use the following as indicators of anticipated therapeutic response to the recommended intensity of statin therapy. Focus is on the intensity of the statin therapy. As an aid to monitoring: a) High-intensity statin therapy generally results in an average LDL-C reduction of â‰¥ 50% from the untreated baseline; b) Moderate-intensity statin therapy generally results in an average LDL-C reduction of 30 to < 50% from the untreated baseline. [5]

5 . References

1. Praluent Prescribing Information. Regeneron Pharmaceuticals, Inc. July 2015.
2. Repatha Prescribing Information. Amgen Inc. August 2015.
3. WHO Familial Hypercholesterolemia Consultation Group. Familial Hypercholesterolemia (FH): report of a second WHO consultation. Geneva: World Health Organization; 1999.
4. Scientific Steering Committee on behalf of the Simon Broome Register Group. Risk of fatal coronary heart disease in familial hypercholesterolaemia. BMJ. 1991;303:893-6.
5. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2889-934.
6. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med. 2015a; DOI: 10.1056/NEJMoa1410489 [Epub ahead of print].
7. The Lipid Research Clinics Coronary Primary Prevention Trial results. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA. 1984;251:365-74.
8. ATP III Final Report PDF. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. Circulation. 2002;106:3143-3421.
9. Per clinical drug consult with cardiologist. August 3, 2015.
10. Blom DJ, Hala T, Bolognese M, et al. A 52-week placebo-controlled trial of evolocumab in hyperlipidemia. N Engl J Med. 2014;370:1809-19.
11. Raal FJ, Santos RD. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. Atherosclerosis. 2012;223:262-8.
12. Raal FJ, Honarpour N, Blom DJ, et al. Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial. Lancet. 2015;385:341-50.
13. Cuchel M, Bruckert E, Ginsberg HN, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercohlesterolaemia of the European Atherosclerosis Society. Eur Heart J. 2014;35:2146-57.
14. Schwartz GG, Bessac L, Berdan LG, et al. Effect of alirocumab, a monoclonal antibody to PCSK9, on long-term cardiovascular outcomes following acute coronary syndromes: a rationale and design of the ODYSSEY outcomes trial. Am Heart J. 2014;168:682-9.

15. American Board of Clinical Lipidology website. www.lipidboard.org. Accessed September 23, 2015.
16. Accreditation Council for Clinical Lipidology website. www.lipidspecialist.org. Accessed September 23, 2015.

Prior Authorization Guideline

GL-17349 Perjeta (pertuzumab)

Formulary OptumRx SP

Formulary Note

Approval Date 5/22/2013

Revision Date 5/23/2016

Technician Note :

P& Approval Date: 8/21/2012; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Perjeta (pertuzumab)

Indications

Metastatic Breast Cancer (first-line therapy)

Indicated in combination with trastuzumab and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

Neoadjuvant Treatment of Breast Cancer

Indicated for use in combination with trastuzumab and docetaxel for the neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer. This indication is based on demonstration of an improvement in pathological complete response rate. No data are available demonstrating improvement in event-free survival or overall survival. Limitations of use: (1) The safety of Perjeta as part of a doxorubicin-containing regimen has not been established; (2) The safety of Perjeta administered for greater than 6 cycles for early breast cancer has not been established.

Off Label Uses

Metastatic Breast Cancer (second-line therapy) [3]

May be considered in combination with trastuzumab with or without cytotoxic therapy (eg, vinorelbine or taxane) for one line of therapy beyond first-line therapy in patients previously treated with chemotherapy and trastuzumab in the absence of pertuzumab.

2 . Criteria

Product Name: Perjeta

Diagnosis	Metastatic breast cancer
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of HER2-positive metastatic breast cancer

AND

2 One of the following:

2.1 Both of the following:

2.1.1 Patient has not received prior anti-HER2 therapy or chemotherapy for metastatic disease [2,A]

AND

2.1.2 Used in combination with both of the following: [2,A]

- Herceptin (trastuzumab)
- A taxane (e.g., docetaxel, paclitaxel)

OR

2.2 Both of the following:

2.2.1 Patient was previously treated with chemotherapy and Herceptin (trastuzumab) without Perjeta [2,A]

AND

2.2.2 Used in combination with Herceptin (trastuzumab) [2,A]

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Perjeta

Diagnosis	Metastatic breast cancer
Approval Length	12 Month
Therapy Stage	Reauthorization

Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Perjeta therapy

Product Name: Perjeta

Diagnosis	Early Stage, Locally-Advanced, or Inflammatory Breast Cancer
Approval Length	6 Month* [B]
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following diagnoses: [C]

- HER2-positive early stage breast cancer
- HER2-positive locally advanced breast cancer
- HER2-positive inflammatory breast cancer

AND

2 Used in combination with both of the following: [C]

- Herceptin (trastuzumab)
- A taxane (e.g., docetaxel, paclitaxel)

AND

3 Prescribed by or in consultation with an oncologist

Notes	*There is insufficient evidence to recommend continued use of Perjeta for greater than 6 cycles for early breast cancer. [1]

3 . Endnotes

A. Perjeta is used for recurrent or metastatic human epidermal growth factor receptor 2-positive disease that is either hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory or with symptomatic visceral disease: (1) as preferred first-line therapy in combination with trastuzumab with docetaxel or paclitaxel; or (2) may be considered in combination with trastuzumab with or without cytotoxic therapy (eg, vinorelbine or taxane) for one line of therapy beyond first-line therapy in patients previously treated with chemotherapy and trastuzumab in the absence of pertuzumab. [3]
B. The safety of Perjeta administered for greater than 6 cycles for early breast cancer has not been established. Perjeta should be administered every 3 weeks for 3 to 6 cycles as part of one of the following treatment regimens for early breast cancer. [1]
C. A pertuzumab-containing regimen can be administered to patients with T2 or N1, HER2-positive, early stage breast cancer. Patients who have not received a neoadjuvant pertuzumab-containing regimen can receive adjuvant pertuzumab. [2]

4 . References

1. Perjeta Prescribing Information. Genentech, Inc., September 2013.
2. National Comprehensive Cancer Network. Clinical practice guidelines in oncology: breast cancer. v.1.2014. Available at: http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 6,2014.
3. National Comprehensive Cancer Network. NCCN Drugs & Biologics Compendium: Pertuzumab. 2014. Available at: http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=383. Accessed January 6, 2014.
4. Baselga J, Cortes J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med. 2012;366:109-19.

Prior Authorization Guideline

GL-15525 Pomalyst (pomalidomide)

Formulary OptumRx SP

Formulary Note

Approval Date 7/11/2013

Revision Date 4/21/2016

Technician Note :

P&T Approval Date: 2/19/2013; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Pomalyst (pomalidomide)

Indications

Multiple myeloma

Indicated for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval is based on response rate. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

2 . Criteria

Product Name: Pomalyst

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple myeloma [1]

AND

2 History of failure, contraindication, or intolerance to at least two prior therapies including both of the following:

- Revlimid (lenalidomide)
- proteasome inhibitor (eg, Velcade [bortezomib], Kyprolis [carfilzomib])

AND

3 Patient has experienced disease progression on or within 60 days of completion of last therapy

AND

4 Used in combination with dexamethasone **AND** **5** Prescribed by or in consultation with a hematologist/oncologist

Product Name: Pomalyst

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Patient does not show evidence of progressive disease while on Pomalyst therapy	

3 . References

1. Pomalyst Prescribing Information, Celgene Corporation, Summit, NJ. May 2014.
2. National Comprehensive Cancer Network. Practice Guidelines in Oncology – Multiple Myeloma v.4.2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed April 20, 2015.

Prior Authorization Guideline

GL-14602 Portrazza (necitumumab)

Formulary OptumRx SP

Formulary Note

Approval Date 3/18/2016

Revision Date 3/18/2016

Technician Note :

P&T Approval Date: 2/25/2016

1 . Indications

Drug Name: Portrazza

Indications

Non-small cell lung cancer

Indicated, in combination with gemcitabine and cisplatin, for first-line treatment of patients with metastatic squamous non-small cell lung cancer (NSCLC). LIMITATIONS OF USE: Portrazza is NOT indicated for treatment of non-squamous non-small cell lung cancer.

2 . Criteria

Product Name: Portrazza

Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of metastatic squamous non-small cell lung cancer

AND

2 Used in combination with gemcitabine and cisplatin

AND

3 Used as first-line treatment

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Portrazza

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has not experienced disease progression

3 . Endnotes

A. A quantity limit was developed to ensure use does not exceed the FDA recommendation of 800 mg as an intravenous infusion on days 1 and 8 of each 3 week cycle [1].

4 . References

1. Portrazza prescribing information. Eli Lilly and Company. Indianapolis, IN. November 2015.
2. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology™. Prostate Cancer v.3.2016. Available from: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed December 23, 2015.
3. P&T Consultant Review. January 20, 2016.

Prior Authorization Guideline

GL-16233 Procysbi (cysteamine bitartrate)

Formulary OptumRx SP

Formulary Note

Approval Date 5/23/2016

Revision Date 5/23/2016

Technician Note :

P&T Approval Date: 10/22/2014; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Procysbi (cysteamine bitartrate)

Indications

Nephropathic cystinosis

Indicated for the management of nephropathic cystinosis in adults and children ages 2 years and older.

2 . Criteria

Product Name: Procysbi

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of nephropathic cystinosis

AND

2 Diagnosis is confirmed by elevated leukocyte cystine levels (LCL) or genetic analysis of the CTNS gene [A, 2, 3]

AND

3 History of failure or intolerance to Cystagon (immediate-release cysteamine bitartrate)

AND

4 Patient is 2 years of age or older

3 . Endnotes

A. A definitive diagnosis can be verified by measuring leukocyte cystine levels or genetic analysis of the CTNS gene [2-3]

4 . References

1. Procysbi prescribing information. Raptor Pharmaceuticals, Inc. Novato, CA. 2015.
2. Emma F, Nesterva G, Langman C, et al. Nephropathic cystinosis: an international consensus document. Nephrol Dial Transplant (2014) 29: iv87–iv94.
3. Wilmer MJ, Schoeber JP, van den Heuvel LP, Levtchenko EN. Cystinosis: practical tools for diagnosis and treatment [educational review]. Pediatric Nephrology 2011; 26: 205-15.

Prior Authorization Guideline

GL-17281 Prolia (denosumab)

Formulary OptumRx SP

Formulary Note

Approval Date 3/14/2013

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 8/17/2010; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Prolia (denosumab)

Indications

Treatment of postmenopausal women with osteoporosis at high risk for fracture

Indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia reduces the incidence of vertebral, nonvertebral, and hip fractures.

Treatment to increase bone mass in men with osteoporosis

Indicated for treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

Treatment of bone loss in men receiving androgen deprivation therapy for nonmetastatic prostate cancer [A]

Indicated as a treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolia also reduced the incidence of vertebral fractures. NOTE: The use of Prolia for the treatment of bone loss in men receiving androgen deprivation therapy for nonmetastatic prostate cancer should not be confused with the use of Xgeva (another injectable formulation of denosumab) for the prevention of skeletal-related events (SREs) in patients with bone metastases from solid tumors (including breast cancer and prostate cancer).

Treatment of bone loss in women receiving adjuvant aromatase inhibitor therapy for breast cancer [B]

Indicated as a treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer. NOTE: The use of Prolia for the treatment of bone loss in women receiving adjuvant aromatase inhibitor therapy for breast cancer should not be confused with the use of Xgeva (another injectable formulation of denosumab) for the prevention of skeletal-related events (SREs) in patients with bone metastases from solid tumors (including breast cancer and prostate cancer).

Off Label Uses

Postmenopausal osteoporosis; prophylaxis

Has been used for prophylaxis of postmenopausal osteoporosis [18, 19]

2 . Criteria

Product Name: Prolia

Diagnosis	Bone loss in men receiving androgen deprivation therapy for nonmetastatic prostate cancer
Approval Length	12 months [D]

Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of nonmetastatic prostate cancer

AND

2 Patient is undergoing androgen deprivation therapy with one of the following: [11, A]

2.1 Luteinizing hormone-releasing hormone (LHRH)/gonadotropin releasing hormone (GnRH) agonist [e.g., Eligard/Lupron (leuprolide), Trelstar (triptorelin), Vantas (histrelin), and Zoladex (goserelin)]

OR

2.2 Bilateral orchiectomy (i.e., surgical castration)

AND

3 One of the following:

3.1 Age greater than or equal to 70 years [11, C]

OR

3.2 Both of the following:

3.2.1 Age less than 70 years [11]

AND

3.2.2 One of the following:

3.2.2.1 Bone mineral density (BMD) scan T-score less than -1.0 (1.0 standard deviation or greater below the mean for young adults) [11]

OR

3.2.2.2 History of one of the following from minimal trauma: [9, 11]

- Vertebral compression fracture
- Fracture of the hip
- Fracture of the distal radius

Product Name: Prolia

Diagnosis	Bone loss in men receiving androgen deprivation therapy for nonmetastatic prostate cancer
Approval Length	12 months [D]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is undergoing androgen deprivation therapy with one of the following: [11, A]

1.1 Luteinizing hormone-releasing hormone (LHRH)/gonadotropin releasing hormone (GnRH) agonist [e.g., Eligard/Lupron (leuprolide), Trelstar (triptorelin), Vantas (histrelin), and Zoladex (goserelin)]

OR

1.2 Bilateral orchiectomy (i.e., surgical castration)

AND

2 No evidence of metastases

AND

3 Patient is benefiting from therapy (e.g., improved or stabilized BMD, no new fractures, improved biochemical markers, etc.)

Product Name: Prolia

Diagnosis	Bone loss in women receiving adjuvant aromatase inhibitor therapy for breast cancer
Approval Length	12 months [D]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of breast cancer

AND

2 Patient is receiving adjuvant aromatase inhibitor therapy [e.g., Arimidex (anastrozole), Aromasin (exemestane), Femara (letrozole)] [12, B]

AND

3 One of the following:

3.1 Bone mineral density (BMD) scan T-score less than -1.0 (1.0 standard deviation or greater below the mean for young adults) [12, E]

OR

3.2 History of one of the following from minimal trauma: [9]

- Vertebral compression fracture
- Fracture of the hip
- Fracture of the distal radius

AND

4 One of the following:

4.1 Patient has a documented trial and therapeutic failure with a bisphosphonate, where therapeutic failure is defined as the presence of at least one of the following:

- New fractures in compliant patients on therapy for at least 6 months
- Failure to produce a clinically significant change in a biochemical marker(s) of bone turnover
- Significant loss of bone mineral density on follow-up scans after 12 to 24 months of therapy

OR

4.2 Patient has a documented contraindication or intolerance to bisphosphonate therapy

OR

4.3 Patient is unable to comply with appropriate administration recommendations for oral or injectable bisphosphonate therapy

Product Name: Prolia

Diagnosis	Bone loss in women receiving adjuvant aromatase inhibitor therapy for breast cancer
Approval Length	12 months [D]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is receiving adjuvant aromatase inhibitor therapy [e.g., Arimidex (anastrozole), Aromasin (exemestane), Femara (letrozole)] [12]

AND

2 Patient is benefiting from therapy (e.g., improved or stabilized BMD, no new fractures, improved biochemical markers, etc.)

Product Name: Prolia

Diagnosis	Prevention of postmenopausal osteoporosis [off-label]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 For prevention of postmenopausal osteoporosis

AND

2 BMD scan indicative of osteopenia: T-Score -1.0 to -2.5

AND

3 One of the following:

3.1 Patient has a documented trial and therapeutic failure with a bisphosphonate, where therapeutic failure is defined as the presence of at least one of the following:

- New fractures in compliant patients on therapy for at least 6 months
- Failure to produce a clinically significant change in a biochemical marker(s) of bone turnover
- Significant loss of bone mineral density on follow-up scans after 12 to 24 months of therapy

OR

3.2 Patient has a documented contraindication or intolerance to bisphosphonate therapy

OR

3.3 Patient is unable to comply with appropriate administration recommendations for oral or injectable bisphosphonate therapy

Product Name: Prolia

Diagnosis	Prevention of postmenopausal osteoporosis [off-label]
Approval Length	12 Month
Therapy Stage	Reauthorization

Guideline Type	Prior Authorization

Approval Criteria

1 Patient is benefiting from therapy (e.g., improved or stabilized BMD, no new fractures, improved biochemical markers, etc.)

Product Name: Prolia

Diagnosis	Postmenopausal women with osteoporosis at a high risk for fracture
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of postmenopausal osteoporosis [2]

AND

2 One of the following:

2.1 Bone mineral density (BMD) scan indicative of osteoporosis: T-score less than or equal to -2.5 (2.5 standard deviations or greater below the mean for young adults)

OR

2.2 History of one of the following from minimal trauma:

- Vertebral compression fracture
- Fracture of the hip

- Fracture of the distal radius

AND

3 One of the following:

3.1 Patient has a documented trial and therapeutic failure with a bisphosphonate, where therapeutic failure is defined as the presence of at least one of the following:

- New fractures in compliant patients on therapy for at least 6 months
- Failure to produce a clinically significant change in a biochemical marker(s) of bone turnover
- Significant loss of bone mineral density on follow-up scans after 12 to 24 months of therapy

OR

3.2 Patient has a documented contraindication or intolerance to bisphosphonate therapy

OR

3.3 Patient is unable to comply with appropriate administration recommendations for oral or injectable bisphosphonate therapy

Product Name: Prolia

Diagnosis	Postmenopausal women with osteoporosis at a high risk for fracture
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is benefiting from therapy (e.g., improved or stabilized BMD, no new fractures, improved biochemical markers, etc.)

Product Name: Prolia

Diagnosis	Increase bone mass in men at high risk for fracture
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is a male with osteoporosis

AND

2 One of the following:

2.1 Bone mineral density (BMD) scan indicative of osteoporosis: T-score less than or equal to -2.0 (2.0 standard deviations or greater below the mean for young adults) [3, 16]

OR

2.2 History of one of the following from minimal trauma:

- Vertebral compression fracture
- Fracture of the hip
- Fracture of the distal radius

AND

3 One of the following:

3.1 Patient has a documented trial and therapeutic failure with a bisphosphonate, where therapeutic failure is defined as the presence of at least one of the following:

- New fractures in compliant patients on therapy for at least 6 months
- Failure to produce a clinically significant change in a biochemical marker(s) of bone turnover
- Significant loss of bone mineral density on follow-up scans after 12 to 24 months of therapy

OR

3.2 Patient has a documented contraindication or intolerance to bisphosphonate therapy

OR

3.3 Patient is unable to comply with appropriate administration recommendations for oral or injectable bisphosphonate therapy

Product Name: Prolia

Diagnosis	Increase bone mass in men at high risk for fracture
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is benefiting from therapy (e.g., improved or stabilized BMD, no new fractures, improved biochemical markers, etc.)

3 . Background

Benefit/Coverage/Program Information **Quantity Limit** This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Definitions

Definition	Description
Bone mineral density (BMD) [3]	A risk factor for fractures. By DXA, BMD is expressed as the amount of mineralized tissue in the area scanned (g/cm(to the power of 2)); with some technologies, BMD is expressed as the amount per volume of bone (g/cm(to the power of 3)). Hip BMD by DXA is considered the best predictor of hip fracture; it appears to predict other types of fractures as well as measurements made at other skeletal sites. Spine BMD may be preferable to assess changes early in menopause and after bilateral ovariectomy.
Dual x-ray absorptiometry (DXA) [3]	A diagnostic test used to assess bone density in the spine, hip, or wrist using radiation exposure about one tenth that of a standard chest x-ray. Central DXA (spine, hip) is the preferred measurement for definitive diagnosis and for monitoring the effects of therapy.
Fracture [3]	Breakage of a bone, either complete or incomplete. Most studies of osteoporosis focus on hip, vertebra and/or distal forearm fractures. Vertebral fractures include morphometric as well as clinical fractures.
Osteopenia [3]	The designation for bone density between 1.0 and 2.5 standard deviations below the mean for young normal adults

	(T-score between -1 and -2.5).
Osteoporosis [3]	A chronic, progressive disease characterized by low bone mass, microarchitectural deterioration and decreased bone strength, bone fragility and a consequent increase in fracture risk; bone density 2.5 or more standard deviations below the young normal mean (T-score at or below -2.5).
Peripheral DXA [3]	A DXA test used to assess bone density in the forearm, finger and heel.
Quantitative computed tomography (QCT) [3]	A diagnostic test used to assess bone density; reflects three-dimensional bone mineral density. Usually used to assess the lumbar spine, but has been adapted for other skeletal sites. It is also possible to measure trabecular and cortical bone density in the periphery by peripheral QCT (pQCT).
Quantitative ultrasound densitometry (QUS) [3]	A diagnostic test used to assess bone density at the calcaneus or patella. Ultrasound measurements correlate only modestly with other assessments of bone density in the same patient, yet some prospective studies indicate that ultrasound may predict fractures as well as other measures of bone density.
Remodeling [3]	The ongoing dual processes of bone formation and bone resorption after cessation of growth.
Resorption [3]	The loss of substance (in this case, bone) through physiological or pathological means.
Risk factors [3]	For osteoporotic fractures, includes low BMD, parental history of hip fracture, low body weight, previous fracture, smoking, excess alcohol intake, glucocorticoid use, secondary osteoporosis (e.g., rheumatoid arthritis) and history of falls. These readily accessible and commonplace factors are associated with the risk of hip fracture and, in most cases, with that of vertebral and other types of fracture as well.
Severe or “established” osteoporosis [3]	Osteoporosis characterized by bone density that is 2.5 standard deviations or more below the young normal mean (T-score at or below -2.5), accompanied by the occurrence of at least one fragility-related fracture.

T-score [3]	In describing bone mineral density, the number of standard deviations above or below the mean for young normal adults of the same sex.
Z-score [3]	In describing bone mineral density, the number of standard deviations above or below the mean for persons of the same age and sex.

5 . Endnotes

A. Androgen deprivation therapy (ADT) is commonly used in the treatment of prostate cancer. ADT can be accomplished using luteinizing hormone-releasing hormone (LHRH) agonists (medical castration), also known as gonadotropin releasing hormone (GnRH) agonists, or bilateral orchiectomy (surgical castration), which are equally effective. [13] Examples of LHRH agonists include Eligard/Lupron (leuprolide), Trelstar (triptorelin), Vantas (histrelin), and Zoladex (goserelin).
B. Aromatase inhibitors (AIs) include selective, nonsteroidal AIs (Arimidex [anastrozole] and Femara [letrozole]) and steroidal AIs (Aromasin [exemestane]).
C. Meta-analyses have shown that advancing age increases fracture risk beyond that predicted by age related loss of BMD. Although typical changes in BMD would predict a 4-fold increase in fracture risk from ages 50 to 90 years, fracture risk actually increases 30-fold. Estimated fracture rates using FRAX calculations reflect a strong influence of older age on risk for clinical fracture. When clinical factors were used without BMD in one cross-sectional study, FRAX estimated that 76.6% of men in their 70s and virtually all men 80 years old or older exceeded the NOF recommended risk threshold for drug therapy. [14]
D. Most men run a 2-year course of androgen deprivation therapy while most women receive treatment with aromatase inhibitors for about 5 years. A one year treatment authorization is reasonable. [15]
E. Owing to the rate of bone loss associated with breast cancer treatments (i.e., aromatase inhibitors), and uncertainties about the interaction between aromatase inhibitor use and BMD for fracture risk, the threshold for intervention has been set at a higher level than that generally recommended for postmenopausal osteoporosis.[8]

6 . References

1. Prolia Prescribing Information. Amgen, April 2016.
2. Cummings SR, Martin JS, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. NEJM. 2009;361:756-765.
3. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. Washington (DC): National Osteoporosis Foundation; 2013.
4. North American Menopause Society. Management of postmenopausal osteoporosis in postmenopausal women: 2010 position statement of the North American Menopause Society. Menopause 2010;17(1):25-54.

5. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the prevention and treatment of postmenopausal osteoporosis: 2010 edition. Available at: https://www.aace.com/sites/default/files/OsteoGuidelines2010.pdf. Accessed July 20, 2012.
6. Qaseem A, Snow V, Shekelle P, Hopkins Jr. R, Forciea MA, Owens DK, for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Pharmacologic treatment of low bone density or osteoporosis to prevent fractures: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2008;149:404-415.
7. Watts NB, Bilezikian JP, Camacho PM, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis. Endocr Pract. 2010;16 Suppl 3:1-37.
8. Reid DM, Doughty J, Eastell R, et al. Guidance for the management of breast cancer treatment-induced bone loss: a consensus position statement from a UK Expert Group. Cancer Treat Rev. 2008;34 Suppl 1:S3-S18.
9. Body JJ, Bergmann P, Boonen S, et al. Management of cancer treatment-induced bone loss in early breast cancer and prostate cancer – a consensus paper of the Belgian Bone Club. Osteoporos Int. 2007;18:1439-1450.
10. Hillner BE, Ingle JN, Chlebowski RT, et al. American Society of Clinical Oncology 2003 update on the role of bisphosphonates and bone health issues in women with breast cancer. J Clin Oncol. 2003;21:4042-4057.
11. Smith MR, Egerdie B, Toriz NH, et al. Denosumab in men receiving androgen-deprivation therapy for prostate cancer. N Engl J Med. 2009;361:745-755.
12. Ellis GK, Bone HG, Chlebowski R, et al. Randomized trial of denosumab in patients receiving adjuvant aromatase inhibitors for nonmetastatic breast cancer. J Clin Oncol. 2008 Oct 20. 26:2875-4882.
13. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed October 21, 2015.
14. Saylor PJ, Kaufman DS, Michaelson MD, Lee RJ, Smith MR. Application of a fracture risk algorithm to men treated with androgen deprivation therapy for prostate cancer. J Urol. 2010;183:2200-2205.
15. Per clinical consult with oncologist. December 19, 2011
16. Watts NB, Adler RA, Bilezikian JP, Drake MT, Eastell R, Orwoll ES, Finkelstein JS; Endocrine Society. Osteoporosis in men: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012;97(6):1802-22.
17. Committee on Practice Bulletins-Gynecology, The American College of Obstetricians and Gynecologists. ACOG Practice Bulletin N. 129. Osteoporosis. Obstet Gynecol. 2012 Sep;120(3):718-34.
18. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed October 21, 2015.
19. Bone HG, Bolognese MA, Yuen CK, Kendler DL, Wang H, Liu Y, San Martin J. Effects of denosumab on bone mineral density and bone turnover in postmenopausal women. J Clin Endocrinol Metab. 2008 Jun;93(6):2149-57.

Prior Authorization Guideline

GL-17387 Promacta (eltrombopag)

Formulary OptumRx SP

Formulary Note

Approval Date 3/7/2013

Revision Date 6/1/2016

Technician Note :

P&T Approval Date: 2/17/2009; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Promacta (eltrombopag)

Indications

Treatment of Thrombocytopenia in Patients with Chronic Idiopathic Thrombocytopenic Purpura (ITP)

Indicated for the treatment of thrombocytopenia in adult and pediatric patients 1 year and older with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Limitations of use: • Promacta should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.

Treatment of Thrombocytopenia in Patients with Hepatitis C Infection

Indicated for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. Limitations of use: • Promacta should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy. • Safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection.

Treatment of Severe Aplastic Anemia

Indicated for the treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy.

2 . Criteria

Product Name: Promacta

Diagnosis	Chronic Idiopathic Thrombocytopenic Purpura (ITP)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of relapsed/refractory chronic immune (idiopathic) thrombocytopenic purpura (ITP) for greater than 6 months

AND

2 Patient’s baseline platelet count is less than 50,000/mcL

AND

3 History of failure, contraindication, or intolerance to at least one of the following: [2, 3]

- Corticosteroids
- Immunoglobulins
- Splenectomy

AND

4 Patient's degree of thrombocytopenia and clinical condition increase the risk of bleeding

AND

5 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Promacta

Diagnosis	Chronic Hepatitis C-Associated Thrombocytopenia
Approval Length	9 weeks [A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic hepatitis C

AND

2 One of the following:

2.1 Patient has thrombocytopenia defined as platelets less than 90,000/mcL for initiation (pre-treatment) of interferon-based therapy

OR

2.2 Patient has thrombocytopenia defined as platelets less than 75,000/mcL for maintenance of optimal interferon-based therapy

AND

3 Prescribed by or in consultation with one of the following:

- Hematologist/oncologist
- Gastroenterologist
- Hepatologist
- Infectious disease specialist

Product Name: Promacta

Diagnosis	Chronic Hepatitis C-Associated Thrombocytopenia
Approval Length	24 weeks
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria	

1 Diagnosis of chronic hepatitis C

AND

2 One of the following:

2.1 Patient has thrombocytopenia defined as platelets less than 90,000/mcL for initiation (pre-treatment) of interferon-based therapy

OR

2.2 Patient has thrombocytopenia defined as platelets less than 75,000/mcL for maintenance of optimal interferon-based therapy

AND

3 Prescribed by or in consultation with one of the following:

- Hematologist/oncologist
- Gastroenterologist
- Hepatologist
- Infectious disease specialist

Product Name: Promacta

Diagnosis	Severe Aplastic Anemia
Approval Length	16 weeks [B]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of severe aplastic anemia

AND

2 History of failure, contraindication, or intolerance to immunosuppressive therapy with antithymocyte globulin (ATG) and cyclosporine [5, 6, 7]

AND

3 Patient has thrombocytopenia defined as platelet count less than 30,000/mcL

AND

4 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Promacta

Diagnosis	Severe Aplastic Anemia
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Promacta therapy as evidenced by an increase in platelet count

Product Name: Promacta

Diagnosis	Chronic Idiopathic Thrombocytopenic Purpura (ITP)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Promacta therapy as evidenced by an increase in platelet count to a level sufficient to avoid clinically important bleeding

3 . Endnotes

A. Promacta was studied in two phase 3 trials for chronic hepatitis C-associated thrombocytopenia in two periods. Patients received Promacta in the first period for a maximum of 9 weeks in order to achieve a pre-specified threshold platelet count (greater than or equal to 90 x 10^9/L for Trial 1 and greater than or equal to 100 x 10^9/L for Trial 2); if the pre-specified threshold platelet count was reached, initiation of antiviral therapy in combination with interferon and ribavirin was administered for up to 48 weeks in the second period. The lowest dose of Promacta should be used to achieve and maintain a platelet count necessary to initiate and maintain interferon-based therapy. Dose adjustments are based upon the platelet count response. [1]
B. In patients with severe aplastic anemia, hematologic response requires dose titration, generally up to 150 mg, and may take up to 16 weeks after starting Promacta. The dose should be adjusted every 2 weeks as necessary to achieve the target platelet count

greater than or equal to 50 x 10^9/L. If no hematologic response has occurred after 16 weeks of therapy with Promacta, therapy should be discontinued. [1]

4 . References

1. Promacta Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; August 2015.
2. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 Evidence-based practice guideline for immune thrombocytopenia. Available at: http://www.hematology.org/Practice/Guidelines/2934.aspx. Accessed October 16, 2014.
3. Bussel JB, Cheng G, Saleh MN, et al. Eltrombopag for the treatment of chronic idiopathic thrombocytopenic purpura. New Engl J Med. 2007;357(22):2237-47.
4. Saleh MN, Bussel JB, Cheng G, et al. Safety and efficacy of eltrombopag for treatment of chronic immune thrombocytopenia: results of the long-term, open-label EXTEND study. 2013;121:537-45.
5. Promacta product dossier. Research Triangle Park, NC: GlaxoSmithKline; 2014.
6. Desmond R, Townsley DM, Dumitriu B, et al. Eltrombopag restores trilineage hematopoiesis in refractory severe aplastic anemia that can be sustained on discontinuation of drug. Blood. 2014;123(12):1818-25.
7. Marsh JC, Ball SE, Cavenagh J, et al. Guidelines for the diagnosis and management of aplastic anemia. Br J Haematol. 2009;147(1):43-70.

Prior Authorization Guideline

GL-14648 Pulmonary Arterial Hypertension Agents

Formulary OptumRx SP

Formulary Note

Approval Date 3/14/2013

Revision Date 3/17/2016

Technician Note :

P&T Approval Date: 8/15/2005; P&T Revision Date: 2/25/2016

1 . Indications

Drug Name: Adcirca (tadalafil) Tablets

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with New York Heart Association (NYHA) Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).

Drug Name: Adempas (riociguat) Tablets

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for treatment of adults with PAH (WHO Group 1) to improve exercise capacity, WHO functional class, and to delay clinical worsening. Efficacy was shown in patients on riociguat monotherapy or in combination with endothelin receptor antagonists or prostanoids. Studies establishing effectiveness included predominantly patients with WHO functional class II to III and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (25%).

Chronic-Thromboembolic Pulmonary Hypertension (CTEPH)

Indicated for treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH), (WHO Group 4) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class.

Drug Name: Flolan (epoprostenol sodium) Injection

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of PAH (WHO Group I) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Drug Name: Letairis (ambrisentan) Tablets

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of pulmonary PAH (WHO Group 1) to improve exercise ability and delay clinical worsening. Studies establishing effectiveness included predominantly patients with WHO Class II-III symptoms and etiologies of idiopathic or heritable PAH (64%) or PAH associated with connective tissue diseases (32%).

Drug Name: Opsumit (macitentan) Tablets

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of PAH (WHO Group 1) to delay disease progression. Disease progression included: death, initiation of intravenous or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms, and need for additional PAH treatment). Macitentan also reduced hospitalization for PAH. Effectiveness was established in a long-term study in PAH patients with predominantly WHO functional class II to III symptoms treated for an average of 2 years. Patients were treated with macitentan monotherapy or in combination with phosphodiesterase-5 inhibitors or inhaled prostanoids. Patients had idiopathic and heritable PAH (57%), PAH caused by connective tissue disorders (30%), and PAH caused by congenital heart disease with repaired shunts (8%).

Drug Name: Orenitram (treprostinil) Tablets

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of PAH (WHO Group 1) to improve exercise capacity. The study that established effectiveness included predominantly patients with WHO functional class II to III symptoms and etiologies of idiopathic or heritable PAH (75%) or PAH associated with connective tissue disease (19%). When used as the sole vasodilator, the effect of Orenitram on exercise is about 10% of the deficit, and the effect, if any, on a background of another vasodilator is probably less than this. Orenitram is probably most useful to replace subcutaneous, intravenous, or inhaled treprostinil, but this has not been studied.

Drug Name: Remodulin (treprostinil sodium) Injection

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for: •Treatment of PAH (WHO Group 1) to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (58%), PAH associated with congenital systemic-to-pulmonary shunts (23%), or PAH associated with connective tissue diseases (19%). It may be administered as a continuous subcutaneous infusion or continuous intravenous

infusion; however, because of the risks associated with chronic indwelling central venous catheters, including serious blood stream infections, continuous intravenous infusion should be reserved for patients who are intolerant of the subcutaneous route, or in whom these risks are considered warranted. •Patients who require transition from Flolan, to reduce the rate of clinical deterioration. The risks and benefits of each drug should be carefully considered prior to transition.

Drug Name: Revatio (sildenafil) Injection, Tablets, Oral Suspension

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of PAH (WHO Group I) [A] in adults to improve exercise ability and delay clinical worsening. The delay in clinical worsening was demonstrated when Revatio was added to background epoprostenol (Flolan) therapy. Studies establishing effectiveness were short-term (12 to 16 weeks), and included predominately patients with NYHA Functional Class II-III symptoms and idiopathic etiology (71%) or associated with connective tissue disease (25%). Revatio injection is for the continued treatment of patients with PAH who are currently prescribed oral Revatio and who are temporarily unable to take oral medication. Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity.

Drug Name: Tracleer (bosentan) Tablets

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of PAH (WHO Group I), to improve exercise ability and decrease clinical worsening. Studies establishing effectiveness included predominately patients with WHO Class II-IV symptoms and etiologies of idiopathic or heritable PAH (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital heart disease with left-to-right shunts (18%). Considerations for use: Patients with WHO Class II symptoms showed reduction in the rate of clinical deterioration and a trend for improvement in walk distance. Physicians should consider whether these benefits are sufficient to offset the risk of hepatotoxicity in WHO Class II patients, which may preclude future use as their disease progresses.

Drug Name: Tyvaso (treprostinil) Inhalation Solution

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of PAH (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%). The effects diminish over the minimum recommended dosing interval of 4 hours; treatment timing can be adjusted for planned activities. While there are long-term data on use of inhaled treprostinil by other routes of administration, nearly all controlled clinical experience with inhaled treprostinil has been on a background of bosentan (an endothelin receptor antagonist) or sildenafil (a phosphodiesterase type 5 inhibitor). The controlled clinical experience was limited to 12 weeks in duration.

Drug Name: Veletri (epoprostenol) Injection

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Drug Name: Ventavis (iloprost) Inhalation Solution

Indications

Pulmonary Arterial Hypertension (PAH)

Indicated for the treatment of PAH (WHO Group I) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration. Studies establishing effectiveness included predominately patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH (65%) or PAH associated with connective tissue diseases (23%).

Drug Name: Uptravi (selexipag)

Indications

Pulmonary Arterial Hypertension

Indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH. Effectiveness was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms. Patients had idiopathic and heritable PAH (58%), PAH associated with connective tissue disease (29%), PAH associated with congenital heart disease with repaired shunts (10%).

2 . Criteria

Product Name: Adcirca tablet, Adempas tablets, Brand Flolan injection, Generic epoprostenol injection, Letairis tablets, Opsumit tablet, Orenitram tablets, Remodulin injection, Brand Revatio tablet, Generic sildenafil tablet, Tracleer tablets, Tyvaso inhalation solution, Tyvaso Refill inhalation solution, Tyvaso Starter inhalation solution, Veletri injection, or Ventavis inhalation solution

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pulmonary arterial hypertension [1, 11, 22-28, 31-33]

AND

2 Pulmonary arterial hypertension is symptomatic [1, 11, 22-28, 31-33]

AND

3 One of the following:

3.1 Diagnosis of pulmonary arterial hypertension was confirmed by right heart catheterization [B]

OR

3.2 Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension

AND

4 Prescribed by or in consultation with a pulmonologist or cardiologist

Product Name: Brand Revatio injection or Generic sildenafil injection

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pulmonary arterial hypertension [11]

AND

2 Pulmonary arterial hypertension is symptomatic [11]

AND

3 One of the following

3.1 Diagnosis of pulmonary arterial hypertension was confirmed by right heart catheterization [B]

OR

3.2 Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension

AND

4 Prescribed by or in consultation with a pulmonologist or cardiologist

AND

5 Patient is temporarily unable to take oral medications [11]

Product Name: Revatio oral suspension

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pulmonary arterial hypertension [11]

AND

2 Pulmonary arterial hypertension is symptomatic [11]

AND

3 One of the following:

3.1 Diagnosis of pulmonary arterial hypertension was confirmed by right heart catheterization [B]

OR

3.2 Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension

AND

4 Prescribed by or in consultation with a pulmonologist or cardiologist

AND

5 One of the following:

5.1 History of intolerance to generic Revatio tablets

OR

5.2 Patient is unable to ingest a solid dosage form (eg, an oral tablet or capsule) due to one of the following:

- Age
- Oral-motor difficulties
- Dysphagia

Product Name: Adempas tablets

Diagnosis	Chronic Thromboembolic Pulmonary Hypertension (CTEPH)
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Both of the following: [32]

1.1.1 Diagnosis of inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH)

AND

1.1.2 CTEPH is symptomatic

OR

1.2 Patient is currently on any therapy for the diagnosis of CTEPH

AND

2 Prescribed by or in consultation with a pulmonologist or cardiologist

Product Name: Adcirca tablet, Adempas tablets, Brand Flolan injection, Generic epoprostenol injection, Letairis tablets, Opsumit tablet, Orenitram tablets, Remodulin injection, Brand Revatio injection, Generic sildenafil injection, Brand Revatio tablet, Generic sildenafil tablet, Tracleer tablets, Tyvaso inhalation solution, Tyvaso Refill inhalation solution, Tyvaso Starter inhalation solution, Veletri injection, or Ventavis inhalation solution

Diagnosis	All indications listed above
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to therapy

Product Name: Revatio oral suspension

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to therapy

AND

2 One of the following:

2.1 History of intolerance to generic Revatio tablets

OR

2.2 Patient is unable to ingest a solid dosage form (eg, an oral tablet or capsule) due to one of the following:

- Age
- Oral-motor difficulties
- Dysphagia

Product Name: Uptravi

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of pulmonary arterial hypertension [34]

AND

2 Pulmonary arterial hypertension is symptomatic [34]

AND

3 One of the following:

3.1 Diagnosis of pulmonary arterial hypertension was confirmed by right heart catheterization [B]

OR

3.2 Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension

AND

4 One of the following:

4.1 Both of the following:

4.1.1 History of failure, contraindication, or intolerance to one of the following:

- PDE-5 inhibitor (ie, Adcirca, Revatio)
- Adempas (riociguat)

AND

4.1.2 History of failure, contraindication, or intolerance to an endothelin receptor antagonist [e.g. Letairis (ambrisentan), Opsumit (macitentan), or Tracleer (bosentan)]

OR

4.2 For continuation of prior Uptravi therapy

AND

5 Not taken in combination with a prostanoid/prostacyclin analogue (eg, epoprostenol, iloprost, treprostinil)

AND

6 Prescribed by or in consultation with a pulmonologist or cardiologist

Product Name: Uptravi

Diagnosis	Pulmonary Arterial Hypertension
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Uptravi therapy

AND

2 Not taken in combination with a prostanoid/prostacyclin analogue (eg, epoprostenol, iloprost, treprostinil)

3 . Definitions

Definition	Description
Pulmonary arterial hypertension (PAH)	Is characterized by a progressive increase in pulmonary vascular resistance leading to right ventricular failure and death. [2]
Revised World Health Organization Clinical Classification of Pulmonary Hypertension (Nice 2013) [9]	Group 1. Pulmonary Arterial Hypertension (PAH) 1.1 Idiopathic PAH 1.2 Heritable PAH 1.2.1 BMPR2 1.2.2 ALK-1, ENG, SMAD9, CAV1, KCNK3 1.2.3 Unknown 1.3 Drug- and toxin-induced 1.4 Associated with: 1.4.1 Connective tissue disease 1.4.2 HIV infection 1.4.3 Portal hypertension 1.4.4 Congenital heart disease 1.4.5 Schistosomiasis 1.5 Persistent pulmonary hypertension of the newborn 1’ Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis 1’’ Persistent pulmonary hypertension of the newborn Group 2. Pulmonary hypertension due to left heart disease Group 3. Pulmonary hypertension owing to lung diseases and/or hypoxemia Group 4. Chronic thromboembolic pulmonary hypertension (CTEPH) Group 5. Pulmonary hypertension with unclear multifactorial mechanisms
World Health Organization Functional Classes	PAH severity is quantified using the WHO classification of functional status, which is the NYHA functional classification modified to describe PAH symptoms: [7, 8] Class I: Patients with pulmonary hypertension in whom there is no limitation of usual physical activity; ordinary physical activity does not cause increased dyspnea, fatigue, chest pain, or presyncope. Class II: Patients with pulmonary hypertension who have mild limitation of physical activity. There is no discomfort at rest, but normal physical activity causes increased dyspnea, fatigue, chest pain, or presyncope. Class III: Patients with pulmonary hypertension who have a marked limitation of physical activity. There is no discomfort at rest, but less than ordinary activity causes increased dyspnea, fagitue, chest pain, or presyncope. Class IV: Patients with pulmonary

	hypertension who are unable to perform any physical activity at rest and who may have signs of right ventricular failure. Dyspnea and/or fatigue may be present at rest and symptoms are increased by almost any physical activity.

4 . Endnotes

A. WHO group I and WHO functional class I are distinct. WHO group I is not a measure of PAH severity but rather a diagnostic description that includes idiopathic pulmonary hypertension, familial pulmonary hypertension, and associated pulmonary hypertension. [8, 9]
B. Require right heart catheterization in order to confirm pulmonary arterial hypertension diagnosis: Per cardiologist consult, PAH specialist consult, and P&T committee recommendation, 2/20/2014

5 . References

1. Flolan Prescribing Information. GlaxoSmithKline, April 2015.
2. Badesch D, Abman S, Simonneau G, et al. Medical therapy for pulmonary arterial hypertension: Updated ACCP evidence-based clinical practice guidelines. Chest. 2007;131:1917-1928.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 Expert consensus document on pulmonary hypertension: a report of the American College of Cardiology Foundation Task Force on expert consensus documents and the American Heart Association. J Am Coll Cardiol. 2009;53:1573-1619.
4. Barst RJ, et al. A comparison of continuous intravenous Flolan (prostacyclin) with conventional therapy for primary pulmonary hypertension. N Engl J Med 1996;334:296-301.
5. McLaughlin VV, et al. Survival in primary pulmonary hypertension; the impact of Flolan therapy. Circulation 2002;106:1477-1482.
6. Badesch DB, Tapson VF, McGoon MD, et al. Continuous intravenous Flolan for pulmonary hypertension due to the scleroderma spectrum of disease. A randomized controlled trial. Ann Intern Med 2002;132:425-34.
7. Barst J, McGoon M, Torbicki A, et al. Diagnosis and differential assessment of pulmonary arterial hypertension. J Am Coll Cardiol. 2004;43:40S-47S.
8. Rubin L. Introduction: diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Chest. 2004;126:7-10.
9. Simonneau G, Gatzoulis MA, Adatia I, et al. Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol. 2013;62(25 Suppl):D34-41.
10. McCrory D, Lewis S. Methodology and grading for pulmonary hypertension evidence review and guideline development. Chest. 2004;126:11-13.
11. Revatio Prescribing Information. Pfizer Inc., May 2015.
12. Barst R on behalf of the 1140 (SUPER 1) Study Group. Hemodynamic effects of Revatio Injection citrate in patients with pulmonary arterial hypertension: results of a

multinational, international, randomized, double blind, placebo controlled trial. Presented at the 54th Annual Scientific Session of the American College of Cardiology (ACC) in Orlando, FL from March 5th-8th, 2005.
13. Ghofrani H. Efficacy and safety of Revatio Injection citrate in pulmonary arterial hypertension: results of a multinational, randomized, double-blind, placebo-controlled trail. Presented on Wednesday, October 27, 2004 in the Late Breaking Abstract Session at CHEST 2004 Annual Scientific Assembly, Seattle, WA, USA.
14. Data on file, Pfizer Inc.
15. Galie N, Burgess G, Parpia T, et al. Effects of Revatio Injection on 1-year survival of patients with idiopathic pulmonary arterial hypertension (PAH) [abstract]. Presented at the 101st International Conference of the American Thoracic Society (ATS); San Diego, CA; May 2005.
16. Rubin L, Burgess G, Parpia T, et al. Effects of Revatio Injection on 6 minute walk distance (6MWD) and WHO functional class (FC) after 1 year of treatment [abstract]. Presented at the 101st International Conference of the American Thoracic Society (ATS); San Diego, CA; May 2005.
17. Sastry B, Narasimhan C, Krishna N, Raju B. Clinical efficacy of Revatio Injection in primary pulmonary hypertension: a randomized, placebo-controlled, double-blind, crossover study. J Am Coll Cardiol. 2004;43:1149-1153.
18. Badesch D, Abman S, Simonneau G, et al. Medical therapy for pulmonary arterial hypertension: Updated ACCP evidence-based clinical practice guidelines. Chest. 2007;131:1917-1928.
19. Barst RJ, McGoon M, Torbicki A, et al. Diagnosis and differential assessment of pulmonary arterial hypertension. J Am Coll Cardiol. 2004;43:40S-47S.
20. Simonneau G, Galie N, Rubin LJ, et al. Clinical classification of pulmonary hypertension. J Am Coll Cardiol 2004;43:5S-12S.
21. Simmoneau G, Rubin LJ, Galié N, et al. Addition of Revatio Injection to long-term intravenous Flolan therapy in patients with pulmonary arterial hypertension. Ann Int Med. 2008;149:521-30.
22. Ventavis Prescribing Information. Actelion Pharmaceuticals US, Inc. November 2013.
23. Tyvaso Prescribing Information. United Therapeutics Corp, August 2014.
24. Remodulin Prescribing Information. United Therapeutics Corp, December 2014.
25. Adcirca Prescribing Information. Eli Lilly and Company, July 2015.
26. Letairis Prescribing Information. Gilead Sciences, Inc., March 2015.
27. Tracleer Prescribing Information. Actelion Pharmaceuticals US, Inc., October 2012.
28. Veletri Prescribing Information. Actelion Pharmaceuticals US, Inc., June 2012.
29. Simonneau G, Robbins, IM, Behetti M, et al. Updated Clinical Classification of Pulmonary Hypertension. J Am Coll Cardiol 2009;54:S43–54.
30. U.S. Food and Drug administration. FDA Drug Safety Communication: FDA recommends against use of Revatio (sildenafil) in children with pulmonary hypertension. http://www.fda.gov/Drugs/DrugSafety/ucm317123.htm; Accessed January 23, 2013.
31. Opsumit Prescribing Information. Actelion Pharmaceuticals US, Inc., May 2015.
32. Adempas Prescribing Information. Bayer HealthCare Pharmaceuticals Inc., August 2014.
33. Orenitram Prescribing Information. United Therapeutics Corp., October 2014.
34. Uptravi Prescribing Information. Actelion Pharmaceuticals US, Inc., December 2015

Prior Authorization Guideline

GL-17156 Pulmozyme (dornase alfa inhalation solution)

Formulary OptumRx SP

Formulary Note

Approval Date 5/31/2016

Revision Date 5/31/2016

Technician Note :

P&T Approval date: 5/27/2015; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Pulmozyme (dornase alpha) Inhalation Solution

Indications

Cystic Fibrosis

Indicated for daily administration in conjunction with standard therapies for the management of cystic fibrosis (CF) patients to improve pulmonary function. In CF patients with an FVC greater than or equal to 40% of predicted, daily administration of Pulmozyme has also been shown to reduce the risk of respiratory tract infections requiring parenteral antibiotics.

2 . Criteria

Product Name: Pulmozyme*

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization
Approval Criteria **1** Diagnosis of cystic fibrosis (CF)	
Notes	*Prior Authorization may not apply depending on the plan

Product Name: Pulmozyme*

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Diagnosis of cystic fibrosis (CF) **AND** **2** Documentation of positive clinical response (i.e., improvement in lung function [forced expiratory volume in one second {FEV1}], decreased number of pulmonary exacerbations) to Pulmozyme therapy	

Notes	*Prior Authorization may not apply depending on the plan

3 . References

1. Pulmozyme Prescribing Information. Genentech, Inc, December 2014.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. Am J Respir Crit Care Med. 2013;187(7):680-9.
3. Flume PA, O'Sullivan BP, Robinson KA et al. Cystic fibrosis pulmonary guidelines. Am J Respir Crit Care Med. 2007;176:957-969

Prior Authorization Guideline

GL-17082 Ravicti (glycerol phenylbutyrate)

Formulary OptumRx SP

Formulary Note

Approval Date 4/10/2013

Revision Date 4/29/2016

Technician Note :

P&T Approval Date: 4/9/2013; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Ravicti (glycerol phenylbutyrate)

Indications

Urea cycle disorders (UCDs)

Indicated for use as a nitrogen-binding agent for chronic management of adult and pediatric patients greater than or equal to 2 years of age with urea cycle disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Ravicti must be used with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements). Limitations of use: Ravicti is not indicated for treatment of acute hyperammonemia in patients with UCDs. Safety and

efficacy for treatment of N-acetylglutamate synthase (NAGS) deficiency has not been established. The use of Ravicti in patients less than 2 months of age is contraindicated.

2 . Criteria

Product Name: Ravicti

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of urea cycle disorders (UCDs)

AND

2 Age greater than 2 months [A]

AND

3 Inadequate response to one of the following:

- Dietary protein restriction
- Amino acid supplementation

AND

4 Will be used concomitantly with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements)

Product Name: Ravicti

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Ravicti therapy

AND

2 Patient is actively on dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements)

3 . Endnotes

A. Ravicti is contraindicated in patients less than 2 months of age. Children < 2 months of age may have immature pancreatic exocrine function, which could impair hydrolysis of Ravicti, leading to impaired absorption of phenylbutyrate and hyperammonemia. [1]

4 . References

1. Ravicti Prescribing Information. Hyperion Therapeutics, Inc. September 2013.

Prior Authorization Guideline

GL-17146 Relistor (methylnaltrexone bromide)

Formulary OptumRx SP

Formulary Note

Approval Date 2/19/2015

Revision Date 5/25/2016

Technician Note :

P&T Approval Date: 8/18/2008; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Relistor (methylnaltrexone bromide)

Indications

Opioid-Induced Constipation (cancer pain, other advanced illnesses)

Indicated for the treatment of opioid-induced constipation (OIC) in adult patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient. Use of Relistor beyond four months has not been studied.

Opioid-Induced Constipation (chronic non-cancer pain)

Indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain.

2 . Criteria

Product Name: Relistor

Approval Length	4 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of opioid-induced constipation

AND

2 One of the following:

2.1 Patient is an adult with a diagnosis of chronic non-cancer pain

OR

2.2 Patient is receiving palliative care for an advanced illness

AND

3 Patient has used opioid medications for a minimum of 4 weeks

AND

4 One of the following:

4.1 Patient is experiencing fewer than 3 bowel movements in a week

OR

4.2 Patient has not experienced a bowel movement for longer than 2 days

AND

5 Patient has tried and had an insufficient response to a stool softener and a stimulant laxative regimen, plus one additional laxative trial from a different class

Product Name: Relistor

Approval Length	4 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of opioid-induced constipation

AND

2 One of the following:

2.1 Patient is an adult with a diagnosis of chronic non-cancer pain

OR

2.2 Patient is receiving palliative care for an advanced illness

AND

3 Documentation of positive clinical response to Relistor therapy (e.g., increase in bowel movements)

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. The efficacy and safety of Relistor in the treatment of opioid-induced constipation (OIC) in advanced illness patients receiving palliative care was demonstrated in 2 randomized, double-blind, placebo-controlled studies. [1] In these studies, the median age was 68 years (range 21 to 100) and patients had advanced illness and received care to control their symptoms. [1] The majority of patients had a primary diagnosis of incurable cancer; other primary diagnoses included endstage chronic obstructive pulmonary disease (COPD)/emphysema, cardiovascular disease/heart failure, Alzheimer's disease/dementia, HIV/AIDS, or other advanced illnesses. [1]
B. Authorization limit was set to 4 months because Relistor has not been studied in patients for this indication beyond 4 months. [1]
C. Stimulant and osmotic laxatives should be tried/failed first before patients are placed on OIC agents (ie, Relistor and Movantik). [11]
D. The efficacy and safety of Relistor in the treatment of OIC in patients with chronic non-cancer pain were evaluated in a randomized, double-blind, placebo-controlled study comparing 4 weeks of treatment on Relistor 12 mg once daily with placebo. [1] Patients had a history of chronic non-cancer pain for which they were taking opioids. [1] The majority of patients had a primary diagnosis of back pain; other primary diagnoses included joint/extremity pain, fibromyalgia, neurologic/neuropathic pain, and rheumatoid arthritis. [1]

5 . References

1. Relistor Prescribing Information. Salix Pharmaceuticals, April 2015.
2. Grunkemeier DM, Cassara JE, Dalton CB, Drossman DA. The narcotic bowel syndrome: clinical features, pathophysiology, and management. Clinical Gastroenterology and Hepatology. 2007;5:1126-1139.
3. Miles CL, Fellowes D, Goodman ML, Wilkinson S. Laxatives for the management of constipation in palliative care patients. Cochrane Database Syst Rev. 2006;18(4):CD003448.
4. Herndon CM, Jackson KC, Hallin PA. Management of opioid-induced gastrointestinal effects in patients receiving palliative care. Pharmacotherapy. 2002;22(2):240-250.
5. American College of Gastroenterology Chronic Constipation Task Force. An evidence-based approach to the management of chronic constipation in North America. American Journal of Gastroenterology. 2005;100:S1-S4.
6. National Comprehensive Cancer Network (NCCN). Palliative care: Clinical practice guidelines in oncology. Version 2.2015. National Comprehensive Cancer Network, Inc. http://www.nccn.org/professionals/physician_gls/pdf/palliative.pdf. Accessed on July 21, 2015.
7. Thomas J et al. Methylnaltrexone for opioid-induced constipation in advanced illness. N Eng J Med. 2008;358:2332-43.
8. DRUGDEX System [Internet database]. Greenwood Village, Colorado: Thomson Micromedex. Accessed on July 20, 2015.
9. Yuan CS, Foss JF, O'Connor M, Osinski J, et al. Methylnaltrexone for reversal of constipation due to chronic methadone use: a randomized controlled study. JAMA. 2000;283:367-372.
10. Siemens W, Gaertner J, Becker G. Advances in pharmacotherapy for opioid-induced constipation - a systematic review. Expert Opin Pharmacother. 2014:1-18.

11. Per clinical consult with gastroenterologist and family medicine specialists, May 20, 2015.
12. Facts and Comparisons [Internet database]. Clinical Drug Information, LLC. Accessed on July 16, 2015.

Prior Authorization Guideline

GL-17133 Revlimid (lenalidomide)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/25/2016

Technician Note :

P&T Approval Date: 6/6/2006; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Revlimid (lenalidomide)

Indications

Myelodysplastic Syndromes

Indicated for the treatment of patients with transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q abnormality with or without additional cytogenetic abnormalities.

Multiple Myeloma

In combination with dexamethasone is indicated for the treatment of patients with multiple myeloma.

Mantle Cell Lymphoma (MCL)

Indicated for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.

Limitations of Use

Not indicated and is not recommended for the treatment of patients with CLL outside of controlled clinical trials.

2 . Criteria

Product Name: Revlimid

Diagnosis	Myelodysplastic Syndromes (MDS)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of symptomatic or transfusion-dependent anemia due to myelodysplastic syndrome (MDS) associated with a deletion 5q abnormality

AND

2 Prescribed by or in consultation with an oncologist/hematologist

Notes	Reauthorization criteria for all indications appear at the end of the criteria section.

Product Name: Revlimid

Diagnosis	Multiple Myeloma (MM)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple myeloma

AND

2 Prescribed by or in consultation with an oncologist/hematologist

Notes	Reauthorization criteria for all indications appear at the end of the criteria section.

Product Name: Revlimid

Diagnosis	Mantle Cell Lymphoma (MCL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of relapsed or progressed mantle cell lymphoma (MCL)

AND

2 History of failure, contraindication, or intolerance to two prior MCL therapies (e.g., bortezomib, bendamustine, cladribine, rituximab) [5, C]

AND

3 Prescribed by or in consultation with an oncologist/hematologist

Notes	Reauthorization criteria for all indications appear at the end of the criteria section.

Product Name: Revlimid

Diagnosis	Myelodysplastic Syndromes, Multiple Myeloma, Mantle Cell Lymphoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Revlimid therapy

3 . Endnotes

A. Current NCCN practice guideline does not recommend treatment for smoldering or Durie-Salmon stage I MM. Close observation for disease progression every 3 to 6 months is recommended. [5]
B. Current NCCN practice guideline recommends single agent lenalidomide for maintenance of MM. [5]

4 . References

1. Revlimid Prescribing Information. Celgene Corporation. February 2015.
2. National Comprehensive Cancer Network (NCCN), Clinical Practice Guidelines in Oncology. Myelodysplastic Syndromes. V.1.2016. http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf Accessed September 18, 2015.
3. List A, Kurtin S, Roe DJ, et al. Efficacy of lenalidomide in myelodysplastic syndrome. N Engl J Med. 2005;352:549-557.
4. Raza A, Reeves JA, Feldman EJ, et al. Phase 2 study of lenalidomide in transfusion-dependent, low-risk, and intermediate-1 risk myelodysplastic syndromes with karyotypes other than deletion 5q. Blood. 2008;111(1):86-93.
5. National Comprehensive Cancer Network (NCCN), Clinical Practice Guidelines in Oncology. Non-Hodgkin's Lymphomas. V2.2015. http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf. Accessed on September 18, 2015.
6. Chanan-Khan A, Miller KC, Musial L, et al. Clinical efficacy of lenalidomide in patients with relapsed or refractory chronic lymphocytic leukemia: results of a phase II study. J Clin Oncol. 2006;24(34):5343-9.
7. Ferrajoli A, Lee BN, Schlette EJ, et al. Lenalidomide induced complete and partial remission in patients with relapsed and refractory chronic lymphocytic leukemia. Blood 2008;111(11):5291-97.

Prior Authorization Guideline

GL-17348 Rituxan (rituximab)

Formulary OptumRx SP

Formulary Note

Approval Date 4/10/2013

Revision Date 5/18/2016

Technician Note :

P&T Approval Date: 2/7/2005; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Rituxan (rituximab)

Indications

Non-Hodgkin's Lymphoma (NHL)

Indicated for the treatment of patients with: a. Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell non-Hodgkin's lymphoma as a single agent. b. Previously untreated diffuse large B-cell, CD20-positive non-Hodgkin's lymphoma in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or other anthracycline-based chemotherapy regimens. c. Previously untreated follicular, CD20-positive, B-cell non-Hodgkin's lymphoma in combination with first-line chemotherapy and, in patients achieving a complete or

partial response to Rituxan in combination with chemotherapy, as a single-agent maintenance therapy. d. Non-progressing (including stable disease) low-grade, CD20-positive, B-cell non-Hodgkin's lymphoma, as a single agent, after first-line CVP chemotherapy. Limitations of Use: Rituxan is not recommended for use in patients with severe, active infections.

Rheumatoid Arthritis (RA)

In combination with methotrexate, is indicated for the treatment of adult patients with moderately- to severely-active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies. Limitations of Use: Rituxan is not recommended for use in patients with severe, active infections.

Chronic Lymphocytic Leukemia (CLL)

Indicated, in combination with fludarabine and cyclophosphamide, for the treatment of patients with previously untreated and previously treated CD20-positive CLL. Limitations of Use: Rituxan is not recommended for use in patients with severe, active infections.

Granulomatosis with Polyangiitis (GPA) (Wegener’s Granulomatosis) and Microscopic Polyangiitis (MPA)

In combination with glucocorticoids, is indicated for the treatment of adult patients with Granulomatosis with Polyangiitis (GPA) (Wegener’s Granulomatosis) and Microscopic Polyangiitis (MPA). Limitations of Use: Rituxan is not recommended for use in patients with severe, active infections.

Off Label Uses

Immune Thrombocytopenic Purpura (ITP) [17-18]

Has been used for the treatment of immune or idiopathic thrombocytopenic purpura. [17-18] Overall response rates of 35% to 52% in patients with refractory idiopathic thrombocytopenic purpura. [6,7]

Waldenstrom's Macroglobulinemia [17-18]

Has been used for the treatment of relapsed/refractory Waldenstrom's macroglobulinemia. [17-18] Rituximab monotherapy (1 to 8 cycles) has shown efficacy in limited studies. [8-11]

2 . Criteria

Product Name: Rituxan

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	1 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately- to severely-active rheumatoid arthritis

AND

2 One of the following:

2.1 Patient is concurrently on methotrexate [1]

OR

2.2 History of contraindication or intolerance to methotrexate [21,27,C]

AND

3 One of the following:

3.1 History of failure, contraindication, or intolerance to two of the following:

- Cimzia (certolizumab)
- Humira (adalimumab)
- Simponi (golimumab) or Simponi Aria (golimumab IV)

OR

3.2 Continuation of prior Rituxan therapy

AND

4 Prescribed by or in consultation with a rheumatologist

AND

5 Not received in combination with a biologic DMARD [e.g., Enbrel (etanercept), Orencia (abatacept), Kineret (anakinra)] [19]

AND

6 Not received in combination with a janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [19]

Product Name: Rituxan

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	1 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Rituxan therapy

AND

2 At least 16 weeks have elapsed since last course of therapy [1,B]

AND

3 Not received in combination with a biologic DMARD [e.g., Enbrel (etanercept), Orencia (abatacept), Kineret (anakinra)] [19]

AND

4 Not received in combination with a janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [19]

Product Name: Rituxan

Diagnosis	Wegener's Granulomatosis and Microscopic Polyangiitis
Approval Length	3 Month
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following diagnoses: [1,24]

- Wegener's Granulomatosis [1,24]
- Microscopic Polyangiitis [1,24]

AND

2 One of the following:

2.1 Patient is concurrently on glucocorticoids (e.g., prednisone) [1,24]

OR

2.2 History of contraindication or intolerance to glucocorticoids (e.g., prednisone) [28,E]

AND

3 Prescribed by or in consultation with one of the following:

- Nephrologist
- Pulmonologist
- Rheumatologist

Product Name: Rituxan

Diagnosis	Non-Hodgkin's Lymphoma
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Both of the following: [1]

- Diagnosis of diffuse large B-cell, CD20-positive, non-Hodgkin’s lymphoma
- Used as first-line treatment in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or other anthracycline-based chemotherapy regimens

OR

1.2 Both of the following: [1]

- Diagnosis of follicular, CD20-positive, B-cell non-Hodgkin's lymphoma
- Used as first-line treatment in combination with chemotherapy

OR

1.3 All of the following: [1]

- Diagnosis of follicular, CD20-positive, B-cell non-Hodgkin's lymphoma
- Used as a single-agent maintenance therapy
- Patient achieved a complete or partial response to Rituxan in combination with chemotherapy

OR

1.4 Both of the following: [1]

1.4.1 Diagnosis of low-grade, CD20-positive, B-cell non-Hodgkin's lymphoma

AND

1.4.2 One of the following:

- Patient has stable disease following first-line treatment with CVP (cyclophosphamide, vincristine, prednisolone/ prednisone) chemotherapy
- Patient achieved a partial or complete response following first-line treatment with CVP (cyclophosphamide, vincristine, prednisolone/ prednisone) chemotherapy

OR

1.5 Diagnosis of relapsed or refractory, low grade or follicular CD20-positive, B-cell non-Hodgkin’s lymphoma. [1]

Product Name: Rituxan

Diagnosis	Immune or Idiopathic Thrombocytopenic Purpura [17-18] (Off-Label)
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of immune or idiopathic thrombocytopenic purpura (off-label) [6,7,29]

AND

2 Prescribed by or in consultation with a hematologist/oncologist

AND

3 History of failure, contraindication, or intolerance to at least one of the following: [23]

- Corticosteroids
- Immunoglobulins
- Splenectomy

AND

4 Documented platelet count of less than 50 x 10^9 / L [29]

Product Name: Rituxan

Diagnosis	Other Indications

Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Diagnosis of chronic lymphocytic leukemia [1-5,12,18]

OR

1.2 Diagnosis of Waldenstrom's macroglobulinemia (off-label) [8-11,17-18]

3 . Endnotes

A. Aggressive, continuous and early treatment with DMARDs may slow the destructive processes in RA by preventing or delaying cartilage and bone destruction. [13] Often used in combination, the most commonly prescribed DMARDs include hydroxychloroquine, sulfasalazine, leflunomide and methotrexate, with methotrexate being the gold standard.
B. An open-label extension analysis of RA patients previously treated with Rituxan was conducted. Patients were eligible for the second course if they demonstrated a greater than or equal to 20% reduction in both swollen joint count and the tender joint count at any visit 16 weeks after initial treatment or later and had active disease (swollen joint count greater than or equal to 8 and tender joint count greater than or equal to 8). Repeat courses of treatment were administered at the investigator's discretion, with a minimum interval between treatment courses of 16 weeks. [22]
C. A number of patients have absolute (eg, severe skin rash, cytopenia) or relative (hepatic disease, GI intolerance, other significant intolerance) contraindication to use of MTX. For such patients, it is reasonable to approve Rituxan treatment without concurrent MTX therapy.

D. Limited data are available on the safety and efficacy of subsequent courses of Rituxan in patients with Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA). The safety and efficacy of retreatment with Rituxan have not been established. [1]
E. Glucocorticoids were included in the approved indication because this was how the clinical studies were conducted. Clinicians will use pulse steroids ~1g/day with slow taper until other immunosuppressants kick in. This is usually done unless there is a good reason not to give steroids. Exception is when patient cannot tolerate high dose steroids (eg, patients with diabetes). For such patients, it is reasonable to approve Rituxan treatment without concurrent glucocorticoid therapy. [28]

4 . References

1. Rituxan Prescribing Information. Genentech, Inc., August 2014.
2. Byrd JC, Murphy T, Howard RS, et al. Rituximab using a thrice weekly dosing schedule in B-cell chronic lymphocytic leukemia and small lymphocytic lymphoma demonstrates clinical activity and acceptable toxicity. J Clin Oncol. 2001;19:2153-2164.
3. Byrd JC, Peterson BL, Morrison VA, et al. Randomized phase II study of fludarabine with concurrent versus sequential treatment with rituximab in symptomatic, untreated patients with B-cell chronic lymphocytic leukemia: results from Cancer and Leukemia Group B 9712 (CALGB 9712). Blood. 2003;101:6-14.
4. Schulz H, Klein SK, Rehwald U, et al. Phase 2 study of a combined immunochemotherapy using rituxumab and fludarabine in patients with chronic lymphocytic leukemia. Blood. 2002;100:3115-3120. .
5. Keating MJ, O'Brien S, Albitar M, et al. Early results of a chemoimmunotherapy regimen of fludarabine, cyclophosphamide, and rituxumab as initial therapy for chronic lymphocytic leukemia. J Clin Oncol. 2005;23:4079-4088.
6. Stasi R, Pagano A, Stipa E, et al. Rituximab chimeric anti-CD20 monoclonal antibody treatment for adults with chronic idiopathic thrombocytopenic purpura. Blood. 2001;98:952-7.
7. Saleh MN, Moore M, Feinberg B, et al. A pilot study of anti-CD20 MoAB rituximab in patients with refractory immune thrombocytopenic purpura (ITP). Blood. 2001;96:521a.
8. Dimopoulos MA, Kiamouris C, Karkantaris C, et al. Prospective evaluation of rituximab for the treatment of waldenstrom's macroglobulinemia. Blood. 2000;96:169a.
9. Treon SP, Agus DB, Link B, et al. Rituximab is an active agent in waldenstrom's macroglobulinemia (WM).Proc Am Soc Clin Oncol. 2000;19:6a.
10. Weide R, Heymanns J, & Koppler H. The polyneuropathy associated with Waldenstrom's macroglobulinaemia can be treated effectively with chemotherapy and the anti-CD20 monoclonal antibody rituximab. Br J Haematol. 2000a;109:838-841.
11. Byrd JC, White CA, Link B, et al. Rituximab therapy in Waldenstrom's macroglobulinemia: preliminary evidence of clinical activity. Ann Oncol. 1999a;10:1525-7.
12. National Comprehensive Cancer Network. Practice Guidelines in Oncology – v. 2.2015. Non-Hodgkin’s Lymphomas. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf. Accessed July 27, 2015.
13. The Canadian Coordinating Office for Health Technology Assessment (CCOHTA) Abatacept as add-on therapy for rheumatoid arthritis. September 2005. Issue #71 Available at: http://www.cadth.ca/media/pdf/359_Abatacept_cetap_e.pdf. Accessed July 27, 2015.

14. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995;38(6):727-735.
15. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum. 1993;36:729-740.
16. Edwards JCW, Szczepanski L, Szechinski J, et al. Efficacy of B-cell-targeted therapy with rituximab in patients with rheumatoid arthritis. N Engl J Med. 2004;350:2572-2581.
17. DRUGDEX Information System [Internet database]. Greenwood Village, Colorado: Thomson Micromedex. Accessed on July 27, 2015.
18. AHFS Drug Information (Adult and Pediatric) [Internet database]. Hudson, Ohio: Lexicomp. Accessed on July 27, 2015.
19. American College of Rheumatology 2008 Recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum. 2008;59(6):762-784.
20. Mease PJ, Cohen S, Gaylis NB, Chubick A, Kaell AT, Greenwald M, Agarwal S, Yin M, Kelman A. Efficacy and safety of retreatment in patients with rheumatoid arthritis with previous inadequate response to tumor necrosis factor inhibitors: results from the SUNRISE trial. J Rheumatol. 2010;37(5):917-27.
21. Per clinical consult with rheumatologist, December 18, 2009.
22. Keystone E, Fleischmann R, Emery P, et al. Safety and Efficacy of Additional Courses of Rituximab in Patients with Active Rheumatoid Arthritis: An Open-Label Extension Analysis. Arthritis Rheum. 2007;56(12):3896-3908.
23. George JN, Woolf SH, Raskob GE, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood. 1996;88:3-40.
24. Stone JH, Merkel PA, Spiera R, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. N Engl J Med. 2010;363:221-32.
25. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012;64(5):625-39.
26. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA; American Society of Hematology. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;21;117(16):4190-207.
27. Owczarczyk K, Hellmann M, Fliedner G, Röhrs T, Maizus K, Passon D, Hallek M, Rubbert A. Clinical outcome and B cell depletion in patients with rheumatoid arthritis receiving rituximab monotherapy in comparison with patients receiving concomitant methotrexate. Ann Rheum Dis. 2008;67(11):1648-9.
28. Per clinical consult with rheumatologist, March 10, 2014.
29. Gudbrandsdottir S, Birgens HS, Frederiksen H, et al. Rituximab and dexamethasone vs dexamethasone monotherapy in newly diagnosed patients with primary immune thrombocytopenia. Blood. 2013;121(11):1976-81.

Prior Authorization Guideline

GL-15507 Sabril (vigabatrin)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/1/2016

Technician Note :

P&T Approval Date: 11/13/2012; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Sabril (vigabatrin)

Indications

Refractory Complex Partial Seizures

Indicated as adjunctive therapy for adult patients and pediatric patients 10 years of age and older with refractory complex partial seizures (CPS) who have inadequately responded to several alternative treatments and for whom the potential benefits outweigh the risk of vision loss. Sabril is not indicated as a first line agent for complex partial seizures.

Infantile Spasms (1 Month to 2 Years of Age)
Indicated as monotherapy for pediatric patients with infantile spasms (IS) 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss.

2 . Criteria

Product Name: Sabril

Approval Length	12 months [A]
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Diagnosis of infantile spasms [A]

OR

1.2 All of the following: [A]

1.2.1 Diagnosis of complex partial seizures

AND

1.2.2 Used as adjunctive therapy

AND

1.2.3 History of failure, contraindication, or intolerance to two formulary anticonvulsants [e.g., Lamictal (lamotrigine), Depakene (valproic acid), Dilantin (phenytoin)]

3 . Endnotes

A. Sabril Risk Evaluation and Mitigation Strategy (REMS) program overview: Lundbeck has created the SHARE (Support Help And Resources for Epilepsy) System to facilitate the activities associated with implementation and maintenance of the Sabril REMS program that act as the hub for a network of select specialty pharmacies. The REMS includes the following elements utilizing SHARE database: 1) Medication Guide: outlines the vision loss that can occur with Sabril treatment; 2) Communication Plan for ophthalmic professionals with education to reinforce key risk messages; 3) Elements to Assure Safe Use (ETASU): Lundbeck will maintain a database of certified prescribers (eg, experience in treating epilepsy; assessing the effectiveness of Sabril; ordering and reviewing visual assessment; enrolling patients taking Sabril in the REMS program) and will ensure that prescribers comply with the requirements of the REMS and may de-enroll noncompliant prescribers. Assessing the effectiveness of Sabril should be done within 12 weeks for CPS patients and within 2-4 weeks for IS. Vision monitoring is mandatory in adults and it is required to the extent possible in infants at baseline (no later than 4 weeks after starting Sabril) and at least 3 months while on therapy. Vision testing is also required about 3-6 months after the discontinuation of Sabril therapy. Under REMS requirement, pharmacies that dispense Sabril will be specially certified. Lundbeck Inc. will ensure that each patient treated with Sabril is enrolled in the Sabril REMS before Sabril is dispensed and that Sabril will be dispensed to patients with evidence or other documentation of safe-use conditions. 4) Implementation system: Lundbeck will ensure that the REMS coordinating center receives completed Treatment Maintenance Form documenting an assessment of risk-benefit prior to authorizing the maintenance phase of therapy; ensure that the REMS coordinating center obtains the completed Ophthalmologic Assessment Form for all registered patients at 3-month intervals prior to authorizing continued dispensing of refills; ensure that certified pharmacies dispense Sabril only if they receive authorization for each dispensing from the REMS coordinating center; ensure that patients who do not comply with the vision monitoring requirements of the REMS are tapered from Sabril. [2,3]

4 . References

1. Sabril (vigabatrin) [package insert]. Deerfield, IL: Lundbeck Inc. (formerly Ovation Pharmaceuticals, Inc.) October 2013.
2. Sabril Risk Evaluation and Mitigation Strategy. Sabril Formulary Dossier. Lundbeck August 2009.

3. Mackay MT, Weiss SK, Adams-Webber T, Ashwal S, Stephens D, Ballaban-Gill K, et al. Practice parameter: medical treatment of infantile spasms: report of the American Academy of Neurology and the Child Neurology Society. Neurology 2004;62(10):1668-1681.
4. Go CY, Mackay MT, Weiss SK, et al. Evidence-based guideline update: Medical treatment of infantile spasms: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2012 Jun 12;78(24):1974-80.
5. American Academy of Neurology and the American Epilepsy Society. Efficacy and tolerability of the new antiepileptic drugs II: treatment of refractory epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2004;62:1261-73.

Prior Authorization Guideline

GL-16901 Sandostatin, Sandostatin LAR (octreotide)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 1/19/2001; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Sandostatin (octreotide acetate)

Indications

Acromegaly

Indicated to reduce blood levels of growth hormone and IGF-1 (somatomedin C) in acromegaly patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine at maximally tolerated doses. The goal is to achieve normalization of growth hormone and IGF-I (somatomedin C) levels. In patients with acromegaly, Sandostatin reduces growth hormone to within normal ranges in 50% of patients and reduces IGF-I (somatomedin C) to within normal ranges in 50%-60% of patients. Since the

effects of pituitary irradiation may not become maximal for several years, adjunctive therapy with Sandostatin to reduce blood levels of growth hormone and IGF-I (somatomedin C) offers potential benefit before the effects of irradiation are manifested. Improvement in clinical signs and symptoms or reduction in tumor size or rate of growth were not shown in clinical trials performed with Sandostatin; these trials were not optimally designed to detect such effects.

Diarrhea and Flushing associated with Carcinoid Tumors

Indicated for the symptomatic treatment of patients with metastatic carcinoid tumors where it suppresses or inhibits the severe diarrhea and flushing episodes associated with the disease. Studies were not designed to show an effect on the size, rate of growth, or development of metastases.

Vasoactive Intestinal Peptide Tumors (VIPomas)

Indicated for the treatment of the profuse watery diarrhea associated with VIP secreting tumors. Studies were not designed to show an effect on the size, rate of growth, or development of metastases.

Drug Name: Sandostatin LAR Depot (octreotide acetate)

Indications

General

Indicated in patients in whom initial treatment with Sandostatin Injection has been shown to be effective and tolerated.

Acromegaly

Indicated for long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option. The goal of treatment in acromegaly is to reduce GH and IGF-1 levels to normal.

Diarrhea and Flushing associated with Carcinoid Tumors

Indicated for long-term treatment of the severe diarrhea and flushing episodes associated with metastatic carcinoid tumors.

Vasoactive Intestinal Peptide Tumors (VIPomas)

Indicated for long-term treatment of the profuse watery diarrhea associated with VIP-secreting tumors. The effect of Sandostatin LAR on tumor size, rate of growth and development of metastases, has not been determined.

2 . Criteria

Product Name: Brand Sandostatin, Generic octreotide, or Sandostatin LAR

Diagnosis	Acromegaly
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of acromegaly

AND

2 One of the following:

2.1 Inadequate response to one of the following:

- Surgery
- Pituitary irradiation

OR

2.2 Not a candidate for surgical resection and pituitary irradiation

AND

3 History of failure or intolerance to a dopamine agonist (e.g., bromocriptine or cabergoline) at maximally tolerated doses **AND** **4** For Sandostatin LAR, patient has had a trial of short-acting octreotide and responded to and tolerated therapy

Product Name: Brand Sandostatin, Generic octreotide, or Sandostatin LAR

Diagnosis	Acromegaly
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Documentation of positive clinical response to therapy (e.g., reduction or normalization of IGF-1/GH level for same age and sex, reduction in tumor size)	

Product Name: Brand Sandostatin, Generic octreotide, or Sandostatin LAR

Diagnosis	Carcinoid Tumors, for Symptomatic Treatment of Diarrhea or Flushing
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of metastatic carcinoid tumor, for symptomatic treatment of severe diarrhea or flushing

AND

2 For Sandostatin LAR, patient has had a trial of short-acting octreotide and responded to and tolerated therapy

Product Name: Brand Sandostatin, Generic octreotide, or Sandostatin LAR

Diagnosis	Carcinoid Tumors, for Symptomatic Treatment of Diarrhea or Flushing
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of an improvement in the number of diarrhea and flushing episodes

Product Name: Brand Sandostatin, Generic octreotide, or Sandostatin LAR

Diagnosis	Vasoactive Intestinal Peptide Tumors, for Symptomatic Treatment of Diarrhea
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of metastatic vasoactive intestinal peptide tumor, for symptomatic treatment of profuse watery diarrhea

AND

2 For Sandostatin LAR, patient has had a trial of short-acting octreotide and responded to and tolerated therapy

Product Name: Brand Sandostatin, Generic octreotide, or Sandostatin LAR

Diagnosis	Vasoactive Intestinal Peptide Tumors, for Symptomatic Treatment of Diarrhea
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of an improvement in the number of diarrhea episodes

3 . References

1. Sandostatin Prescribing Information. Novartis, March 2012.
2. Sandostatin LAR Prescribing Information. Novartis, July 2014.

Prior Authorization Guideline

GL-17399 Selzentry (maraviroc)

Formulary OptumRx SP

Formulary Note

Approval Date 11/13/2013

Revision Date 5/31/2016

Technician Note :

P&T Approval Date: 11/12/2013; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Selzentry (maraviroc)

Indications

CCR5-tropic HIV-1

Indicated, in combination with other antiretroviral agents, for adult patients infected with only C-C motif chemokine receptor 5 (CCR5)-tropic human immunodeficiency virus type 1 (HIV-1). This indication is based on analyses of plasma HIV-1 RNA levels in 2 controlled trials of maraviroc in treatment-experienced subjects and one trial in treatment-naive subjects. Both trials in treatment-experienced subjects were conducted in clinically advanced, 3-class antiretroviral-experienced (nucleoside reverse transcriptase inhibitor [NRTI], non-nucleoside reverse

transcriptase inhibitor [NNRTI], protease inhibitor [PI], or enfuvirtide) adults with evidence of HIV-1 replication despite ongoing antiretroviral therapy. The following points should be considered when initiating therapy with maraviroc: - Adult patients infected with only CCR5-tropic HIV-1 should use maraviroc; - Tropism testing must be conducted with a highly sensitive tropism assay that has demonstrated the ability to identify patients appropriate for use of maraviroc. Outgrowth of pre-existing low-level CXCR4- or dual/mixed-tropic HIV-1 not detected by tropism testing at screening has been associated with virologic failure on maraviroc; - Use of maraviroc is not recommended in subjects with CXCR4- or dual/mixed-tropic HIV-1 as efficacy was not demonstrated in a Phase 2 trial of this patient group; - The safety and efficacy of maraviroc have not been established in pediatric patients; - In treatment-naive subjects, more subjects treated with maraviroc experienced virologic failure and developed lamivudine resistance compared with efavirenz.

2 . Criteria

Product Name: Selzentry

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of CCR5-tropic HIV-1 infection as confirmed by a highly sensitive tropism assay

AND

2 Patient is currently taking or will be prescribed an optimized background antiretroviral therapy regimen

AND

3 Prescribed by or in consultation with a clinician with HIV expertise

Product Name: Selzentry

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Selzentry therapy

AND

2 Prescribed by or in consultation with a clinician with HIV expertise

3 . References

1. Selzentry [Package Insert]. Research Triangle Park, NC: ViiV Healthcare; September 2013.
2. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. February 12, 2013; 1–267. Available at

http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed October 7, 2013.

Prior Authorization Guideline

GL-16788 Signifor, Signifor LAR (pasireotide)

Formulary OptumRx SP

Formulary Note

Approval Date 3/10/2015

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 2/19/2013; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Signifor LAR (pasireotide) **Indications** **Acromegaly** Indicated for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option.
Drug Name: Signifor (pasireotide)

Indications

Cushing's disease

Indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

2 . Criteria

Product Name: Signifor LAR

Diagnosis	Acromegaly
Approval Length	6 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of acromegaly

AND

2 One of the following:

- Inadequate response to surgery
- Patient is not a candidate for surgery

Product Name: Signifor LAR

Diagnosis	Acromegaly

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Signifor LAR therapy (e.g., patient's growth hormone level or insulin-like growth factor 1 level for age and gender has normalized/improved)

Product Name: Signifor

Diagnosis	Cushing's disease
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of endogenous Cushing's disease

AND

2 One of the following:

2.1 Patient has failed pituitary surgery

OR

2.2 Patient is not a candidate for surgery

Product Name: Signifor

Diagnosis	Cushing's disease
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Signifor therapy (e.g., a clinically meaningful reduction in 24-hour urinary free cortisol levels, improvement in signs or symptoms of the disease)

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

These products are subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . References

1. Signifor LAR Prescribing Information. Novartis, December 2014.
2. Signifor Prescribing Information. Novartis Pharmaceuticals, March 2015.

Prior Authorization Guideline

GL-16843 Simponi, Simponi Aria (golimumab)

Formulary OptumRx SP

Formulary Note

Approval Date 10/8/2013

Revision Date 4/14/2016

Technician Note :

P&T Approval Date: 6/23/2009; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Simponi (golimumab) - for subcutaneous use

Indications

Rheumatoid Arthritis (RA)

In combination with methotrexate, indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis.

Psoriatic Arthritis (PsA)

Alone or in combination with methotrexate, indicated for the treatment of adult patients with

active psoriatic arthritis.

Ankylosing Spondylitis (AS)

Indicated for the treatment of adult patients with active ankylosing spondylitis.

Ulcerative Colitis (UC)

Indicated in adult patients with moderately to severely active ulcerative colitis who have demonstrated corticosteroid dependence or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine or 6-mercaptopurine for: (1) inducing and maintaining clinical response, (2) improving endoscopic appearance of the mucosa during induction, (3) inducing clinical remission, and (4) achieving and sustaining clinical remission in induction responders.

Drug Name: Simponi Aria (golimumab) - for intravenous use

Indications

Rheumatoid Arthritis (RA)

In combination with methotrexate, indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis.

2 . Criteria

Product Name: Simponi or Simponi Aria

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active RA

AND

2 One of the following:

2.1 Patient is receiving concurrent therapy with methotrexate (Rheumatrex, Trexall)

OR

2.2 History of failure, contraindication or intolerance to methotrexate (Rheumatrex, Trexall)

AND

3 Prescribed by or in consultation with a rheumatologist

AND

4 Patient is not receiving the requested medication in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)] [A,B,C]

AND

5 Patient is not receiving the requested medication in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [A,B,C]

Product Name: Simponi or Simponi Aria

Diagnosis	Rheumatoid Arthritis (RA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to therapy

AND

2 Patient is not receiving the requested medication in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)] [A,B,C]

AND

3 Patient is not receiving the requested medication in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [A,B,C]

Product Name: Simponi

Diagnosis	Psoriatic Arthritis (PsA)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active PsA

AND

2 Prescribed by or in consultation with one of the following:

- Dermatologist
- Rheumatologist

AND

3 Patient is not receiving Simponi in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)] [A,C]

AND

4 Patient is not receiving Simponi in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [A,C]

Product Name: Simponi

Diagnosis	Psoriatic Arthritis (PsA)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Simponi therapy

AND

2 Patient is not receiving Simponi in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)] [A,C]

AND

3 Patient is not receiving Simponi in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [A,C]

Product Name: Simponi

Diagnosis	Ankylosing Spondylitis (AS)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of active ankylosing spondylitis

AND

2 History of failure, contraindication, or intolerance to two NSAIDs [6,14]

AND

3 Prescribed by or in consultation with a rheumatologist

AND

4 Patient is not receiving Simponi in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)] [A,C]

AND

5 Patient is not receiving Simponi in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [A,C]

Product Name: Simponi

Diagnosis	Ankylosing Spondylitis (AS)
Approval Length	24 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Simponi therapy

AND

2 Patient is not receiving Simponi in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)] [A,C]

AND

3 Patient is not receiving Simponi in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [A,C]

Product Name: Simponi

Diagnosis	Ulcerative Colitis (UC)
Approval Length	10 Week
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderately to severely active ulcerative colitis

AND

2 One of the following:

2.1 Patient is corticosteroid dependent (I.e., an inability to successfully taper corticosteroids

without a return of the symptoms of UC)

OR

2.2 History of failure, contraindication, or intolerance to one of the following conventional therapies: [15]

- 6-mercaptopurine (Purinethol)
- Aminosalicylate [e.g., mesalamine (Asacol, Pentasa, Rowasa), olsalazine (Dipentum), sulfasalazine (Azulfidine, Sulfazine)]
- Azathioprine (Imuran)
- Corticosteroids (e.g., prednisone, methylprednisolone)

AND

3 Prescribed by or in consultation with a gastroenterologist

AND

4 Patient is not receiving Simponi in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)] [A,C]

AND

5 Patient is not receiving Simponi in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [A,C]

Product Name: Simponi

Diagnosis	Ulcerative Colitis (UC)
Approval Length	24 Month

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Simponi therapy

AND

2 Patient is not receiving Simponi in combination with a biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Orencia (abatacept)] [A,C]

AND

3 Patient is not receiving Simponi in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [A,C]

3 . Endnotes

A. The concomitant use of Simponi with biologics approved to treat RA, PsA, or AS is not recommended because of the possibility of an increased risk of infection. [1]
B. The concomitant use of Simponi Aria with biologics approved to treat RA is not recommended because of the possibility of an increased risk of infection. [16]
C. Xeljanz should not be used in combination with biologic DMARDs. [17]

D. The American Academy of Dermatology 2011 recommendations for PsA places the TNF blockers as first line therapy options alongside methotrexate. [4]

4 . References

1. Simponi Prescribing Information. Janssen Biotech Inc., December 2014.
2. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care & Research. 2012;64(5):625-639.
3. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011. Ann Rheum Dis. 2012;71(Supp II):i2–i45.
4. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis -- Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: Case-based presentations and evidence-based conclusions. J Am Acad Dermatol. 2011;65:137-174.
5. Kyle S, Chandler D, Griffiths EM, et al. Guideline for anti-TNF-? therapy in psoriatic arthritis. Rheumatology. 2005;44:390-397.
6. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of Ankylosing spondylitis. Ann Rheum Dis. 2011;70:896-904.
7. Inman RD, Davis Jr. JC, van der Heijde D, et al. Efficacy and safety of golimumab in patients with ankylosing spondylitis: Results of a randomized, double-blind, placebo-controlled, Phase III Trial. Arthritis Rheum. 2008; 58(11): 3402-3412.
8. Kavanaugh A, McInnes I, Mease P, et al. Golimumab, a new tumor necrosis factor ? antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis. Arthritis Rheum. 2009; 60(4): 976-986.
9. Keystone EC, Genovese MC, Klareskog L, et al. Golimumab, a human antibody to tumor necrosis factor ? given by monthly subcutaneous injections, in active rheumatoid arthritis despite methotrexate therapy: the GO-FORWARD Study. Ann Rheum Dis. 2009; 68:789-796.
10. Keats A, Barkham A, Bhalla K, et al. on the behalf of the BSR Standards, Guidelines and Audit Working Group. British Society for Rheumatology (BSR) Guideline for prescribing TNF? blockers in adults with ankylosing spondylitis. Report of a working party of the British Society of Rheumatology. Rheumatol 2005; 44:939-947.
11. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum. 1995;38:727-735.
12. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum. 1993; 36 (6): 729-740.
13. Per clinical consult with rheumatologist, June 30, 2011.
14. van der Heijde, Sieper J, Maksymowych WP, et al. 2010 update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. Ann Rheum Dis. 2011;70:905-908.
15. Kornbluth A, Sachar DB, and Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2010;105(3):501-23.
16. Simponi Aria Prescribing Information. Janssen Biotech, Inc., December 2014.

17. Xeljanz Prescribing Information. Pfizer, Inc., November 2013.

Prior Authorization Guideline

GL-17248 Soliris (eculizumab)

Formulary OptumRx SP

Formulary Note

Approval Date 6/29/2016

Revision Date 6/29/2016

Technician Note :

P&T Approval Date: 11/19/2014; P&T Revision Date: 6/22/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Soliris (eculizumab)

Indications

Paroxysmal Nocturnal Hemoglobinuria (PNH) Indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.

Atypical Hemolytic Uremic Syndrome (aHUS) Indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

2 . Criteria

Product Name: Soliris

Diagnosis	Paroxysmal Nocturnal Hemoglobinuria (PNH), Atypical Hemolytic Uremic Syndrome (aHUS)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 All of the following:

1.1 The member has one of the following diagnoses:

- Atypical hemolytic uremic syndrome (aHUS)
- Paroxysmal nocturnal hemoglobinuria (PNH) [4, A]

and

1.2 The member does not have an unresolved N. meningitidis infection

and

1.3 One of the following:

1.3.1 The member has received a meningococcal vaccination at least two weeks prior to the initiation of therapy with Soliris [5, D]

OR

1.3.2 Both of the following:

1.3.2.1 The member has not received a meningococcal vaccination at least two weeks prior to the initiation of therapy with Soliris

and

1.3.2.2 The risks of delaying Soliris therapy outweigh the risks of developing a meningococcal infection

and

1.4 The prescriber is enrolled in the Soliris REMS Program [C]

Product Name: Soliris

Diagnosis	Paroxysmal Nocturnal Hemoglobinuria (PNH), Atypical Hemolytic Uremic Syndrome (aHUS)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response (e.g., hemoglobin stabilization or a decrease in the number of red blood cell transfusions for PNH; increase in mean platelet counts or hematologic normalization for aHUS) to Soliris therapy

3 . Endnotes

A. The FDA approved eculizumab in March 2007 to treat paroxysmal nocturnal hemoglobinuria (PNH). Currently, eculizumab is the first-line therapy for PNH compared to the supportive therapy (steroid or other immune system suppressive agents)(Risitano, 2008). Bone marrow transplantation remains the only cure for PNH but should be reserved for patients with suboptimal response to eculizumab (Brodskey, 2014).
B. In September 2011, eculizumab was approved to treat atypical hemolytic uremic syndrome (aHUS), a rare and chronic blood disease that disproportionately affects children (FDA News Release, 2011). There are no other FDA-approved treatments for aHUS, and the safety and effectiveness of current standard treatment, plasma therapy (plasma exchange or fresh frozen plasma infusion), have not been studied in well controlled trials (FDA News Release, 2011). Eculizumab is considered as an optimal first-line therapy for this condition and potentially prevent serious outcomes such as renal failure, stroke or death (FDA News Release, 2011).
C. REMS components: Elements to Assure Safe Use; Medication Guide. Access is restricted through a REMS program. Prescribers must be enrolled in the program; enrollment information is available at 1-888-765-4747. Counsel patients on the risk of meningococcal infection; ensure patients are vaccinated and provide educational materials. This is a boxed warning (Soliris prescribing information, 2014).
D. Meningococcal infection: Meningococcal infections have occurred in patients receiving eculizumab; may be fatal or life-threatening if not detected and treated promptly. Monitor for early signs of meningococcal infection; evaluate and treat promptly if suspected. Follow current meningococcal immunization recommendations for patients with complement deficiencies. Vaccinate with meningococcal vaccine at least 2 weeks prior to initiation of treatment; revaccinate according to current guidelines. Polyvalent meningococcal vaccines are recommended. If urgent treatment is necessary in an unvaccinated patient, administer meningococcal vaccine as soon as possible. Although the risk/benefits of prophylactic meningococcal antibiotic therapy have not been determined, prophylactic antibiotics were administered in clinical studies until at least 2 weeks after vaccination. Meningococcal infections developed in some patients despite vaccination. Discontinue eculizumab during the treatment of serious meningococcal infections. This is a boxed warning (Soliris prescribing information, 2014).
Immunizations: Patients should be up to date with all immunizations before initiating therapy (Soliris prescribing information, 2014).

4 . References

1. Brodskey RA. Paroxysmal nocturnal hemoglobinuria. Blood. 2014 Sep 18. pii: blood-2014-02-522128. [Epub ahead of print]
2. FDA News Release. FDA approves Soliris for rare pediatric blood disorder. U.S. Food and Drug Administration; September 23, 2011. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm272990.htm. Accessed October 15, 2014.
3. Micromedex Healthcare Series [internet database]. Greenwood Village, Colorado: Thomson Reuters (Healthcare) Inc. Updated periodically. Available by subscription from: http://www.thomsonhc.com/home/dispatch. Accessed October 15, 2014.

4. Risitano AM, Rotoli B. Paroxysmal nocturnal hemoglobinuria: pathophysiology, natural history and treatment options in the era of biological agents. Biologics. 2008 June; 2(2): 205â€“222.
5. Soliris prescribing information. Alexion Pharmaceuticals, Inc. Cheshire, CT. April 2014.

Prior Authorization Guideline

GL-16889 Somatuline Depot (lanreotide)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/25/2016

Technician Note :

P&T Approval Date: 11/13/2007; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Somatuline Depot (lanreotide)

Indications

Acromegaly

Indicated for the long-term treatment of acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option. The goal of treatment in acromegaly is to reduce growth hormone (GH) and insulin growth factor-1 (IGF-1) levels to normal.

Advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NET)
Indicated for the treatment of patients with unresectable, well-or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.

2 . Criteria

Product Name: Somatuline Depot

Diagnosis	Acromegaly
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of acromegaly

AND

2 One of the following:

2.1 Inadequate response to one of the following:

- Surgery
- Radiotherapy

OR

2.2 Not a candidate for surgery

Product Name: Somatuline Depot

Diagnosis	Acromegaly
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Somatuline Depot therapy, such as a reduction or normalization of IGF-1/GH level for same age and sex

Product Name: Somatuline Depot

Diagnosis	Advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NET)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of gastroenteropancreatic neuroendocrine tumor (GEP-NET)

AND

2 Disease is one of the following:

- Unresectable, locally advanced
- Metastatic

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Somatuline Depot

Diagnosis	Advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NET)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Somatuline Depot therapy

3 . References

1. Somatuline Depot Prescribing Information. Ipsen Pharma Biotech, December 2014.

Prior Authorization Guideline

GL-16794 Somavert (pegvisomant)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 7/14/2006; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Somavert (pegvisomant)

Indications

Acromegaly

Indicated for the treatment of acromegaly in patients who have had an inadequate response to surgery or radiation therapy, or for whom these therapies are not appropriate. The goal of treatment is to normalize serum insulin-like growth factor-I (IGF-I) levels.

2 . Criteria

Product Name: Somavert

Approval Length	12 Week
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of acromegaly

AND

2 One of the following:

2.1 Inadequate response to one of the following:

- Surgery
- Radiation therapy
- Dopamine agonist (e.g., bromocriptine, cabergoline) therapy

OR

2.2 Not a candidate for all of the following:

- Surgery
- Dopamine agonist (e.g., bromocriptine, cabergoline) therapy
- Radiation therapy

AND

3 History of failure, contraindication, or intolerance to generic octreotide (a somatostatin analogue)

Product Name: Somavert

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Documentation of positive clinical response to Somavert therapy (such as biochemical control; decrease or normalization of IGF-1 levels)	

3 . References

1. Somavert Prescribing Information. Pfizer Inc., August 2014.

Prior Authorization Guideline

GL-31230 Sprycel (dasatinib)

Formulary OptumRx SP

Formulary Note

Approval Date 8/8/2016

Revision Date 8/8/2016

Technician Note :

P&T Approval Date: 10/3/2006; P&T Revision Date: 2/25/2016 **Effective 8/22/2016**

1 . Indications

Drug Name: Sprycel (dasatinib)

Indications

Newly diagnosed Chronic Myelogenous Leukemia Indicated for the treatment of adults with newly diagnosed Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase. The effectiveness of Sprycel and Tasigna is based on cytogenetic response and major molecular response rates. The respective trials are ongoing and further data will be required to determine long-term outcome.

Resistant or intolerant Chronic Myelogenous Leukemia Indicated for the treatment of adults

with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib.

Acute Lymphoblastic Leukemia (ALL) Indicated for the treatment of adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy.

2 . Criteria

Product Name: Sprycel

Diagnosis	Acute Lymphoblastic Leukemia/Acute Lymphoblastic Lymphoma (ALL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL)

and

2 Prescribed by or in consultation with an oncologist and/or hematologist

Product Name: Sprycel

Diagnosis	Acute Lymphoblastic Leukemia/Acute Lymphoblastic Lymphoma (ALL)
Approval Length	12 Month

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on therapy

Product Name: Sprycel

Diagnosis	Chronic Myelogenous/Myeloid Leukemia (CML)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Philadelphia chromosome-positive chronic myelogenous/myeloid leukemia (Ph+ CML)

and

2 Prescribed by or in consultation with an oncologist and/or hematologist

and

3 One of the following:

3.1 Both of the following:

3.1.1 Newly diagnosed disease [A]

and

3.1.2 Diagnosis has been confirmed to be Philadelphia chromosome positive or BCR-ABL positive as detected by bone marrow cytogenetics, FISH, or PCR

OR

3.2 Both of the following: [B]

3.2.1 History of failure, contraindication, or intolerance to at least one prior tyrosine kinase inhibitor (such as Gleevec [imatinib])

and

3.2.2 Patient does not have the T315I mutation

Product Name: Sprycel

Diagnosis	Chronic Myelogenous/Myeloid Leukemia (CML)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on therapy

3 . Endnotes

A. According to NCCN recommendations, imatinib, dasatinib, and nilotinib are all first-line therapies for chronic myelogenous/myeloid leukemia. Since all 3 agents are appropriate as a first-line option, a step through any of the 3 products is inappropriate. [2]
B. According to NCCN recommendations, patients with disease that is resistant to first-line imatinib should be treated with nilotinib, dasatinib, or bosutinib in the second-line setting. Patients with disease that is resistant to first-line nilotinib or dasatinib could be treated with an alternate TKI (other than imatinib) in the second-line setting. Dasatinib and nilotinib are effective against a majority of mutations resistant to imatinib, except for the T315I mutation. Consider clinical trial, ponatinib, omacetaxine, or hematopoietic cell transplantation (HCT) for patients with a T315I mutation. [2]

4 . References

1. Sprycel Prescribing Information. Bristol-Myers Squibb Company, June 2013.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia - Version 1.2016. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed August 5, 2016.

Prior Authorization Guideline

GL-17442 Stivarga (regorafenib)

Formulary OptumRx SP

Formulary Note

Approval Date 4/10/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 2/192013; P&T Revision Date: 2/25/2016; ** Effective 7/1/2016 **

1 . Indications

Drug Name: Stivarga (regorafenib)

Indications

Metastatic Colorectal Cancer (mCRC)

Indicated for the treatment of patients with mCRC who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if KRAS wild type, an anti-EGFR therapy.

Gastrointestinal STromal Tumor (GIST)

Indicated for the treatment of patients with locally advanced, unresectable or metastatic GIST who have been previously treated with imatinib mesylate and sunitinib malate.

2 . Criteria

Product Name: Stivarga

Diagnosis	Metastatic Colorectal Cancer (mCRC)
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of metastatic colorectal cancer (mCRC)

AND

2 History of failure, contraindication or intolerance to fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy

AND

3 History of failure, contraindication or intolerance to an anti-VEGF therapy (e.g. Avastin [bevacizumab])

AND

4 One of the following:

4.1 KRAS mutation

OR

4.2 Both of the following:

- KRAS Wild-Type
- History of failure, contraindication or intolerance to an anti-EGFR therapy [e.g. Vectibix (panitumumab), Erbitux (cetuximab)]

AND

5 Prescribed by or in consultation with an oncologist

Product Name: Stivarga

Diagnosis	Metastatic Colorectal Cancer (mCRC)
Approval Length	3 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Stivarga therapy

Product Name: Stivarga

Diagnosis	Gastrointestinal Stromal Tumor (GIST)
Approval Length	3 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST)

AND

2 History of failure, contraindication or intolerance to both of the following:

- Gleevec (imatinib mesylate)
- Sutent (sunitinib malate)

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Stivarga

Diagnosis	Gastrointestinal Stromal Tumor (GIST)
Approval Length	3 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Stivarga therapy

3 . Dosing

Drug Name	Description
Stivarga	Recommended Dose: 160 mg orally, once daily for the first 21 days of each 28-day cycle. Take Stivarga with food (a low-fat breakfast).

4 . Availability

Drug Name	Description
Stivarga	40 mg regorafenib tablets

5 . Background

Clinical Practice Guidelines

National Comprehensive Cancer Network (2013) [2,3,4]

NCCN categories of evidence and consensus

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is

appropriate

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate

Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

NCCN recommended use:

a. Colon Cancer: Therapy for patients who have unresectable advanced or metastatic disease and have not previously received regorafenib (NCCN Category 2A)

- As a single agent after first progression in patients (KRAS mutant only) previously receiving FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen
- As a single agent after second progression in patients with KRAS mutations or in patients previously receiving cetuximab or panitumumab
- As a single agent after third progression

b. Rectal Cancer: Therapy for patients who have unresectable advanced or metastatic disease and have not previously received regorafenib (NCCN Category 2A)

- As a single agent after first progression in patients (KRAS mutant only) previously receiving FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen
- As a single agent after second progression in patients with KRAS mutations or in patients previously receiving cetuximab or panitumumab
- As a single agent after third progression

c. Soft Tissue Sarcoma – Gastrointestinal Stromal Tumors (GIST): Treatment for progressive disease when patient is no longer receiving benefit from imatinib or sunitinib (NCCN Category

2A)

6 . References

1. Stivarga Prescribing Information. Bayer HealthCare Pharmaceuticals, February 2013.
2. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Colorectal Cancer Version 3.2013. Accessed February 8, 2013.
3. National Comprehensive Cancer Network (NCCN). NCCN Drugs&Biologics Compendium Colon Cancer Version 3.2013. Accessed February 25, 2013.
4. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Soft Tissue Carcinoma Version 3.2012. Access February 8, 2013

Prior Authorization Guideline

GL-14417 Strensiq (asfotase alfa)

Formulary OptumRx SP

Formulary Note

Approval Date 1/4/2016

Revision Date 1/4/2016

Technician Note :

CPS Approval Date: 12/18/2015

1 . Indications

Drug Name: Strensiq (asfotase alfa)

Indications

Perinatal/infantile- and juvenile-onset hypophosphatasia (HPP)

Indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

2 . Criteria

Product Name: Strensiq 18 mg/0.45 mL, Strensiq 28 mg/0.7 mL, Strensiq 40 mg/mL

Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of perinatal/infantile or juvenile-onset hypophosphatasia (HPP) [A-C]

AND

2 Prescribed by or in consultation with a specialist experienced in the treatment of inborn errors of metabolism [A]

Product Name: Strensiq 80 mg/0.8 mL

Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of perinatal/infantile or juvenile-onset hypophosphatasia (HPP) [A-C]

AND

2 Prescribed by or in consultation with a specialist experienced in the treatment of inborn errors of metabolism [A]

AND

3 Patient's weight is greater than or equal to 40 kg [D]

3 . Endnotes

A. HPP is a rare metabolic disease characterized by low serum alkaline-phosphatase activity which results in bone mineralization defects and various systemic complications [2, 6] The disease arises from a genetic mutation within the tissue-nonspecific isozyme of alkaline phosphatase (TNSALP). The mutation results in a loss of function which leads to an accumulation of TNSALP substrates (e.g., inorganic pyrophosphate and pyridoxal 5?-phosphate (PLP). Given the complexities and rarity of the condition, the criteria requires the medication to be prescribed by or in consultation with a specialist experienced in the treatment of inborn errors of metabolism, this aims to ensure proper diagnosis.
B. Generally, HPP can be confidently diagnosed when there is low serum ALP activity in conjunction with physical and radiographic findings consistent with the disease. [2] Also, other chemical hallmarks of the disease include an elevated plasma PLP, elevated serum inorganic pyrophosphate, and an elevated serum or urinary phosphoethanolamine.
C. The inclusion criteria used in the pivotal trials varied depending on study design, however all included verification of the diagnosis as evident by a low ALP activity level, high PLP level, and/or some type of radiographic findings consistent with the disease [3-6]
D. The 80 mg/0.8 mL vial should not be used in patients weighing less than 40 kg, as the systemic exposure of the drug is lower than that achieved within the lower strengths. Use in these patients could result in inadequate exposure and poor treatment outcomes. [1]

4 . References

1. Strensiq prescribing information, Alexion Pharmaceuticals. Cheshire, CT.October 2015.

2. Hickman-Simmons, Jill. Best Practices in: Recognizing and Diagnosing Hypophosphatasia. Clinical Endocrinology News. November 2013. Accessed 12/3/2015. Available at: http://www.clinicalendocrinologynews.com
3. Hofmann C, Rockman-greenberg C, Harmatz P, Moseley S, Odrljin T, Liese J. Improvement in bone manifestations and respiratory status in infants and young children with HPP treated with asfotase alfa: An update on the ENB-010-10 trial. In: Oral Presentation Presented at the 7th International Conference on Children's Bone Health. 27-30 June 2015. Salzburg, Austria.
4. Madson KL, Rockman-Greenberg C, Melian A, et al. Asfotase alfa: long-term safety and efficacy in children with hypophosphatasia. Poster presented at the Pediatric Academic Societies and Asian Society for Pediatric Research Joint Meeting; May 3-6, 2014; Vancouver, Canada.
5. Rockman-Greenberg C, Vockley J, Harmatz P, et al. Asfotase alfa improves skeletal mineralization and respiratory function in infants and young children with hypophosphatasia: results from up to 12 months' treatment. Poster presented at the 2014 ACMG Annual Meeting; March 25-29, 2014; Nashville, TN.
6. Whyte MP, Greenberg CR, Salman N, et al. Enzyme-replacement therapy in life-threatening hypophosphatasia. N Engl J Med. 2012; 366(10):904-913.

Prior Authorization Guideline

GL-16892 Sutent (sunitinib)

Formulary OptumRx SP

Formulary Note

Approval Date 7/11/2013

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 4/4/2006; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Sutent (sunitinib)

Indications

Advanced pancreatic neuroendocrine tumors (pNET)

Indicated for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease.

Gastrointestinal stromal tumor (GIST)

Indicated for the treatment of gastrointestinal stromal tumor after disease progression on or

intolerance to imatinib mesylate.

Renal cell carcinoma (RCC)

Indicated for the treatment of advanced renal cell carcinoma.

2 . Criteria

Product Name: Sutent

Diagnosis	Gastrointestinal Stromal Tumor (GIST)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of gastrointestinal stromal tumor (GIST)

AND

2 History of disease progression, contraindication, or intolerance to Gleevec (imatinib)

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Sutent

Diagnosis	Gastrointestinal Stromal Tumor (GIST)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Sutent therapy

Product Name: Sutent

Diagnosis	Pancreatic Neuroendocrine Tumors (pNET)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of progressive, well-differentiated pancreatic neuroendocrine tumors (pNET)

AND

2 One of the following:

- unresectable locally advanced disease
- metastatic disease

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Sutent

Diagnosis	Pancreatic Neuroendocrine Tumors (pNET)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Sutent therapy

Product Name: Sutent

Diagnosis	Renal Cell Carcinoma (RCC)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced/metastatic renal cell carcinoma (RCC)

AND

2 Prescribed by or in consultation with an oncologist

Product Name: Sutent

Diagnosis	Renal Cell Carcinoma (RCC)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Patient does not show evidence of progressive disease while on Sutent therapy	

3 . References

1. Sutent Prescribing Information. Pfizer Labs, June 2014.

Prior Authorization Guideline

GL-16784 Sylatron (peginterferon alfa-2b)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 7/12/2011; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Sylatron (peginterferon alfa-2b)

Indications

Melanoma

Indicated for the adjuvant treatment of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy.

2 . Criteria

Product Name: Sylatron

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of melanoma with microscopic or gross nodal involvement

AND

2 The prescribed medication will be used as adjuvant therapy within 84 days of definitive surgical resection, including complete lymphadenectomy

AND

3 Prescribed by or in consultation with an oncologist or dermatologist

Product Name: Sylatron

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1	Patient does not show evidence of progressive disease while on Sylatron therapy

3 . References

1. Sylatron Prescribing Information. Schering Corporation. September 2015.

Prior Authorization Guideline

GL-17438 Synagis (palivizumab)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/31/2016

Technician Note :

P&T Approval Date: 3/17/2000; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Synagis (palivizumab)

Indications

Prophylaxis of respiratory syncytial virus (RSV)

Indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in children at high risk of RSV disease. Safety and efficacy were established in infants with bronchopulmonary dysplasia (BPD), infants with a history of premature birth (less than or equal to 35 weeks gestational age), and children with hemodynamically significant congenital heart disease (CHD).

2 . Criteria

Product Name: Synagis

Diagnosis	Premature Infants (without other indications)
Approval Length	5 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Born prematurely at or before 29 weeks, 0 days gestation [2, B]

AND

2 Age < 12 months at the start of the RSV season [A]

AND

3 Used for the prevention of serious lower respiratory tract disease caused by RSV during the RSV season for the patient's geographic region

Notes	Authorization will be issued for up to a maximum of 5 months (5 doses) during RSV season. Initiation of Synagis prophylaxis after start of RSV season will not require all 5 doses for these conditions. [A]

Product Name: Synagis

Diagnosis	Chronic Lung Disease of Prematurity
Approval Length	5 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Chronic lung disease (CLD) of prematurity [2]

AND

2 Born before 32 weeks, 0 days gestation [2]

AND

3 Received greater than 21% oxygen supplementation for at least the first 28 days after birth

AND

4 One of the following:

4.1 Age < 12 months at the start of the RSV season

OR

4.2 Both of the following:

- Age at least 12 to < 24 months at the start of the RSV season

- Received medical support (i.e., chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) within 6 months before the start of the second RSV season

AND

5 Prescribed by or in consultation with one of the following:

- Pediatric pulmonologist
- Neonatologist
- Pediatric intensivist
- Infectious disease specialist

AND

6 Used for the prevention of serious lower respiratory tract disease caused by RSV during the RSV season for the patient's geographic region

Notes	Authorization will be issued for up to a maximum of 5 months (5 doses) during RSV season. Initiation of Synagis prophylaxis after start of RSV season will not require all 5 doses for these conditions. [A]

Product Name: Synagis

Diagnosis	Hemodynamically Significant Congenital Heart Disease
Approval Length	5 Month
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Age < 12 months at the start of the RSV season, with one of the following: [C]

1.1.1 All of the following:

- Acyanotic heart failure
- Receiving medication to control congestive heart failure
- Patient will require a cardiac surgical procedure

OR

1.1.2 Moderate to severe pulmonary hypertension

OR

1.1.3 Cyanotic heart defect

OR

1.2 Both of the following*: [D]

- Age < 24 months
- Patient will or has undergone a cardiac transplantation during the RSV season

AND

2 Prescribed by or in consultation with a pediatric cardiologist

AND

3 Used for the prevention of serious lower respiratory tract disease caused by RSV during the RSV season for the patient's geographic region

Notes	Authorization will be issued for up to a maximum of 5 months (5 doses) during RSV season. Initiation of Synagis prophylaxis after start of RSV season will not require all 5 doses for these conditions. *ONE additional postoperative dose allowed for patients undergoing cardiac

	transplantation, cardiac bypass or extracorporeal membrane oxygenation. [A, D]

Product Name: Synagis

Diagnosis	Pulmonary Abnormality or Neuromuscular Disorder
Approval Length	5 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Pulmonary abnormalities (e.g., pulmonary malformations, tracheoesophageal fistula, conditions requiring tracheostomy) or neuromuscular disease (e.g., cerebral palsy) [2]

AND

2 Age < 12 months at the start of the RSV season

AND

3 Impaired ability to clear secretions from the upper airway due to an ineffective cough

AND

4 Prescribed by or in consultation with one of the following:

- Pediatric pulmonologist

- Neurologist

AND

5 Used for the prevention of serious lower respiratory tract disease caused by RSV during the RSV season for the patient's geographic region

Notes	Authorization will be issued for up to a maximum of 5 months (5 doses) during RSV season. Initiation of Synagis prophylaxis after start of RSV season will not require all 5 doses for these conditions. [A]

Product Name: Synagis

Diagnosis	Immunocompromised Children
Approval Length	5 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Received or will receive a solid organ transplant, hematopoietic stem cell transplant, or chemotherapy during the RSV season

AND

2 Age < 24 months

AND

3 Lymphocyte count is below the normal range for patient's age

AND

4 Prescribed by or in consultation with one of the following:

- Pediatric pulmonologist
- Infectious disease specialist
- Pediatric intensivist

AND

5 Used for the prevention of serious lower respiratory tract disease caused by RSV during the RSV season for the patient's geographic region

Notes	Authorization will be issued for up to a maximum of 5 months (5 doses) during RSV season. Initiation of Synagis prophylaxis after start of RSV season will not require all 5 doses for these conditions. [A]

Product Name: Synagis

Diagnosis	Children with Cystic Fibrosis
Approval Length	5 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cystic fibrosis [2]

AND

2 One of the following:

2.1 Both of the following:

- Age < 12 months
- Clinical evidence of CLD and/or nutritional compromise (i.e., failure to thrive)

OR

2.2 Both of the following:

- Age at least 12 to < 24 months
- Severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life, abnormalities on chest radiography or chest computed tomography that persist when stable) or weight for length < 10th percentile on pediatric growth chart [E]

Notes	Authorization will be issued for up to a maximum of 5 months (5 doses) during RSV season. Initiation of Synagis prophylaxis after start of RSV season will not require all 5 doses for these conditions. [A]

3 . Endnotes

A. Five monthly doses of palivizumab will provide more than 6 months of prophylactic serum palivizumab concentrations. Administration of more than five monthly doses is not recommended. If RSV season onset is in November, the first dose should be administered in November, and the fifth and final dose should be administered in March. If RSV season onset is in November and the first dose is given in January, the third and final dose should be administered in March. In most of North America, peak RSV activity typically occurs between November and March, usually beginning in November or December, peaking in January or February, and ending by the end of March or sometime in April. Communities in the southern United States, particularly some

communities in the state of Florida, tend to experience the earliest onset of RSV. Data from the Centers for Disease Control and Prevention (CDC) have identified variations in the onset and offset of the RSV “season” in the state of Florida that could affect the timing of palivizumab administration. [2] For analysis of National Respiratory and Enteric Virus Surveillance System (NREVSS) reports in the CDC Morbidity and Mortality Weekly Report (MMWR), season onset is defined as the first of 2 consecutive weeks during which the mean percentage of specimens testing positive for RSV antigen is at least 10% and RSV season offset is defined as the last of 2 consecutive weeks during which the mean percentage of positive specimens is at least 10%. [3] NREVSS surveillance data can be viewed here (http://www.cdc.gov/surveillance/nrevss/rsv/)

B. Palivizumab prophylaxis is not recommended for otherwise healthy infants born at or after 29 weeks, 0 days' gestation. [2]
C. The following conditions are NOT considered hemodynamically significant congenital heart disease: secundum atrial septal defect, small ventricular septal defect, pulmonary stenosis, uncomplicated aortic stenosis, mild coaractation of the aorta, and patent ductus arteriosus; lesions adequately corrected by surgery, unless continuing required medication for congestive heart failure; mild cardiomyopathy and not receiving medical therapy for the condition; children in the second year of life. [2]
D. Pediatric growth charts can be viewed here (http://www.cdc.gov/growthcharts/who_charts.htm)
E. Children undergoing these procedures should receive an additional dose of palivizumab as soon as possible after the procedure. Thereafter, doses should be administered monthly as scheduled. [2]
F. Monthly prophylaxis should be discontinued in any infant or child who experiences a breakthrough RSV hospitalization. [2]
G. Palivizumab prophylaxis is not recommended for prevention of health care-associated RSV disease. [2]
H. The burden of RSV disease and costs associated with transport from remote locations may result in a broader use of palivizumab for RSV prevention in Alaska Native populations and possibly in selected other American Indian populations. [2]

4 . References

1. Synagis Prescribing Information. MedImmune, LLC, March 2014.
2. Commitee on Infectious Diseases and Bronchiolitis Guidelines Committee. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalizations for respiratory syncytial virus infection. Pediatrics. 2014 Aug;134(2):415-20. doi: 10.1542/peds.2014-1665.
3. Panozzo CA, Stockman LJ, et al. Use of respiratory syncytial virus surveillance data to optimize the timing of immunoprophylaxis. Pediatrics. 2010 Jul;126(1):e116-23.

Prior Authorization Guideline

GL-16994 Synribo(omacetaxine mepesuccinate)

Formulary OptumRx SP

Formulary Note

Approval Date 3/13/2013

Revision Date 4/26/2016

Technician Note :

P&T Approval Date: 2/19/2013; P&T revision date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Synribo (omacetaxine mepesuccinate)

Indications

Resistant or intolerant Chronic Myeloid Leukemia

Is indicated for the treatment of adult patients with chronic or accelerated phase chronic myeloid leukemia (CML) with resistance and/or intolerance to two or more tyrosine kinase inhibitors (TKIs).

2 . Criteria

Product Name: Synribo

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic myelogenous leukemia in the chronic or accelerated phase

AND

2 Patient is 18 years of age or older

AND

3 Prescribed by or in consultation with a hematologist/oncologist

AND

4 Patient has tried and has had resistance, relapse, inadequate response, intolerance or is contraindicated to TWO tyrosine kinase inhibitors (i.e., GLEEVEC, SPRYCEL, TASIGNA, BOSULIF, ICLUSIG)

Product Name: Synribo

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has not experienced disease progression

3 . Endnotes

A. Resistance was defined as one of the following: no complete hematologic response (CHR) by 12 weeks (whether lost or never achieved); or no cytogenetic response by 24 weeks (i.e., 100% Ph positive [Ph+]) (whether lost or never achieved); or no major cytogenetic response (MCyR) by 52 weeks (i.e., greater than or equal to 35% Ph+) (whether lost or never achieved); or progressive leukocytosis. Intolerance was defined as one of the following: 1) Grade 3-4 non-hematologic toxicity that does not resolve with adequate intervention; or 2) Grade 4 hematologic toxicity lasting more than 7 days; or 3) any Grade greater than or equal to 2 toxicity that is unacceptable to the patient. [1]
B. Synribo should be prepared in a healthcare facility and administered by a healthcare professional. As omacetaxine mepesuccinate is an antineoplastic product, special handling and disposal procedures should be followed. [1]
C. In patients with chronic phase CML, the median duration of major cytogenetic response (MCyR) was 12.5 months. The median duration of major hematologic response (MaHR) in patients with accelerated phase CML was 4.7 months. [1]

4 . References

1. Synribo [Package Insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc. April, 2014

2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia -Version 3.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf

Prior Authorization Guideline

GL-15721 Tafinlar (dabrafenib)

Formulary OptumRx SP

Formulary Note

Approval Date 7/11/2013

Revision Date 3/30/2016

Technician Note :

P&T Approval Date: 7/9/2013 P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Tafinlar (dabrafenib)

Indications

BRAF V600E mutation-positive unresectable or metastatic melanoma

Indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test. Limitation of use: Tafinlar is not indicated for treatment of patients with wild-type BRAF melanoma.

BRAF V600E or V600K mutation-positive unresectable or metastatic melanoma

Indicated in combination with trametinib for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test. This indication is based on the demonstration of durable response rate. Improvement in disease-related symptoms or overall survival has not been demonstrated for Tafinlar in combination with trametinib. Limitation of use: Tafinlar is not indicated for treatment of patients with wild-type BRAF melanoma.

2 . Criteria

Product Name: Tafinlar

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following diagnoses: [1]

- Unresectable melanoma
- Metastatic melanoma

AND

2 Cancer is BRAFV600 mutant type (MT) as detected by an FDA-approved test (THxID-BRAF Kit) or performed at a facility approved by Clinical Laboratory Improvement Amendments (CLIA) [2]

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Tafinlar

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Patient does not show evidence of progressive disease while on Tafinlar therapy	

3 . References

1. Tafinlar Prescribing Information. GlaxoSmithKline, January 2014.
2. National Comprehensive Cancer Network. Clinical practice guidelines in oncology: melanoma. v.3.2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf. Accessed May 12, 2015.

Prior Authorization Guideline

GL-17413 Tagrisso (osimertinib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 6/1/2016

Technician Note :

P&T Approval Date: 1/27/2016; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Tagrisso (osimertinib)

Indications

Non-small cell lung cancer

Indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR TKI therapy.

2 . Criteria

Product Name: Tagrisso

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of metastatic non-small cell lung cancer (NSCLC)

AND

2 Tumors are positive for epidermal growth factor receptor (EGFR) T790M mutation

AND

3 The patient has experienced disease progression on or after one of the following EGFR Tyrosine Kinase Inhibitors (TKIs): [1]

- Gilotrif (afatinib)*
- Iressa (gefitinib)*
- Tarceva (erlotinib)*

AND

4 Prescribed by or in consultation with an oncologist	
Notes	*This product may require prior authorization.

Product Name: Tagrisso

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Tagrisso therapy [A]

AND

2 Patient has not developed interstitial lung disease

AND

3 Patient has not developed QTc interval prolongation with sign and symptoms of life threatening arrhythmia

AND

4 Patient has not developed symptomatic congestive heart failure

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to a standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. Osimertinib may be continued as a single agent therapy in patients with NSCLC and known sensitizing EGFR mutation following disease progression (Category 2A). [1]

5 . References

1. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed December 14, 2015.
2. Tagrisso Prescribing Information. AstraZeneca Pharmaceuticals, November 2015.

Prior Authorization Guideline

GL-16871 Tarceva (erlotinib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 7/14/2003; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Tarceva (erlotinib)

Indications

Non-Small Cell Lung Cancer (NSCLC)

Indicated for: • The first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test. • The maintenance treatment of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy. • The treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior

chemotherapy regimen. Limitations of use: • Tarceva is not recommended for use in combination with platinum-based chemotherapy. • Safety and efficacy of Tarceva have not been evaluated as first-line treatment in patients with metastatic NSCLC whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution.

Pancreatic Cancer

Indicated for the first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer in combination with gemcitabine.

2 . Criteria

Product Name: Tarceva

Diagnosis	Non-Small Cell Lung Cancer (NSCLC)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of locally advanced or metastatic (stage III or IV) non-small cell lung cancer (NSCLC)

AND

2 One of the following:

2.1 Both of the following:

2.1.1 History of failure to at least one prior chemotherapy regimen

AND

2.1.2 Tarceva will be used as monotherapy

OR

2.2 Both of the following:

2.2.1 No evidence of disease progression after four cycles of first-line platinum-based chemotherapy (i.e., Tarceva used as maintenance treatment)

AND

2.2.2 Tarceva will be used as monotherapy

OR

2.3 Patient has known active epidermal growth factor receptor (EGFR) exon 19 deletions, exon 21 (L858R) substitution, exon 18 (G719X, G719) or exon 20 (S7681) mutation as detected by an FDA-approved test or Clinical Laboratory Improvement Amendments-approved facility

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Tarceva

Diagnosis	Non-Small Cell Lung Cancer (NSCLC)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Tarceva therapy

Product Name: Tarceva

Diagnosis	Pancreatic Cancer
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following diagnoses:

- Locally advanced pancreatic cancer
- Unresectable pancreatic cancer
- Metastatic pancreatic cancer

AND

2 Used in combination with Gemzar (gemcitabine)

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Tarceva

Diagnosis	Pancreatic Cancer
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Tarceva therapy

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to an OptumRx standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . References

1. Tarceva Prescribing Information. Genentech, Inc., April 2015.

Prior Authorization Guideline

GL-16834 Targretin (bexarotene)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/7/2016

Technician Note :

P&T Approval Date: 11/17/2009; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Targretin (bexarotene) capsules **Indications** **Cutaneous T-Cell Lymphoma** Indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma in patients who are refractory to at least one prior systemic therapy.
Drug Name: Targretin (bexarotene) gel 1%

Indications

Cutaneous T-Cell Lymphoma

Indicated for the topical treatment of cutaneous lesions in patients with cutaneous T-cell lymphoma (Stage 1A and 1B) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.

2 . Criteria

Product Name: Brand Targretin capsules, Generic bexarotene capsules, or Targretin gel

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cutaneous T-cell lymphoma (CTCL) [A]

AND

2 History of failure, contraindication, or intolerance to at least one prior therapy (including skin-directed therapies [eg, corticosteroids {ie, clobetasol, diflorasone, halobetasol, augmented betamethasone dipropionate}, phototherapy] or systemic therapies [eg, interferons])

AND

3 Prescribed by or in consultation with one of the following:

- Oncologist
- Dermatologist

Product Name: Brand Targretin capsules, Generic bexarotene capsules, or Targretin gel

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has not had disease progression while on therapy

3 . Endnotes

A. Cutaneous T-cell lymphomas (CTCLs) are a group of non-Hodgkin's lymphomas (NHLs) primarily developing in the skin and ultimately involve lymph nodes, blood, and visceral organs. CTCLs include Mycosis fungoides (MF) and Sezary syndrome (SS), the most common types of CTCLs. MF accounts for 50-70% of cases of CTCL and SS accounts for only 1-3% of cases. MF is an extranodal NHL of mature T-cells with primary cutaneous involvement. SS is an erythrodermic, leukemic variant of CTCL and is characterized by significant blood involvement and lymphadenopathy. [3]

4 . References

1. Targretin Capsules Prescribing Information. Valeant, Inc., May 2013.
2. Targretin gel 1% Prescribing Information. Valeant, Inc., July 2013.

3. National Comprehensive Cancer Network (NCCN). Non-Hodgkins Lymphoma v.2.2015. Available at: http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf. Accessed on September 10, 2015.

Prior Authorization Guideline

GL-31241 Tasigna (nilotinib)

Formulary OptumRx SP

Formulary Note

Approval Date 8/8/2016

Revision Date 8/8/2016

Technician Note :

P&T Approval Date: 10/3/2006; P&T Revision Date: 2/25/2016. **Effective 8/22/2016**

1 . Indications

Drug Name: Tasigna (nilotinib)

Indications

Resistant or intolerant Chronic Myelogenous Leukemia Indicated for the treatment of chronic phase and accelerated phase Ph+ CML in adult patients resistant to or intolerant to prior therapy that included imatinib.

2 . Criteria

Product Name: Tasigna

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Philadelphia chromosome-positive chronic myelogenous/myeloid leukemia (Ph+ CML)

and

2 Prescribed by or in consultation with an oncologist and/or hematologist

and

3 One of the following:

3.1 Both of the following:

3.1.1 Newly diagnosed disease [A]

and

3.1.2 Patient is found to be Philadelaphia chromosome positive or BCR-ABL positive as detected by bone marrow cytogenetics, FISH, or PCR

OR

3.2 Both of the following: [B]

3.2.1 History of failure, contraindication, or intolerance to at least one prior tyrosine kinase inhibitor (such as Gleevec [imatinib])

and

3.2.2 Patient does not have the T315I mutation [2]

Product Name: Tasigna

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on therapy

3 . Endnotes

A. According to NCCN recommendations, Gleevec (imatinib), Sprycel (dasatinib), and Tasigna (nilotinib) are all first-line therapies for chronic myelogenous/myeloid leukemia. Since all 3 agents are appropriate as a first-line option, a step through any of the 3 products is inappropriate. [2]
B. According to NCCN recommendations, patients with disease that is resistant to first-line imatinib should be treated with nilotinib, dasatinib, or bosutinib in the second-line setting.

Patients with disease that is resistant to first-line nilotinib or dasatinib could be treated with an alternate TKI (other than imatinib) in the second-line setting. Dasatinib and nilotinib are effective against a majority of mutations resistant to imatinib, except for the T315I mutation. Consider clinical trial, ponatinib, omacetaxine, or HCT for patients with a T315I mutation. [2]

4 . References

1. Tasigna Prescribing Information. Novartis Pharmaceutical Corporation, September 2013.
2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia - Version 1.2016. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed August 5, 2016.

Prior Authorization Guideline

GL-17354 Temodar (temozolomide)

Formulary OptumRx SP

Formulary Note

Approval Date 7/11/2013

Revision Date 5/31/2016

Technician Note :

P&T Approval Date: 7/9/2013; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Temodar (temozolomide)

Indications

Newly Diagnosed Glioblastoma Multiforme

Indicated for the treatment of adult patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment.

Refractory Anaplastic Astrocytoma

Indicated for the treatment of adult patients with refractory anaplastic astrocytoma, i.e., patients

who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine.

2 . Criteria

Product Name: Brand Temodar, Generic temozolomide

Diagnosis	Glioblastoma Multiforme
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of glioblastoma multiforme

AND

2 One of the following:

2.1 Both of the following:

- Patient's condition is newly diagnosed
- Used concomitantly with radiotherapy

OR

2.2 Used as maintenance treatment

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Brand Temodar, Generic temozolomide

Diagnosis	Glioblastoma Multiforme
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Temodar therapy

Product Name: Brand Temodar, Generic temozolomide

Diagnosis	Anaplastic Astrocytoma
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of anaplastic astrocytoma

AND

2 Patient's condition has progressed on a drug regimen containing nitrosourea and procarbazine

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Brand Temodar, Generic temozolomide

Diagnosis	Anaplastic Astrocytoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Temodar therapy

3 . References

1. Temodar Prescribing Information, Merck & Co, Inc. January 2013.

2. Clinical Practice Guidelines in Oncology, v.2. 2013. Central Nervous System Cancers. National Comprehensive Cancer Network (NCCN) Web site. Available at http://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed June 4, 2013

Prior Authorization Guideline

GL-31507 Testosterone Injections

Formulary OptumRx SP

Formulary Note

Approval Date 9/29/2016

Revision Date 9/29/2016

Technician Note :

P&T Approval Date: 10/7/2008; P&T Revision Date: 9/28/2016

1 . Indications

Drug Name: Delatestryl (testosterone enanthate) injection

Indications

Primary hypogonadism (congenital or acquired) Indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone. Primary hypogonadism (congenital or acquired) - Testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy. If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone

deficiency after puberty. Safety and efficacy of Delatestryl in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Hypogonadotropic hypogonadism (congenital or acquired) Indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone. Hypogonadotropic hypogonadism (congenital or acquired) - Gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty. Safety and efficacy of Delatestryl in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Delayed puberty in males Indicated for stimulation of puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every six months to assess the effect of treatment on the epiphyseal centers.

Metastatic mammary cancer in females Indicated for secondary use in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or antiestrogen therapy. This treatment has also been used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

Drug Name: Depo-Testosterone (testosterone cypionate) injection

Indications

Primary hypogonadism (congenital or acquired) Indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone. Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy. Safety and efficacy of Depo-Testosterone (testosterone cypionate) in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Hypogonadotropic hypogonadism (congenital or acquired) Indicated for replacement

therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone. Hypogonadotropic hypogonadism (congenital or acquired) - Gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. Safety and efficacy of Depo-Testosterone (testosterone cypionate) in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Drug Name: Testopel (testosterone) pellets

Indications

Primary hypogonadism (congenital or acquired) Indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone. Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy. If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sex characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty. Safety and efficacy of Testopel in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism" have not been established.

Hypogonadotropic hypogonadism (congenital or acquired) Indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone. Hypogonadotropic hypogonadism (congenital or acquired)-idiopathic gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty. If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sex characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty. Safety and efficacy of Testopel in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism" have not been established.

Delayed puberty in males Indicated for stimulation of puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every six months to assess the effect of treatment on the epiphyseal centers.

Drug Name: Aveed (testosterone undecanoate)

Indications

Primary hypogonadism (congenital or acquired) Indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone. Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range. Aveed should only be used in patients who require testosterone replacement therapy and in whom the benefits of the product outweigh the serious risks of pulmonary oil microembolism and anaphylaxis. Limitations of use: Safety and efficacy of Aveed in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established. Safety and efficacy of Aveed in males less than 18 years old have not been established.

Hypogonadotropic hypogonadism (congenital or acquired) Indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone. Hypogonadotropic hypogonadism (congenital or acquired): idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range. Aveed should only be used in patients who require testosterone replacement therapy and in whom the benefits of the product outweigh the serious risks of pulmonary oil microembolism and anaphylaxis. Limitations of use: Safety and efficacy of Aveed in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established. Safety and efficacy of Aveed in males less than 18 years old have not been established.

Drug Name: Aveed (testosterone undecanoate), Delatestryl (testosterone enanthate) injection, Depo-Testosterone (testosterone cypionate) injection, Testone CIK (testosterone cypionate), Testopel (testosterone) pellets

Off Label Uses

Female-to-male transsexual - Gender identity disorder [25] Effectively produces male characteristics in female-to-male transsexual patients with gender identity disorder in open-label, time-series clinical trials. Produces significant improvements in body weight, BMI, suppression of menses, and secondary sex characteristics. Long-term effects in these patients have not been extensively studied, but 1 trial reports detrimental effects on cholesterol and triglyceride levels. Recommended by the Harry Benjamin International Gender Dysphoria

Association as a standard of care in appropriate individuals.
Drug Name: Testone CIK (testosterone cypionate) **Indications** **Primary hypogonadism (congenital or acquired)** Indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone. Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome; or orchidectomy. **Hypogonadotropic hypogonadism (congenital or acquired)** Indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone. Hypogonadotropic hypogonadism (congenital or acquired) - idiopathic gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation.

2 . Criteria

Product Name: Aveed^, Generic testosterone enanthate^, Brand Depo-Testosterone^, Generic testosterone cypionate^, Testone CIK^, Testopel^, Testosterone injection (250 mg/mL)^, Testosterone implant pellets^, Testosterone EO-PRO-CYP 220^

Diagnosis	Male hypogonadism
Approval Length	6 months for patients new to testosterone therapy; or 12 months for patients continuing testosterone therapy but without a current authorization on file with OptumRx [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization
Approval Criteria **1** Diagnosis of hypogonadism	

AND

2 Male patient

AND

3 One of the following:

3.1 Two pre-treatment serum total testosterone levels less than 280 ng/dL (< 9.7 nmol/L) or less than the reference range for the lab* [5]

OR

3.2 Both of the following:

3.2.1 Patient has a condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity)

AND

3.2.2 One pre-treatment calculated free or bioavailable testosterone level less than 5 ng/dL (< 0.17 nmol/L) or less than the reference range for the lab*

OR

3.3 Patient has a history of one of the following:

- Bilateral orchiectomy
- Panhypopituitarism
- A genetic disorder known to cause hypogonadism (e.g., congenital anorchia, Klinefelter's syndrome)

Notes	^Per the American Geriatrics Society 2012 Beers Criteria Update, testosterone should be avoided in patients greater than or equal to 65 years of age unless indicated for moderate to severe hypogonadism. [G] *This may require treatment to be temporarily held.

Product Name: Aveed^, Generic testosterone enanthate^, Brand Depo-Testosterone^, Generic testosterone cypionate^, Testone CIK^, Testopel^, Testosterone injection (250 mg/mL)^, Testosterone implant pellets^, Testosterone EO-PRO-CYP 220^

Diagnosis	Gender Identity Disorder (off-label) [8]
Approval Length	6 months for patients new to testosterone therapy; or 12 months for patients continuing testosterone therapy but without a current authorization on file with OptumRx [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Age 18 years or older [9, 12]

AND

2 Using hormones to change physical characteristics [9, 12]

AND

3 Demonstrable knowledge of what hormones medically can and cannot do and their social benefits and risks [9, 12]

AND

4 One of the following: [9, 12]

4.1 A documented real-life experience (living as the other gender) of at least three months prior to the administration of hormone

OR

4.2 A period of psychotherapy of a duration specified by the mental health professional after the initial evaluation (usually a minimum of three months)

AND

5 The Covered person must meet the definition of Gender Identity Disorder (see definition below): [9, 12]

5.1 Gender Identity Disorder: A disorder characterized by the following diagnostic criteria:

- A strong and persistent cross-gender identification (not merely a desire for any perceived cultural advantages of being the other sex)
- Persistent discomfort with his or her sex or sense of inappropriateness in the gender role of that sex
- The disturbance is not concurrent with a physical intersex condition
- The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning
- The transsexual identity has been present persistently for at least two years
- The disorder is not a symptom of another mental disorder or a chromosomal abnormality

Notes	^Per the American Geriatrics Society 2012 Beers Criteria Update, testosterone should be avoided in patients greater than or equal to 65 years of age unless indicated for moderate to severe hypogonadism [G]

Product Name: Aveed*, Generic testosterone enanthate*, Brand Depo-Testosterone*, Generic testosterone cypionate*, Testone CIK*, Testopel*, Testosterone injection (250 mg/mL)*, Testosterone implant pellets*, Testosterone EO-PRO-CYP 220*

Diagnosis	Male hypogonadism or Gender Identity Disorder
Approval Length	12 Month [C]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Follow-up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy, or 12 months for patients continuing testosterone therapy, is within or below the normal limits of the reporting lab [D, E, F]

OR

1.2 Follow-up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy, or 12 months for patients continuing testosterone therapy, is outside of upper limits of normal for the reporting lab and the dose is adjusted [D, E, F]

OR

1.3 Both of the following:

1.3.1 Patient has a condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity)

AND

1.3.2 One of the following:

1.3.2.1 Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy, or the past 12 months for patients continuing testosterone therapy, is within or below the normal limits of the reporting lab [D, E, F]

OR

1.3.2.2 Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy, or past 12 months for patients continuing testosterone therapy, is outside of upper limits of normal for the reporting lab and the dose is adjusted [D, E, F]

Notes	*Per the American Geriatrics Society 2012 Beers Criteria Update, testosterone should be avoided in patients greater than or equal to 65 years of age unless indicated for moderate to severe hypogonadism [G]

Product Name: Generic testosterone enanthate*

Diagnosis	Inoperable breast cancer in women
Approval Length	1 Year
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of breast cancer

AND

2 Breast cancer is inoperable

AND

3 Used for palliative treatment

AND

4 Female patient	
Notes	*Per the American Geriatrics Society 2012 Beers Criteria Update, testosterone should be avoided in patients greater than or equal to 65 years of age unless indicated for moderate to severe hypogonadism [G]

Product Name: Generic testosterone enanthate*, Testopel*, Testosterone implant pellets*

Diagnosis	Delayed puberty [A]
Approval Length	6 Month
Guideline Type	Prior Authorization
Approval Criteria **1** Diagnosis of delayed puberty [B] **AND** **2** Male patient	
Notes	*Per the American Geriatrics Society 2012 Beers Criteria Update, testosterone should be avoided in patients greater than or equal to 65 years of age unless indicated for moderate to severe hypogonadism [G]

3 . Endnotes

A. An X-ray of the hand and wrist to determine bone age should be taken every 6 months to assess the effect of treatment on epiphyseal centers. [1, 3]
B. Delayed puberty is defined as the lack of the initial signs of sexual maturation by an age that is more than 2-2.5 standard deviations above the mean for the population (traditionally, the age of 14 years in boys and 13 years in girls). In most cases, delayed puberty is not due to an underlying pathology, but instead represents an extreme end of the normal spectrum of pubertal timing, a developmental pattern referred to as constitutional delay of growth and puberty (CDGP). CDGP is the most common cause of delayed puberty in both sexes, but it can be diagnosed only after underlying conditions have been ruled out. Management of CDGP may involve expectant observation or therapy with low-dose sex steroids. [6]
C. Initial authorization of 6 months, and reauthorization of 12 months is based on the Endocrine Society's Clinical Practice Guideline's recommendation to monitor testosterone level 3 to 6 months after initiation of testosterone therapy, and then annually to assess whether symptoms have responded to treatment and whether the patient is suffering from any adverse effects. [5]
D. For injectable testosterone enanthate or cypionate, serum testosterone levels should be measured midway between injections. If testosteorne is > 700 ng/dL (24.5 nmol/L) or < 400 ng/dL (14.1 nmol/L), dose or frequency should be adjusted. For replacement therapy in male hypogonadism, the suggested dosage for testosterone enanthate or cypionate is 50 to 400 mg intramuscularly every 2 to 4 weeks. [2, 3, 5]
E. For testosterone pellets, serum testosterone levels should be measured at the end of the dosing interval. The dosage guideline for testosterone pellets for replacement therapy in androgen-deficient males is 150 mg to 450 mg subcutaneously every 3 to 6 months. [1, 5]
F. For testosterone undecanoate, serum testosterone levels were measured after the third injection (at steady state) in pivotal trials. The suggested dosage for testosterone undecanoate for replacement therapy in male hypogonadism is 750 mg injected intramuscularly, followed by 750 mg injected after 4 weeks, then 750 mg injected every 10 weeks thereafter. [7]
G. Testosterone is included on the 2012 American Geriatrics Socity (AGS) Beers Criteria list of inappropriate medications in older adults (greater than or equal to 65 years old). [11]

4 . References

1. Testopel Prescribing Information. Slate Pharma. May 2015.
2. Depo-Testosterone Prescribing information. Pfizer. April 2015.
3. Testosterone Enanthate Prescribing Information. Indevus Pharmaceutical. May 2015.
4. AACE Hypoganadism Task Force. American Association of Clinical Endocrinologist (AACE) medical guidelines for Clinical Practices for the Evaluation and Treatment of hypogonadism in adult male patients 2002 update. Endocr Practice 2002;8(6)439-56.
5. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM. Testosterone therapy in adult men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2010; 95(6): 2536-2559.
6. Palmert MR, Dunkel L. Clinical practice. Delayed puberty. N Engl J Med. 2012; 2;366(5):443-53.

7. Aveed Prescribing Information. Endo Pharmaceuticals Solutions Inc. May 2015.
8. DRUGDEX [Internet database]. Greenwood Village, Colo: Thomson MICROMEDEX, updated periodically. Accessed September 20, 2015.
9. Hembree, Wylie C, et al. "Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline." The Journal of clinical endocrinology and metabolism 94.9 (2009):3132-3154.
10. Testone CIK Prescribing Information. Asclemed USA, Inc. December 2014.
11. American Geriatrics Society Updated Beers Criteria for potentially inappropriate medication use in older adults (2012). Available at: www.americangeriatrics.org/files/documents/beers/2012BeersCriteria_JAGS.pdf. Accessed October 5, 2015.
12. Coleman E, Bockting W, Botzer M, et al. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, version 7. International Journal of Transgenderism. 13:165-232, 2011.

Prior Authorization Guideline

GL-17121 Thalomid (thalidomide)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/3/2016

Technician Note :

P&T Approval Date: 5/22/2007; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Thalomid (thalidomide)

Indications

Erythema Nodosum Leprosum (ENL)

Indicated for the acute treatment of the cutaneous manifestations of moderate to severe ENL. Is not indicated as monotherapy for such ENL treatment in the presence of moderate to severe neuritis. Is also indicated as a maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence.

Newly Diagnosed Multiple Myeloma

In combination with dexamethasone is indicated for the treatment of patients with newly diagnosed multiple myeloma. The effectiveness of Thalomid is based on response rates. There are no controlled trials demonstrating a clinical benefit, such as an improvement in survival.

Off Label Uses

Non-FDA approved indications

Has been used in several proposed non-FDA approved indications: 1. Advanced multiple myeloma [2, 3] 2. Treatment of Waldenstrom's Macroglobulinemia (lymphoplasmacytic lymphoma) [2, 3, 38] 3. Aphthous stomatitis or ulcers[2, 3, 34] 4. Crohn's disease [2, 3] 5. Graft-versus-host disease [2, 3] 6. Glioblastoma multiforme [44] 7. Wasting syndrome associated with autoimmune deficiency syndrome (AIDS) [2, 3, 35-37]

2 . Criteria

Product Name: Thalomid

Diagnosis	Erythema Nodosum Leprosum (ENL)
Approval Length	12 months [1, 40]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderate to severe erythema nodosum leprosum (ENL) with cutaneous manifestations [1]

Product Name: Thalomid

Diagnosis	Erythema Nodosum Leprosum (ENL)
Approval Length	12 months [1, 40]

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Thalomid therapy

Product Name: Thalomid

Diagnosis	Multiple Myeloma
Approval Length	12 months [1, 4]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple myeloma [1, 40]

AND

2 Used in combination with dexamethasone, unless the patient has an intolerance to steroids

AND

3 Prescribed by or in consultation with an oncologist/hematologist

Product Name: Thalomid

Diagnosis	Multiple Myeloma
Approval Length	12 months [1, 4]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Thalomid therapy

3 . References

1. Thalomid Prescribing Information. Celgene Corporation, February 2013.
2. McEvoy GK, ed. AHFS Drug Information 2009. Bethesda, MD: American Society of Health-System Pharmacists; 2009.
3. DRUGDEX System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed May 22, 2013.
4. National Comprehensive Cancer Network. Practice Guidelines in Oncology: Multiple Myeloma. Version.2.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed May 30, 2013.
5. Weber D, Rankin K, Gavino M, Delasalle, Alexanian R. Thalidomide alone or with dexamethasone for previously untreated multiple myeloma. J Clin Oncol 2003;21:16-19.
6. Wang M, Weber Dm, Delasalle K, Alexanian R. Thalidomide-Dexamethasone as primary therapy for advanced multiple myeloma. Am J Hematol. 2005;79:194-197.
7. Rajkumar SV, Blood E, Vesole B, Fonseca R, Greipp PR. Phase III clinical trial of thalidomide plus dexamethasone compared with dexamethasone alone in newly diagnosed multiple myeloma: a clinical trial coordinated by the Eastern Cooperative Oncology Group. J Clin Oncol. 2006;24:431-436.
8. Kumar S, Rajkumar SV. Thalomid and lenalidomide in the treatment of multiple myeloma. Euro J Cancer. 2006;42:1612-1622.

9. Palumbo A, Bringhen S, Caravita T, et al. Oral melphalan and prednisone chemotherapy plus thalidomide compared with melphalan and prednisone alone in elderly patients with multiple myeloma: randomized controlled trial. Lancet. 2006;367:825-831.
10. Singhal S, Mehta J, Desikan R, et al. Antitumor activity of thalidomide in refractory multiple myeloma. N Engl J Med. 1999;341:1565-1572.
11. Barlogie B, Tricot G, Anaisse E, et al. Thalidmomide and hematopoietic cell transplant in multiple myeloma. N Eng J Med. 2006;354:1021-1030.
12. Mehta P, Gian VG, Smith SP, Beltz SE, Wingard JR. Thalidomide is not effective for acute graft versus host disease. Blood. 1997; 90: Abstract No. 4423.
13. Mehta P, Kedar A, Graham-Pole J, Skoda-Smith S, Winckler K. Thalidomide in children undergoing bone marrow transplantation: series at a single institution and review of the literature. Pediatrics.1999;103:44.
14. Kulkarni S, Powles R, Sirohi B, et al. Thalidomide after allogeneic haematopoietic stem cell transplantation: activity in chronic but not in acute graft-versus-host disease. Bone Marrow Transpl. 2003;32:165-170.
15. Chao NJ, Parker PM, Niland JC, et al. Paradoxical effect of thalidomide prophylaxis on chronic graft-versus-host disease. Biol Blood Marrow Transpl. 1996;2:86-92.
16. Arora M, Wagner JF, Davies SM, et al. Randomized clinical trial of Thalidomide, cyclosporine, and prednisone versus cyclosporine and prednisone as initial therapy for chronic graft-versus-host disease. Biol Blood Marrow Transp. 2001;7:265-273.
17. Koc S, Leisenring W, Flowers MED, et al. Thalidomide for treatment of patients with chronic graft-versus-host-disease. Blood. 2000;96:3995-3996.
18. Glass J, Gruber ML, Nirenberg A. Phase I/II study of carboplatin and Thalomid in recurrent glioblastoma multiforme. The society of clinical oncology 35th annual meeting, Proceedings of ASCO Altanta Georgia, May 1999. Abstract No. 551.
19. Fine HA, Wen PY, Maher EA , et al. Phase II trial of thalidomide and Carmustine for patients with recurrent high grade gliomas. J Clin Oncol. 2003;21:2299-2304.
20. National Comprehensive Cancer Network. Practice Guidelines in Oncology: Kidney Cancer http://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Version 2.2012. Accessed May 30, 2012.
21. Escudier B, Lassau N, Couanet D, et al. Phase II trial of thalidomide in renal cell carcinoma. Annal Oncol. 2002;13:1029-35.
22. Minor DR, Monroe D, Damico LA, et al. A phase II study of thalidomide in advanced metastatic renal cell carcinoma. Invest New Drugs. 2002;20:389-93.
23. Hernberg M, Virkkunen P, Bono Petri, et al. Interferon alfa-2b three times daily and thalidomide in the treatment of metastatic renal cell carcinoma. J Clin Oncol. 2003;21:3770-3776.
24. Clark PE, Hall MC, Miller A, et al. Phase II trial of combination interferon-alpha and thalidomide as first-line therapy in metastatic renal cell carcinoma. Urology. 2004;63:1061-5.
25. Jacobsen JM, Spritzler J, Fox L, et al. Thalidomide for the treatment of esophageal aphthous ulcers in patients with human immunodeficiency virus infection. J Infectious Dis. 1999;180:61-67.
26. Grinspan D, Blanco GF, Aguero S. Treatment of apthae with Thalidomide. J Am Acad Dermatol. 1989:20:1060-1063.
27. Eggiman P, Chave JP, Glauser MP. Thalidomide for recurrent aphthous ulcerations in HIV-infected patients: a prospective, multicenter, double-blinded controlled study. ICCAC. 1994;N33.
28. University of Texas at Austin, School of Nursing, Family Nurse Practitioner Program. Recommendations for the diagnosis and management of recurrent aphthous stomatitis. Austin (TX): University of Texas at Austin, School of Nursing; 2003 May Available at:

http://www.guideline.gov/summary/summary.aspx?doc_id=4368&nbr=003290&string= Accessed March 7, 2006.
29. Griepp PR. Miguel JS, Durie BGM, et al. International staging system for multiple myeloma. J Clinical Oncol. 2005;23:3412-3420.
30. Richardson P. Management of relapsed/refractory myeloma patient: strategies incorporating lenalidomide. Semin Hematol. 2005;42(Suppl 4):S9-15.
31. Ferrara JLM. 2000. Graft-versus-host disease and graft-versus leukemia effect. In: Hoffman R, Benz JB, Shattil SJ, et al. Hematology: Basic Principles and Practice. 3rd Ed. Philadelphia, PA: Churchill Livingston;1659-1671.
32. Vose JM, Kessinger A, Bishop MR, et al. Bone marrow transplantation. In: Abeloff MD, Armitage JO, Licter AS, Niederhuber JE, editors. Clinical Oncology. 2nd Ed. Philadelphia, PA: Churchill Livingstone; 482-493.
33. Hutton KP, Rodgers RS. Recurrent aphthous stomatitis. Dermatologic Clinics. 1987;5:761-768.
34. Scully C. Aphthous ulceration. New Engl J Med. 2006;355:165-72.
35. Polsky B, Kotler D, Steinhart C. Treatment guidelines for HIV-associated wasting. HIV Clin Trials. 2004;5(1):50-61.
36. Federal Bureau of Prisons. Management of HIV. Clinical Practice Guidelines. 2006. Available at: http://www.bop.gov/news/PDFs/hiv.pdf. Accessed March 29, 2010.
37. Reyes-Teran G, Sierra-Madero JG, Martinez del Cerro V, et al. Effects of thalidomide on HIV-associated wasting syndrome: a randomized, double-blind, placebo-controlled clinical trial. AIDS. 1996;10:150107.
38. National Comprehensive Cancer Network. Practice Guidelines in Oncology: Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version.1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed on May 30, 2012.
39. Facts & Comparisons e-answers. Facts & Comparisons Web Site. Available at http://online.factsandcomparisons.com/MonoDisp.aspx?monoID=fandc-hcp12424&quick=714216%7c5&search=714216%7c5&isstemmed=True&fromTop=true#fandc-hcp12424.unlab-dose-section.6. Accessed June 1, 2013.
40. Scollard D, Stryjewska B. Treatment and prevention of leprosy. UpToDate Web Site. Available at www.uptodate.com. Accessed May 30, 2013.
41. Plamondon S, Ng SC, and Kamm MA. Thalidomide in luminal and fistulizing Crohn's disease resistant to standard therapies. Aliment Pharmacol Ther. 2007 Mar 1;25(5):557-67.
42. Sabate JM, Villarejo J, Lemann M, et al. An open-label study of thalidomide for maintenance therapy in responders to infliximab in chronically active and fistulizing refractory Crohn's disease. Aliment Pharmacol Ther. 2002 Jun;16(6):1117-24.
43. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed May 30, 2013.

Prior Authorization Guideline

GL-15712 Thyrogen (thyrotropin alfa for injection)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 3/26/2016

Technician Note :

P&T Approval Date: 1/19/2001; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Thyrogen (thyrotropin alfa for injection)

Indications

Thyroid cancer

Indicated for: 1. Use as an adjunctive diagnostic tool for serum thyroglobulin (Tg) testing with or without radioiodine imaging in the follow-up of patients with well-differentiated thyroid cancer. 2. Use as an adjunctive treatment for radioiodine ablation of thyroid tissue remnants in patients who have undergone a near-total or total thyroidectomy for well-differentiated thyroid cancer and who do not have evidence of metastatic thyroid cancer.

Potential Clinical Uses [1, A]

1. Tg testing may be used in patients with an undetectable Tg on thyroid hormone suppressive therapy to exclude the diagnosis of residual or recurrent thyroid cancer. 2. Treatment may be used in combination with radioiodine to ablate thyroid remnants following total thyroidectomy in patients without evidence of metastatic disease. 3. Testing may be used in patients requiring serum Tg testing and radioiodine imaging who are unwilling to undergo thyroid hormone withdrawal testing and whose treating physician believes that use of a less sensitive test is justified. 4. Testing may be used in patients who are either unable to mount an adequate endogenous TSH response to thyroid hormone withdrawal or in whom withdrawal is medically contraindicated.

2 . Criteria

Product Name: Thyrogen

Approval Length	1 course of therapy
Guideline Type	Prior Authorization

Approval Criteria

1 Patient requires one of the following:

- Blood Thyroglobulin (Tg) testing
- Radioiodine ablation of remnant thyroid tissue after a thyroidectomy

AND

2 One of the following:

2.1 Patient is unable to tolerate thyroid hormone withdrawal (ie, intolerable hypothyroid symptoms) [1,2]

OR

2.2 Thyroid hormone withdrawal is medically contraindicated (ie, exacerbation of comorbid conditions) [1,2]

OR

2.3 Patient has inadequate thyroid stimulating hormone (TSH) response to thyroid hormone withdrawal [1]

OR

2.4 Patient has an undetectable Tg on thyroid hormone suppressive therapy, to exclude the diagnosis of residual or recurrent thyroid cancer [1]

3 . Endnotes

A. Considerations in the Use of Thyrogen: [1] 1. Even when Thyrogen-stimulated Tg testing is performed in combination with radioiodine imaging, there remains a meaningful risk of missing a diagnosis of thyroid cancer or of underestimating the extent of disease. Therefore, thyroid hormone withdrawal Tg testing with radioiodine imaging remains the standard diagnostic modality to assess the presence, location, and extent of thyroid cancer. 2. Although Thyrogen appeared non-inferior to thyroid hormone withholding in a study of postsurgical thyroid remnant ablation, long-term clinical outcome data are limited. Due to the relatively small clinical experience with Thyrogen in remnant ablation, it is not possible to conclude whether long-term thyroid cancer outcomes would be equivalent after use of Thyrogen or use of thyroid hormone withholding for TSH elevation prior to remnant ablation. 3. Clinicians employ a wide range of 131I activities to achieve remnant ablation in patients who have been prepared by withholding of thyroid hormone. The primary study of Thyrogen for remnant ablation employed 100 mCi ± 10% in all patients. Data are inadequate to determine if a lower dose of radioiodine would be effective when Thyrogen is used as an adjunct to radioiodine in postsurgical thyroid remnant ablation. 4. Thyrogen Tg levels are generally lower than, and do not correlate

with Tg levels after thyroid hormone withdrawal. 5. A newly detectable Tg level or a Tg level rising over time after Thyrogen, or a high index of suspicion of metastatic disease, even in the setting of a negative or low-stage Thyrogen radioiodine scan, should prompt further evaluation such as thyroid hormone withdrawal to definitively establish the location and extent of thyroid cancer. On the other hand, none of the 31 patients studied with undetectable Thyrogen Tg levels (< 2.5 ng/mL) had metastatic disease. Therefore, an undetectable Thyrogen Tg level suggests the absence of clinically significant disease. 6. The decisions whether to perform a Thyrogen radioiodine scan in conjunction with a Thyrogen serum Tg test and whether and when to withdraw a patient from thyroid hormone are complex. Pertinent factors in these decisions include the sensitivity of the Tg assay used, the Thyrogen Tg level obtained, and the index of suspicion of recurrent or persistent local or metastatic disease. In the clinical trials, combination Tg and scan testing did enhance the diagnostic accuracy of Thyrogen in some cases. 7. The signs and symptoms of hypothyroidism which accompany thyroid hormone withdrawal are avoided with Thyrogen.

4 . References

1. Thyrogen Package Insert, Genzyme Corporation, March 2014.
2. Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association Management Guidelines. For Patients with Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2009;19 (11):1167-1214.

Prior Authorization Guideline

GL-17306 Tykerb (lapatinib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 5/22/2007; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Tykerb (lapatinib)

Indications

Metastatic breast cancer

(1) In combination with Xeloda (capecitabine), indicated for the treatment of patients with advanced or metastatic breast cancer whose tumors over-express HER2 and who have received prior therapy including an anthracycline, a taxane, and Herceptin (trastuzumab); (2) In combination with Femara (letrozole), indicated for the treatment of postmenopausal women with hormone receptor positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated. Tykerb in combination with an aromatase inhibitor has not

been compared to a trastuzumab-containing chemotherapy regimen for the treatment of metastatic breast cancer.

Off Label Uses

HER2-positive Breast Cancer [5, 6, 7]

Used for the first-line treatment of HER2-positive locally-advanced or metastatic breast cancer.

2 . Criteria

Product Name: Tykerb

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of HER2-positive metastatic or recurrent breast cancer [2-3, 5-7]

AND

2 Used in combination with one of the following: [3]

- Herceptin (trastuzumab)
- Xeloda (capecitabine)
- Aromatase inhibitors [e.g., Aromasin (exemestane), Femara (letrozole), Arimedex (anastrazole)]

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Tykerb

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization
Approval Criteria **1** Patient does not show evidence of progressive disease	

3 . References

1. Tykerb Prescribing Information. GlaxoSmithKline, December 2012.
2. Geyer CE, Forster J, Lindquist D, et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. N Engl J Med. 2006;355(26):2733-2743.
3. National Comprehensive Cancer Network. Clinical practice guidelines in oncology: breast cancer. v. 3.2013. Available at: http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf. Accessed June 5, 2013.
4. The American Joint Committee on Cancer (AJCC) TNM system, 2010. Available at: http://www.springer.com/medicine/surgery/cancer+staging?SGWID=0-40654-0-0-0 March 24, 2010.
5. DRUGDEX System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed June 5, 2013.
6. Moy B, Goss PE. Lapatinib: current status and future directions in breast cancer. Oncologist. 2006;11:1047-57.

7. Gomez H, Doval D, Chavez M, et al. Efficacy and safety of lapatinib as first-line therapy for ErbB2-amplified locally advanced or metastatic breast cancer. J Clin Oncol. 2008 May 5 [Epub ahead of print].

Prior Authorization Guideline

GL-30916 Tysabri (natalizumab)

Formulary OptumRx SP

Formulary Note

Approval Date 8/24/2016

Revision Date 8/24/2016

Technician Note :

P&T Approval Date: 11/20/2000; P&T Revision Date: 8/18/2016 **Effective 9/15/2016**

1 . Indications

Drug Name: Tysabri (natalizumab)

Indications

Multiple Sclerosis (MS) Indicated as monotherapy for the treatment of patients with relapsing forms of MS to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations. The efficacy of Tysabri beyond two years is unknown. Because Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability, Tysabri is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate MS therapy. Safety and efficacy in patients with chronic progressive multiple

sclerosis have not been studied.

Crohnâ€™s Disease (CD) Indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active CD with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-alpha. In CD, Tysabri should not be used in combination with immunosuppressants (eg, 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-alpha.

2 . Criteria

Product Name: Tysabri

Diagnosis	Multiple Sclerosis (MS)
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of a relapsing form of multiple sclerosis (MS) (e.g., relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS with relapses) [C]

AND

2 History of failure, contraindication, or intolerance to one of the following:

- Aubagio (teriflunomide)*
- Avonex (interferon beta-1a)*
- Betaseron (interferon beta-1b)*
- Copaxone (glatiramer acetate)*
- Extavia (interferon beta-1b)*
- Gilenya (fingolimod)*

- Glatopa (glatiramer acetate)*
- Plegridy (peginterferon beta-1a)*
- Rebif (interferon beta-1a)*
- Tecfidera (dimethyl fumarate)*

AND

3 Not used in combination with another disease-modifying therapy for MS [e.g., Aubagio (teriflunomide), Avonex (interferon beta-1a), Betaseron (interferon beta-1b), Copaxone (glatiramer acetate), Extavia (interferon beta-1b), Gilenya (fingolimod), Glatopa (glatiramer acetate), Lemtrada (alemtuzumab), Plegridy (peginterferon beta-1a), Rebif (interferon beta-1a), Tecfidera (dimethyl fumarate)] [A]

Notes	*These products may require Prior Authorization.

Product Name: Tysabri

Diagnosis	Crohnâ€™s Disease (CD)
Approval Length	3 Months [E]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderate to severe Crohn's disease

AND

2 Crohn's disease has evidence of inflammation (e.g., elevated C-reactive protein [CRP], elevated erythrocyte sedimentation rate, presence of fecal leukocytes)

AND

3 History of inadequate response or intolerance to one of the following conventional therapies:

- corticosteroids
- 6-mercaptopurine (6-MP [Purinethol])
- azathioprine (Imuran)
- methotrexate
- aminosalicylates (e.g., sulfasalazine, mesalamine, olsalazine)

AND

4 History of inadequate response or intolerance to a tumor necrosis factor (TNF)-inhibitor (e.g., Cimzia [certolizumab pegol], Humira [adalimumab], Remicade [infliximab])

AND

5 Not used in combination with an immunosuppressant (e.g., 6-MP, azathioprine, cyclosporine, or methotrexate) [B, D]

AND

6 Not used in combination with a TNF-inhibitor (e.g., Enbrel [etanercept], Humira [adalimumab], or Remicade [infliximab]) [B, D]

Product Name: Tysabri

Diagnosis	Crohnâ€™s Disease (CD)
Approval Length	12 Month

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response (e.g., improved disease activity index) to Tysabri therapy

AND

2 Not used in combination with an immunosuppressant (e.g., 6-MP, azathioprine, cyclosporine, or methotrexate) [B, D]

AND

3 Not used in combination with a TNF-inhibitor (e.g., Enbrel [etanercept], Humira [adalimumab], or Remicade [infliximab]) [B, D]

3 . Endnotes

A. There is no evidence to support a washout period following treatment with interferon beta, glatiramer acetate, or corticosteroids. In patients who have received prior immunosuppressive therapy with azathioprine, mycophenolate mofetil, cyclophosphamide, mitoxantrone, and methotrexate, a 6-month washout period is

recommended. For patients on immunosuppressive treatment for an extended period of time, a longer washout period should be considered. Patients treated with long-acting agents (i.e., alemtuzumab, cladribine, mitoxantrone, rituximab) may require a washout period of 1 year or longer. [9]

B. To minimize the risk of progressive multifocal leukoencephalopathy, natalizumab must be administered as a monothreapy without concomitant immunosuppressive therapy. Aminosalicylates may be continued during treatment with Tysabri. [1, 10]
C. Of the four disease courses of MS, relapse-remitting MS (RRMS) is characterized primarily by relapse, while progressive-relapsing MS (PRMS) and secondary-progressive MS (SPMS) have both relapsing and progressive characteristics. Most patients with RRMS eventually develop SPMS. As a person transitions from RRMS to SPMS, the disease begins to worsen more steadily, with or without occasional relapses, slight remissions, or plateaus. As long as the patient continues to have relapses, the SPMS course is considered to be both progressive and relapsing. [12]
D. In the postmarketing setting, additional cases of PML have been reported in multiple sclerosis and Crohnâ€™s disease patients who were receiving no concomitant immunomodulatory therapy. Three factors that are known to increase the risk of PML in TYSABRI-treated patients have been identified: 1) Longer treatment duration, especially beyond 2 years. There is limited experience in patients who have received more than 4 years of TYSABRI treatment. 2) Prior treatment with an immunosuppressant (e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil). 3) The presence of anti-JCV antibodies. Patients who are anti-JCV antibody positive have a higher risk for developing PML. [1]
E. In CD, discontinue Tysabri in patients that have not experienced therapeutic benefit by 12 weeks of induction therapy, and in patients that cannot discontinue chronic concomitant steroids within six months of starting therapy. [1]

4 . References

1. Tysabri Prescribing Information, Biogen Idec/Elan, May 2016.
2. Polman CH, O'Connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. N Engl J Med 2006;354:899-910.
3. Rudick RA, Stuart WH, Calabresi PA et al. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. N Engl J Med 2006; 354:911-23.
4. MacDonald JK, McDonald JWD, Natalizumab for induction of remission in Crohn's disease. Available at: http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD006097/frame.html. Accessed February 26, 2008.
5. Sandborn WJ, Colombel JF, Enns R, et al. Natalizumab induction and maintenance therapy for Crohn's disease. N Engl J Med. 2005;353(18):1912-25
6. Targan SR, Feagan BG, Fedorak RN, et al. Natalizumab for the treatment of active Crohn's disease: results of the ENCORE Trial. Gastroenterology. 2007;132(5):1672-83.
7. Goodin DS, Frohman EM, Garmany, Jr. GP, et al. Disease modifying therapies in multiple sclerosis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for clinical practice guidelines. Neurology 2002; 58:169-78.
8. Lichtenstein GR, Abreu MT, Cohen R, Tremaine W. American Gastroenterological Association Institute medical position statement on corticosteroids, immunomodulators, and infliximab in inflammatory bowel disease. Gastroenterology 2006 Mar;130(3):935-9.

9. Colyle PK, Foley JF, Fox EJ, Jeffery DR, Munschauer FE, Tornatore C. Best practice recommendations for the selection and management of patients with multiple sclerosis receiving natalizumab therapy. Mult Scler. 2009;15:S26-S36.
10. Lichtenstein GR, Hanauer SB, Sandborn WJ, and The Practice Parameters Committee of the American College of Gastroenterology. Management of Crohnâ€™s disease in adults. Am J Gastroenterol. 2009;104:465-483.
11. Goodin DS, Cohen BA, Oâ€™Connor PO, Kappos L, Stevens JC. Assessment: the use of natalizumab (Tysabri) for the treatment of multiple sclerosis (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008;71:766-773.
12. National Multiple Sclerosis Society. About MS: for people with relapsing MS. National Multiple Sclerosis Society. Available at: http://www.nationalmssociety.org/about-multiple-sclerosis/relapsing-ms/index.aspx. Accessed July 25, 2016.
13. FDA Drug Safety Communication: New risk factor for progressive multifocal leukoencephalopathy (PML) associated with Tysabri (natalizumab). January 20, 2012. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm288186.htm. Accessed: July 25, 2016.

Prior Authorization Guideline

GL-17443 Valchlor (mechlorethamine gel)

Formulary OptumRx SP

Formulary Note

Approval Date 2/18/2014

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 2/18/2014; P&T Revision Date: 2/25/2016; ** Effective 7/1/2016 **

1 . Indications

Drug Name: Valchlor (mechlorethamine gel)

Indications

Mycosis fungoides-type cutaneous T-cell lymphoma (MF-CTCL)

Indicated for the topical treatment of Stage IA and IB mycosis fungoides-type cutaneous T-cell lymphoma in patients who have received prior skin-directed therapy.

2 . Criteria

Product Name: Valchlor

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following diagnoses:

- Stage IA mycosis fungoides-type cutaneous T-cell lymphoma (MF-CTCL)
- Stage IB mycosis fungoides-type cutaneous T-cell lymphoma (MF-CTCL)

AND

2 Patient has received at least one prior skin-directed therapy [e.g., topical corticosteroids, phototherapy, bexarotene topical gel (Targretin® topical gel), topical nitrogen mustard, etc.]

AND

3 Prescribed by or in consultation with an oncologist or dermatologist

Product Name: Valchlor

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Valchlor therapy

3 . References

1. Valchlor Prescribing Information, Actelion Pharmaceuticals US, Inc., South San Francisco, CA, September 2013.
2. The NCCN Drugs and Biologics Compendium. Available at http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed January 29, 2014.
3. Lessin SR, Duvic M, Guitart J, et al. Topical chemotherapy in cutaneous T-cell lymphoma: positive results of a randomized, controlled, multicenter trial testing the efficacy and safety of a novel mechlorethamine, 0.02%, gel in mycosis fungoides. JAMA Dermatol. 2013 Jan;149(1):25-32.

Prior Authorization Guideline

GL-15682 Velcade (bortezomib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 4/21/2016

Technician Note :

P&T Approval Date: 10/2/2004; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Velcade (bortezomib)

Indications

Multiple Myeloma

Indicated for the treatment of patients with multiple myeloma

Mantle Cell Lymphoma

Indicated for the treatment of patients with mantle cell lymphoma

2 . Criteria

Product Name: Velcade

Diagnosis	Multiple Myeloma
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of multiple myeloma [1,5]

AND

2 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Velcade

Diagnosis	Mantle Cell Lymphoma
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of mantle cell lymphoma [1,3,4,6]

AND

2 Prescribed by or in consultation with a hematologist/oncologist

3 . References

1. Velcade Prescribing Information. Millennium Pharmaceuticals, Inc., October 2014.
2. Richardson PG, Sonneveld P, Schuster MW, et al. Assessment of Proteasome Inhibition for Extending Remissions (APEX) Investigators. Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. N Engl J Med. 2005 Jun 16;352(24):2487-98.
3. National Cancer Institute. Adult Non-Hodgkin Lymphoma Treatment (PDQ). Available at: http://www.cancer.gov/cancertopics/pdq/treatment/adult-non-hodgkins/healthprofessional. Accessed January 11, 2015.
4. Fisher RI, Bernstein SH, Kahl BS, et al. Multicenter phase II study of bortezomib in patients with relapsed or refractory mantle cell lymphoma. J Clin Oncol.2006;24(30):4867-74.
5. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Multiple Myeloma, Version 2.2015. Available at: http://www.nccn.org/professionals/physician_gls/PDF/myeloma.pdf. Accessed January 11, 2015.
6. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Non-Hodgkin's Lymphomas, Version 1.2015. Available at: http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf. Accessed January 11, 2015.

Prior Authorization Guideline

GL-17263 Vimizim (elosulfase alfa)

Formulary OptumRx SP

Formulary Note

Approval Date 5/27/2016

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 06/24/2015; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Vimizim (elosulfase alfa)

Indications

Mucopolysaccharidosis type IVA

Indicated for patients with Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome).

2 . Criteria

Product Name: Vimizim

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome)

3 . References

1. Vimizim prescribing information. BioMarin Pharmaceutical Inc. Novato, CA. February 2014.
2. Clinical Trials.gov NCT01275066. A double-blind study to evaluate the efficacy and safety of BMN 110 in patients with mucopolysaccharidosis IVA (Morquio A Syndrome). Last updated August 2, 2013. Available at: http://www.clinicaltrials.gov/ct2/show/NCT01275066?term=NCT01275066&rank=1. Accessed March 7, 2014.
3. FDA News Release: FDA approves Vimizim to treat rare congenital enzyme disorder. February 2014. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm386008.htm. Accessed March 20, 2014.
4. Hendriksz CJ, Harmatz P, Beck M, et al. Review of clinical presentation and diagnosis of mucopolysaccharidosis IVA. Mol Genet Metab. 2013 Sep-Oct;110(1-2):54-64.

Prior Authorization Guideline

GL-17426 Votrient (pazopanib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 2/16/2010; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Votrient (pazopanib)

Indications

Renal Cell Carcinoma (RCC)

Indicated for the treatment of patients with advanced RCC.

Soft tissue sarcoma (STS)

Indicated for the treatment of patients with advanced soft tissue sarcoma (STS) who have received prior chemotherapy. Limitation of Use: The efficacy of Votrient for the treatment of

patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

2 . Criteria

Product Name: Votrient

Diagnosis	Renal Cell Carcinoma
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of renal cell carcinoma

AND

2 One of the following:

- Disease is advanced
- Disease is metastatic

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Votrient

Diagnosis	Renal Cell Carcinoma
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Votrient therapy

Product Name: Votrient

Diagnosis	Soft tissue sarcoma (STS)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of advanced soft tissue sarcoma (STS) [A, B]

AND

2 Prescribed by or in consultation with an oncologist

Product Name: Votrient

Diagnosis	Soft tissue sarcoma (STS)

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Votrient therapy

3 . Endnotes

A. The efficacy of Votrient for the treatment of patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated. [1]
B. Votrient is an active drug in anthracycline pretreated STS patients with an increase in median PFS of 13 weeks. [3]

4 . References

1. Votrient Prescribing Information. GlaxoSmithKline, June 2014.
2. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Kidney Cancer v.3.2014. Available at: http://www.nccn.org/professionals/physician_gls/PDF/kidney.pdf. Accessed July 15, 2014.
3. PALETTE: a randomized, double-blind, phase III trial of pazopanib versus placebo in patients (pts) with soft-tissue sarcoma (STS) whose disease has progressed during or following prior chemotherapy-An EORTC STBSG Global Network Study (EORTC 62072). Available at: www.asco.org/ascov2/Meetings/Abstracts?&vmview=abst_detail_view&confID=102&abstractID=83283. Accessed April 30, 2012.
4. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Soft Tissue Sarcoma v.2.2014. Available at: http://www.nccn.org/professionals/physician_gls/PDF/sarcoma.pdf. Accessed July 15, 2014.

5. NCCN Drugs & Biologics Compendium. Pazopanib. Available at: http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=350. Accessed on July 15, 2014.

Prior Authorization Guideline

GL-16880 Xalkori (crizotinib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/20/2016

Technician Note :

P&T Approval Date: 11/15/2011; P&T Revision Date: 4/27/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Xalkori (crizotinib)

Indications

Non-small cell lung cancer (NSCLC)

Indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test Indicated for the treatment of patients with metastatic NSCLC whose tumors are ROS1-positive

2 . Criteria

Product Name: Xalkori

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of locally advanced or metastatic (stage IIIB or IV) non-small cell lung cancer (NSCLC)

AND

2 Prescribed by or in consultation with an oncologist

AND

3 One of the following:

3.1 Patient has an anaplastic lymphoma kinase (ALK)-positive tumor as detected with an FDA-approved test or Clinical Laboratory Improvement Amendments-approved facility

OR

3.2 Patient has MET amplification- or ROS1 rearrangements-positive tumor as detected with an FDA-approved test or Clinical Laboratory Improvement Amendments-approved facility

Product Name: Xalkori

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Xalkori therapy

3 . Endnotes

A. According to recently published guidelines, Xalkori (crizotinib) can be used as first-line therapy for NSCLC recurrence or metastasis in patients with ALK-fusion tumors (4,2). Additionally, Xalkori (crizotinib) can be used as second-line treatment, whether as switch maintenance, continuation maintenance, or subsequent treatment. The ASCO guidelines have not been updated to reflect the place in therapy for crizotinib or targeted therapy for ALK gene arrangements (3).
B. Additionally, Xalkori (critozinib) has been found to be effective in patients with MET amplifications and ROS1 rearrangements, exclusive of ALK-mutations (5,6,7)
C. Patients should have a detected mutation using an FDA approved test or Clinical Laboratory Improvement Amendments-approved facility to ensure validity of the results (1,7)

4 . References

1. Xalkori Prescribing Information. Pfizer, March 2016
2. Alberta Provincial Thoracic Tumour Team. Non-small cell lung cancer stage IV. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2013 Nov. 23 p.
3. Azzoli CG, Temin S, Aliff T, et al. 2011 Focused Update of 2009 American Society of Clinical Oncology Clinical Practice Guideline Update on Chemotherapy for Stage IV Non–Small-Cell Lung Cancer. Journal of Clinical Oncology 2011; 29(28): 3825-32.

4. Reck M, Popat S, Reinmut N, et al. Metastatic NSCLC: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. Annals of Onc, August 2014. 25 (Suppl 3): iii27-iii39.
5. Shaw AT, Ou SH, Bang YJ, et al. Crizotinib in ROS1-Rearranged Non-Small-Cell Lung Cancer. N Engl J Med. 2014 Nov 20;371(21):1963-71.
6. Ou SH, Kwak EL, Siwak-Tapp C, et al. Activity of crizotinib (PF02341066), a dual mesenchymal-epithelial transition (MET) and anaplastic lymphoma kinase (ALK) inhibitor, in a non-small cell lung cancer patient with de novo MET amplification. J Thorac Oncol, 6 (2011), pp. 942–946
7. Medical Review Institute of America, Inc. (MRIoA) review of Xalkori. April 16, 2015.

Prior Authorization Guideline

GL-16337 Xenazine (tetrabenazine)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 3/25/2016

Technician Note :

P&T Approval Date: 4/6/2010; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Xenazine (tetrabenazine)

Indications

Chorea associated with Huntington's disease

Indicated for the treatment of chorea associated with Huntington's disease.

Off Label Uses

Hyperkinetic movement disorders in tardive dyskinesia and Tourette's syndrome [5-16]

Has shown effectiveness in the treatment of hyperkinetic movement disorders (hyperkinesias)

characterized by abnormal involuntary movements such as tics (eye blink, shouting obscenities or profanities, etc.) in Tourette's syndrome (TS) and stereotypies in tardive dyskinesia (TD).

2 . Criteria

Product Name: Brand Xenazine, Generic tetrabenazine

Diagnosis	Chorea associated with Huntington's disease
Approval Length	3 months [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chorea in patients with Huntington's disease

AND

2 Prescribed by or in consultation with a neurologist [B]

Product Name: Brand Xenazine, Generic tetrabenazine

Diagnosis	Chorea associated with Huntington's disease
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to therapy

Product Name: Brand Xenazine, Generic tetrabenazine

Diagnosis	Tardive dyskinesia (Off-label)
Approval Length	3 months [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has stereotypies associated with tardive dyskinesia [5, A]

AND

2 Patient is greater than or equal to 18 years of age

AND

3 Prescribed by or in consultation with one of the following:

- Neurologist
- Psychiatrist

Product Name: Brand Xenazine, Generic tetrabenazine

Diagnosis	Tardive dyskinesia (Off-label)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to therapy

Product Name: Brand Xenazine, Generic tetrabenazine

Diagnosis	Tourette's syndrome (Off-label)
Approval Length	3 Months [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient has tics associated with Tourette's syndrome [5]

AND

2 History of failure, contraindication, or intolerance to Haldol (haloperidol)

AND

3 Prescribed by or in consultation with one of the following:

- Neurologist
- Psychiatrist

Product Name: Brand Xenazine, Generic tetrabenazine

Diagnosis	Tourette's syndrome (Off-label)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to therapy

3 . Endnotes

A. Stereotypy refers to involuntary, coordinated, patterned, repetitive, rhythmic, purposeless, ritualistic movements seen in TD and other medical conditions. The term 'TD' is used as a synonym for all the tardive syndromes that cause abnormal movements. Several tardive phenotypes have been described and these include stereotypy, akathisia, dystonia, myoclonus and tremor.
B. Ensures the requirement for proper diagnosing and quantifying an adequate chorea score (total maximal chorea score of greater than or equal to 10 (moderate to severe chorea) from the subscale of the UHDRS. Note that the pivotal trial that established efficacy of tetrabenazine included patients with a total maximal chorea of greater than or equal to 10. [1]

C. Authorization period is based on the pivotal study duration of 12 weeks. [1]

4 . References

1. Xenazine Prescribing Information, Biovail Laboratories International. June 2015.
2. Bonelli RM, Hofmann P. A systemic review of the treatment studies in Huntington's disease since 1990. Expert Opin. Pharmacother. 2007;8(2):141-153.
3. Bonelli RM, Wenning GK. Pharmacological management of Huntington's disease: an evidence-based review. Curr Pharm Des. 2006;12:2701-2720.
4. Huntington Study Group. An open-label study of tetrabenazine as anti-chorea therapy in Huntington disease. In preparation (unpublished study 007).
5. DRUGDEX System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed October 27, 2015.
6. Kenney C, Jankovic J. Tetrabenazine in the treatment of hyperkinetic movement disorders. Expert Rev. Neurotherapeutics. 2006;6(1):7-17.
7. Jankovic J. Treatment of hyperkinetic movement disorder with tetrabenazine: a double-blind crossover study. Ann Neurol. 1982;11:41-47.
8. Marsden CD. Involuntary movements other than Parkinsonism. Proc Roy Soc Med. 1973;66:27-29.
9. Ondo WG, Hanna PA, Jankovic J. Treatment of Tardive Dyskinesia: assessment by randomized videotapes protocol. Am J Psychiatry. 1999;156:1279-1281.
10. Jankovic J, Orman J. Examine therapy of dystonia, chorea, tics, and other dyskinesias. Neurology. 1988;38:391-394.
11. Asher SW, Aminoff MJ. Tetrabenazine and movement disorders. Neurology. 1981;31:1051-1054.
12. Kingston D. Tetrabenazine for involuntary movement disorders. Med J Aust. 1979;1628-630.
13. Sweet RD, Brauun R, Shapiro E, Shapiro AK. Presynaptic catecholamine antagonists as treatment for Tourette syndrome. Effects of alpha methyl para tyrosine and tetrabenazine. Arch Gen Psych. 1974;31:857-861.
14. Pakkenberg H, Fog R. Spontaneous oral dyskinesia: results of treatment with tetrabenazine, pimozide, or both. Arch Neurol. 1974;31:352-353.
15. Kazamatsuri H, Chien C-P, Cole J. Treatment of Tardive Dyskinesia: clinical efficacy of a dopamine-depleting agent, tetrabenazine. Arch Gen Psychiat. 1972;27:95-99.
16. Ondo WG, Jong D, Davis A. Comparison of weight gain in treatments for Tourette syndrome: tetrabenazine vs. neuroleptic drug. J Child Neurol. 2008.23:435-437.
17. Armstrong MJ, Miyasaki JM. Evidence-based guideline: Pharmacologic treatment of chorea in Huntington disease: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2012 Jul 18. [Epub ahead of print]

Prior Authorization Guideline

GL-14630 Xeomin (incobotulinumtoxinA)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 3/1/2016

Technician Note :

P&T Approval Date: 11/14/2011; P&T Revision Date: 2/25/2016 **Effective 3-15-2016**

1 . Indications

Drug Name: Xeomin (incobotulinumtoxinA)

Indications

Cervical Dystonia

Is indicated for the treatment of adults with cervical dystonia to decrease the severity of abnormal head position and neck pain in both botulinum toxin-naïve and previously treated patients.

Blepharospasm

Is indicated for the treatment of adults with blepharospasm who were previously treated with Botox (onabotulinumtoxinA).

Upper Limb Spasticity

Indicated for the treatment of upper limb spasticity in adult patients.

Glabellar Lines*

Is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients. *Note: Use of Xeomin for the improvement in the appearance of glabellar lines is excluded, as this is considered a cosmetic use.

2 . Criteria

Product Name: Xeomin (incobotulinumtoxinA)

Diagnosis	Cervical Dystonia (also known as spasmodic torticollis)
Approval Length	3 months (for 1 dose) [A]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cervical dystonia (also known as spasmodic torticollis) [1]

Product Name: Xeomin (incobotulinumtoxinA)

Diagnosis	Cervical Dystonia (also known as spasmodic torticollis)
Approval Length	3 months (for 1 dose) [A]
Therapy Stage	Reauthorization

Guideline Type	Prior Authorization

Approval Criteria

1 Confirmed improvement in symptoms with initial Xeomin treatment

AND

2 At least 3 months have elapsed since the last treatment with Xeomin [1]

Product Name: Xeomin (incobotulinumtoxinA)

Diagnosis	Blepharospasm
Approval Length	3 months (for 1 dose) [1, B]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of blepharospasm [1]

AND

2 History of previous use of Botox (onabotulinumtoxinA) for the treatment of blepharospasm

Product Name: Xeomin (incobotulinumtoxinA)

Diagnosis	Blepharospasm

Approval Length	3 months (for 1 dose) [1, 7, C]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Confirmed improvement in symptoms with initial Xeomin treatment

AND

2 At least 3 months have elapsed since the last treatment with Xeomin [C]

Product Name: Xeomin (incobotulinumtoxinA)

Diagnosis	Upper Limb Spasticity
Approval Length	3 months (for 1 dose) [1, 6]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of upper limb spasticity [1]

Product Name: Xeomin (incobotulinumtoxinA)

Diagnosis	Upper Limb Spasticity
Approval Length	3 months (for 1 dose) [1, 6, D]

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Confirmed improvement in symptoms with initial Xeomin treatment

AND

2 At least 3 months have elapsed since the last treatment with Xeomin [D]

3 . Endnotes

A. In a randomized, double-blind, active-controlled, parallel group study, 463 patients with a documented stable therapeutic response to Botox as a result of the last two consecutive injection sessions directly prior to trial entry (70 to 300 Units) were included. Patients in the study received IM injections of 70 to 300 Units of Xeomin or Botox, based on the previous two consecutive doses of Botox prior to study entry. [2]
B. The total initial dose of Xeomin in both eyes should not exceed 70 Units (35 Units/eye). [1]
C. The median onset of treatment effect with incobotulinumtoxinA was 4 days (range, 0 to 30 days), time to waning of treatment effect was 6 weeks (range 1 to 15 weeks), and duration of treatment effect was 10.6 weeks (range, 6.1 to 19.1 weeks). [7]
D. The median overall duration of treatment effect reported by patients for all injection intervals was 99 days. [6]

4 . References

1. Xeomin Prescribing Information. Merz Pharmaceuticals, December 2015.
2. Benecke R, Jost WH, Kanovsky P, Ruzicka E, Comes G, Grafe S. A new botulinum toxin type A free of complexing proteins for treatment of cervical dystonia. Neurology. 2005;64:1949-1951.
3. Roggenkamper P, Jost WH, Bihari K, Comes G, Grafe S. Efficacy and safety of a new botulinum toxin type A free of complexing proteins in the treatment of blepharospasm. J Neural Transm. 2006;113:303-312.
4. Simpson DM, Blitzer A, Brashear A, et al. Assessment: botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008;70:1699-1706.
5. Jankovic J, Kenney C, Grafe S, Goertelmeyer R, Comes G. Relationship between various clinical outcome assessments in patients with blepharospasm. Mov Disord. 2009;24:407-413.
6. Kanovsky P, Slawek J, Denes Z, et al: Efficacy and safety of treatment with incobotulinum toxin A (botulinum neurotoxin type A free from complexing proteins; NT 201) in post-stroke upper limb spasticity. J Rehabil Med 2011; 43(6):486-492.
7. Jankovic J, Comella C, Hanschmann A, et al: Efficacy and safety of incobotulinumtoxinA (NT 201, Xeomin) in the treatment of blepharospasm-a randomized trial. Mov Disord 2011; 26(8):1521-1528.

Prior Authorization Guideline

GL-17444 Xgeva (denosumab)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 4/5/201; P&T Revision Date: 2/25/2016; ** Effective 7/1/2016 **

1 . Indications

Drug Name: Xgeva (denosumab)

Indications

Bone metastasis from solid tumors

Indicated for the prevention of skeletal-related events in patients with bone metastases from solid tumors. Limitation of use: Not indicated for the prevention of skeletal-related events in patients with multiple myeloma.

Giant cell tumor of bone

Indicated for the treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity. **Hypercalcemia of malignancy** Indicated for the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

2 . Criteria

Product Name: Xgeva

Diagnosis	Bone metastasis from solid tumors
Approval Length	12 Month [B]
Guideline Type	Prior Authorization
Approval Criteria **1** Diagnosis of solid tumors (e.g., breast cancer, kidney cancer, lung cancer, prostate cancer, thyroid cancer) **AND** **2** Documented evidence of one or more metastatic bone lesions	
Notes	Xgeva is not indicated for the prevention of skeletal-related events in patients with multiple myeloma. Mortality was higher with Xgeva in a subgroup analysis of patients with multiple myeloma. [A]

Product Name: Xgeva

Diagnosis	Giant cell tumor of bone

Approval Length	6 Month [C]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of giant cell tumor of bone

AND

2 One of the following:

2.1 Tumor is unresectable

OR

2.2 Surgical resection is likely to result in severe morbidity

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Xgeva

Diagnosis	Giant cell tumor of bone
Approval Length	6 Month
Therapy Stage	Reauthorization

Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Xgeva therapy [C]

Product Name: Xgeva

Diagnosis	Hypercalcemia of malignancy
Approval Length	2 Month [D]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of hypercalcemia of malignancy

AND

2 History of failure, contraindication, or intolerance to one intravenous bisphosphonate (e.g., Aredia (pamidronate), Zometa (zoledronic acid) [13, 14]

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Xgeva

Diagnosis	Hypercalcemia of malignancy
Approval Length	2 Month [D]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation of positive clinical response to Xgeva therapy

3 . Endnotes

A. In one phase 3, double-blind, double-dummy, randomized controlled trial involving nearly 1800 patients with solid tumors (other than breast or prostate cancer) or multiple myeloma and evidence of bone metastases, mortality was higher with Xgeva in a subgroup analysis of patients with multiple myeloma (hazard ratio: 2.26; 95% CI: 1.13-4.50; n=180). [1, 4, 5]
B. The optimal duration of treatment with Xgeva is not known. [6, 7]
C. Xgeva should be continued until disease progression in responding patients. [12]
D. Median time on the study for the treatment of hypercalcemia of malignancy was 56 days. [13]

4 . References

1. Xgeva Prescribing Information. Amgen, December 2014.
2. Stopeck AT, Lipton A, Body JJ, et al. Denosumab compared with zoledronic acid for the treatment of bone metastases ni patients with advanced breast cancer: a randomized, double-blind study. J Clin Oncol. 2010;28:5132-39.
3. Fizazi K, Carducci MA, Smith MR, et al. Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study. Lancet. 2011;377(9768):813-22.

4. Henry DH, Costa L, Goldwasser F, et al. Randomized, double-blind study of denosumab versus zoledronic acid in the treatment of bone metastases in patients with advanced cancer (excluding breast and prostate cancer) or multiple myeloma. J Clin Oncol. 2011;29(9):1125-32.
5. Lipton A, Fizazi K, Stopeck AT, Henry DH, et al. Superiority of denosumab to zoledronic acid for prevention of skeletal-related events: a combined analysis of 3 pivotal, randomised, phase 3 trials. Eur J Cancer. 2012;48(16):3082-92.
6. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Breast Cancer (Version 1.2015). Available at: www.nccn.org. Accessed March 5, 2015.
7. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Prostate Cancer (Version 1.2015). Available at: www.nccn.org. Accessed March 5, 2015.
8. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer (Version 4.2015). Available at: www.nccn.org. Accessed March 5, 2015.
9. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Thyroid Carcinoma (Version 2.2014). Available at: www.nccn.org. Accessed March 5, 2015.
10. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Kidney Cancer (Version 3.2015). Available at: www.nccn.org. Accessed March 5, 2015.
11. National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium. Available at: www.nccn.org. Accessed March 5, 2015.
12. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Bone Cancer (Version 1.2015). Available at: www.nccn.org. Accessed March 5, 2015.
13. Hu MI, Glezerman IG, Leboulleux S, et al. Denosumab for treatment of hypercalcemia of malignancy. J Clin Endocinol Metab. 2014;99(9):3144-52.
14. Stewart AF. Hypercalcemia associated with cancer. N Engl J Med. 2005; 352(4):379-9.

Prior Authorization Guideline

GL-16890 Xiaflex (collagenase clostridium histolyticum)

Formulary OptumRx SP

Formulary Note

Approval Date 5/26/2016

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Xiaflex (collagenase clostridium histolyticum)

Indications

Dupuytren's Contracture

Indicated for the treatment of adult patients with Dupuytren's contracture with a palpable cord.

Peyronie's Disease

Indicated for the treatment of adult men with Peyronie's disease with a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy.

2 . Criteria

Product Name: Xiaflex

Diagnosis	Dupuytren's contracture
Approval Length	12 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Dupuytren's contracture with a palpable cord

AND

2 Patient has a positive "table top test" (defined as the inability to simultaneously place the affected finger and palm flat against a table top) [A]

AND

3 Patient has a documented contracture of at least 20 degrees flexion for a metacarpophalangeal joint or a proximal interphalangeal joint [B]

AND

4 Patient has a flexion deformity that results in functional limitations

Product Name: Xiaflex

Diagnosis	Peyronie's disease
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Peyronie's disease

AND

2 Patient has a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy [C]

AND

3 The plaques do not involve the penile urethra

AND

4 Patient has a curvature deformity that results in pain (e.g., pain upon erection or intercourse) [C]

Product Name: Xiaflex

Diagnosis	Peyronie’s disease
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Peyronie’s disease

AND

2 Patient has a palpable plaque and curvature deformity of at least 30 degrees at the start of therapy

AND

3 The plaques do not involve the penile urethra

AND

4 Patient has a curvature deformity that results in pain (e.g., pain upon erection or intercourse)

AND

5	Patient has a new plaque that results in a curvature deformity

3 . Endnotes

A. Dupuytren's disease diagnosis can include a table top test to assess the severity of the disease. When a patient is unable to place his or her palm and the affected finger flat on the table, the test can help diagnosis Dupuytren's disease. [1]
B. Dupuytren's disease is associated with joint contracture. Xiaflex was studied in a patient population with joint contracture of at least 20 degrees. Evidence does not support any benefit in patients with joint contracture less than 20 degrees. Our program requires that the patient has a flexion deformity that results in functional limitations to protect against cosmetic use. [1]
C. Peyronie's disease is characterized by a curvature deformity. Xiaflex was studied in a patient population with a curvature deformity of at least 30 degrees. Evidence does not support any benefit in patients with a curvature deformity less than 30 degrees. To prevent cosmetic use, patients must also have a curvature deformity that results in pain. [1]

4 . References

1. Xiaflex prescribing information. Auxilium Pharmaceuticals, Inc. Malvern, PA. October 2014.

Prior Authorization Guideline

GL-30777 Xolair (omalizumab)

Formulary OptumRx SP

Formulary Note

Approval Date 8/24/2016

Revision Date 8/24/2016

Technician Note :

P&T Approval Date: 7/14/2003; P&T Revision Date: 8/18/2016 **Effective 10/1/2016**

1 . Indications

Drug Name: Xolair (omalizumab)

Indications

Allergic Asthma Indicated for patients 6 years of age and older with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. Xolair has been shown to decrease the incidence of asthma exacerbations in these patients. Important Limitations of Use: Not indicated for treatment of other allergic conditions or other forms of urticaria. Not indicated for the relief of acute bronchospasm or status asthmaticus.

Chronic Idiopathic Urticaria Indicated for the treatment of adults and adolescents (12 years of age and above) with chronic idiopathic urticaria who remain symptomatic despite H1 antihistamine treatment. Important Limitations of Use: Not indicated for treatment of other forms of urticaria.

2 . Criteria

Product Name: Xolair

Diagnosis	Allergic Asthma
Approval Length	6 months [B]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of moderate to severe persistent allergic asthma [1, 2]

AND

2 Pretreatment serum immune globulin (Ig)E level between 30 to 700 IU/mL [9]

AND

3 Positive skin test or in vitro reactivity to a perennial aeroallergen [1, D]

AND

4 Symptoms are not adequately controlled on a high-dose inhaled corticosteroid and a long-acting beta2-agonist combination for at least 3 months [A, C]

AND

5 Prescribed by or in consultation with one of the following specialists:

- pulmonologist
- allergist/immunologist

AND

6 Patient has been adherent within a 12 month period and is currently adherent with asthma therapy

Product Name: Xolair

Diagnosis	Chronic Idiopathic Urticaria
Approval Length	3 months [E]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of chronic idiopathic urticaria [1]

AND

2 Persistent symptoms (itching and hives) for at least 4 consecutive weeks despite titrating to an optimal dose with a second generation H1 antihistamine

AND

3 Patient has tried and had an inadequate response or intolerance at least two of the following additional therapies:

- doxepin
- H1 antihistamine
- H2 antagonist
- hydroxyzine
- leukotriene receptor antagonist

AND

4 Prescribed by or in consultation with one of the following:

- allergist/immunologist
- dermatologist

Product Name: Xolair

Diagnosis	Allergic Asthma
Approval Length	6 months [B]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Reduction in number of asthma exacerbations from baseline (ie, asthma exacerbation requiring treatment with systemic corticosteroids or doubling of inhaled corticosteroid [ICS] dose from baseline)

OR

1.2 Improvement in forced expiratory volume in 1 second (FEV1) from baseline

OR

1.3 Decreased use of rescue medications from baseline

Product Name: Xolair

Diagnosis	Chronic Idiopathic Urticaria
Approval Length	6 months [B]
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patientâ€™s disease status has been re-evaluated since the last authorization to confirm the patientâ€™s condition warrants continued treatment

AND

2 Patient has experienced at least one of the following:

- Reduction in itching severity from baseline
- Reduction in the number of hives from baseline

3 . Endnotes

A. The National Asthma Education and Prevention Program recommends the combination of an inhaled glucocorticosteroid and a long-acting beta2-agonist for the treatment of moderate persistent or severe persistent asthma. [2]
B. Clinical studies for allergic asthma evaluated an initial 16-week steroid stable phase in which subjects received omalizumab with a constant dose of inhaled steroids. This 16-week period may not be sufficient amount of time to show reduction in exacerbations. Reauthorization duration reduced because it may not be worthwhile to continue treatment in this sick population with high drug costs. For allergic asthma, initial authorization duration increased from 16 weeks to 6 months and reauthorization reduced from 1 year to 6 months. [4]
C. Demonstration of uncontrolled asthma may include measures of asthma control. [4] Several standardized measures for assessing clinical control of asthma have been developed, which score the goals of treatment as continuous variables and provide numerical values to distinguish different levels of control. Examples of validated instruments are the Asthma Control Questionnaire (ACT), the Asthma Control Test (ACT), the Childhood Asthma Control Test (C-ACT), the Asthma Control Scoring System. [3]
D. Sensitization to a perennial allergen (eg, mite, cat, dog) should be required. [4] Xolair is indicated for adults and adolescents (12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen. [1]
E. For chronic idiopathic urticaria, response observed at 12 weeks (one 24-week trial with data reported at 12 weeks, and one 12-week trial) [1]

4 . References

1. Xolair Prescribing Information. Genentech, Inc., July 2016.
2. National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of

Asthma. National Institutes of Health Publication No.08-5846. Bethesda, MD, 2007. Available at https://www.nhlbi.nih.gov/guidelines/asthma/. Accessed April 18, 2014.
3. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention - revised 2012. Available at www.ginasthma.com/download.asp?intId=411. Accessed April 18, 2014.
4. Per clinical consult with asthma specialist, January 6, 2011.
5. The Milliman Care GuidelinesÂ®, Omalizumab [ACG: A-0315 (AC)]. http://www.careguidelines.com/. Accessed April 18, 2014.
6. Sorkness CA, Wildfire JJ, Calatroni A, et al. Reassessment of omalizumab-dosing strategies and pharmacodynamics in inner-city children and adolescents. J Allergy Clin Immunol Pract. 2013;1(2):163-71.
7. Aguiar R, Silva P, Duarte F, Mendes A, Costa AC, Barbosa MP. Poster 1012: Safety and efficacy of omalizumab in 10 children with asthma and other allergic comorbidities. World Allergy Organization Journal 2014, 7(Suppl 1):P7.
8. National Institute for Health and Care Excellence (NICE). Omalizumab for treating severe persistent allergic asthma (review of technology appraisal guidance 133 and 201). London (UK): National Institute for Health and Care Excellence (NICE); 2013 Apr. 64 p. (Technology appraisal guidance; no. 278). Available at http://www.guideline.gov/content.aspx?f=rss&id=45128. Accessed May 30, 2014.
9. Xolair Solution for Injection. Omalizumab. Annex I. Summary of Product Characteristics. Nuremberg, Germany: Novartis; October 25, 2010. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000606/WC500057298.pdf. Accessed May 30, 2014.
10. Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol. 2014;133(5):1270-7.
11. Maselli DJ, Singh H, Diaz J, Peters JI. Efficacy of omalizumab in asthmatic patients with IgE levels above 700 IU/mL: a retrospective study. Ann Allergy Asthma Immunol. 2013;110(6):457-61.

Prior Authorization Guideline

GL-15831 Xtandi (enzalutamide)

Formulary OptumRx SP

Formulary Note

Approval Date 4/4/2013

Revision Date 3/31/2016

Technician Note :

P&T Approval Date: 11/13/2012; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Xtandi (enzalutamide)

Indications

Metastatic castration-resistant prostate cancer (mCRPC)

Indicated for the treatment of patients with mCRPC.

2 . Criteria

Product Name: Xtandi

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of metastatic, castration-resistant prostate cancer [2, A]

AND

2 Prescribed by or in consultation with one of the following:

- Oncologist
- Urologist

AND

3 One of the following:

3.1 History of failure, contraindication, or intolerance to Zytiga (abiraterone)* [B]

OR

3.2 For continuation of prior Xtandi therapy

Notes	*Cross-resistance is a common phenomenon between Zytiga and Xtandi.

Product Name: Xtandi

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Xtandi therapy

3 . Endnotes

A. Several different terms have been used to denote patients who progress on androgen deprivation therapy (ADT) in spite of castrate levels of testosterone: castration-resistant or castrate-resistant prostate cancer (CRPC), castration-recurrent prostate cancer (CRPC), hormone-refractory prostate cancer (HRPC), and androgen-independent prostate cancer (AIPC). [3]
B. The NCCN guidelines for prostate cancer recommend both Xtandi and Zytiga (category 1); they may be thus considered interchangeable for the treatment of metastatic castration-resistant prostate cancer (mCRPC). [3]

4 . References

1. Xtandi Prescribing Information. Astellas Pharma Inc., September 2014.
2. Scher HI, Fizazi K, Saad F, et al. AFFIRM Investigators. Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med. 2012 Sep 27;367(13):1187-97. Available at: http://www.nejm.org/doi/full/10.1056/NEJMoa1207506. Accessed January 11, 2015.
3. National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology. Prostate Cancer.v.1.2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed January 11, 2015.

Prior Authorization Guideline

GL-17400 Xyrem (sodium oxybate)

Formulary OptumRx SP

Formulary Note

Approval Date 3/13/2013

Revision Date 6/1/2016

Technician Note :

P&T Approval Date: 5/17/2011; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Xyrem (sodium oxybate) oral solution

Indications

Narcolepsy with Cataplexy (i.e., Narcolepsy Type 1)

Indicated for the treatment of cataplexy in narcolepsy. Limitations of Use: Xyrem may only be dispensed to patients enrolled in the Xyrem REMS Program.

Narcolepsy without Cataplexy (i.e., Narcolepsy Type 2)

Indicated for the treatment of excessive daytime sleepiness (EDS) in narcolepsy. Limitations of

Use: Xyrem may only be dispensed to patients enrolled in the Xyrem REMS Program.

2 . Criteria

Product Name: Xyrem

Diagnosis	Narcolepsy with Cataplexy (Narcolepsy Type 1) [2, 3, A-D]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of narcolepsy as confirmed by sleep study (unless the prescriber provides justification confirming that a sleep study would not be feasible)

AND

2 Symptoms of cataplexy are present

AND

3 Symptoms of excessive daytime sleepiness (e.g., irrepressible need to sleep or daytime lapses into sleep) are present

Product Name: Xyrem

Diagnosis	Narcolepsy with Cataplexy (Narcolepsy Type 1)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following:

1.1 Documentation demonstrating a reduction in the frequency of cataplexy attacks associated with Xyrem therapy

OR

1.2 Documentation demonstrating a reduction in symptoms of excessive daytime sleepiness associated with Xyrem therapy

Product Name: Xyrem

Diagnosis	Narcolepsy without Cataplexy (Narcolepsy Type 2) [2, 3, A-C, E]
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of narcolepsy as confirmed by sleep study (unless the prescriber provides justification confirming that a sleep study would not be feasible)

AND

2 Symptoms of cataplexy are absent

AND

3 Symptoms of excessive daytime sleepiness (e.g., irrepressible need to sleep or daytime lapses into sleep) are present

AND

4 History of failure, contraindication, or intolerance to one of the following [2, 3, E]:

- Amphetamine-based stimulant (e.g., amphetamine, dextroamphetamine)
- Methylphenidate-based stimulant

Product Name: Xyrem

Diagnosis	Narcolepsy without Cataplexy (Narcolepsy Type 2)
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Documentation demonstrating a reduction in symptoms of excessive daytime sleepiness associated with Xyrem therapy

3 . Background

Benefit/Coverage/Program Information

Quantity Limit

This product is subject to a standard quantity limit. The quantity limit may vary from the standard limit based upon plan-specific benefit design. Please refer to your benefit materials.

4 . Endnotes

A. International classification of Sleep Disorder (ICSD) diagnostic criteria for narcolepsy with cataplexy (narcolepsy type 1) include: [4, 5, 6] 1. Daily periods of irrepressible need for sleep or daytime lapses into sleep (i.e., excessive daytime sleepiness) for at least 3 months. 2. One or both of the following: cataplexy and a mean sleep latency of less than or equal to 8 minutes and 2 or more sleep onset REM periods (SOREMPs) on a multiple sleep latency test (MSLT) performed using standard techniques (a SOREMP within 15 minutes of sleep onset on the preceding nocturnal polysomnogram may replace 1 of the SOREMPs on the MSLT); or cerebrospinal fluid (CSF) hypocretin-1 concentration is low (less than 110 pg/mL or one-third of the normative values with the same standardized assay). 3. Exclusion of alternative causes of chronic daytime sleepiness by history, physical exam, and polysomnography. Other conditions that cause chronic daytime sleepiness include insufficient sleep, untreated sleep apnea, periodic limb movements of sleep, and idiopathic hypersomnia (chronic sleepiness but without SOREMPs or other evidence of abnormal REM sleep). In addition, the effects of sedating medications should be excluded.

B. International classification of Sleep Disorder (ICSD) diagnostic criteria for narcolepsy without cataplexy (narcolepsy type 2) include: [4, 5, 6] 1. Daily periods of irrepressible need for sleep or daytime lapses into sleep (i.e., excessive daytime sleepiness) for at least 3 months. 2. Cataplexy is absent 3. CSF hypocretin-1 levels, if measured, must not meet the narcolepsy type 1 criterion. 4. A mean sleep latency of less than or equal to 8 minutes and 2 or more sleep onset REM periods (SOREMPs) on a multiple sleep latency test (MSLT) performed using standard techniques (a SOREMP within 15 minutes of sleep onset on the preceding nocturnal polysomnogram may replace 1 of the

SOREMPs on the MSLT). 5. Exclusion of alternative causes of chronic daytime sleepiness by history, physical exam, and polysomnography. Other conditions that cause chronic daytime sleepiness include insufficient sleep, untreated sleep apnea, periodic limb movements of sleep, and idiopathic hypersomnia (chronic sleepiness but without SOREMPs or other evidence of abnormal REM sleep). In addition, the effects of sedating medications should be excluded.

C. Narcolepsy is often misdiagnosed. Treatment can often be given for the wrong reason if the patient has another condition with symptoms of excessive sleepiness. The diagnosis is the most important, and should be the focus in determining appropriate treatment. Both clinical symptoms and sleep study criteria (both daytime and nighttime tests) are needed to guide the diagnosis. [7]
D. Xyrem is very effective and can be considered a first-line treatment for cataplexy in patients with narcolepsy (narcolepsy type 1). Antidepressants have mixed issues. Currently, there are no safety data with antidepressants for the treatment of cataplexy, and tricyclics and SSRIs cause a lot of side effects including anticholinergic effects, sedation, impotence and EKG changes. Xyrem offers the advantage of treating cataplexy, and giving the patient more energy without the side effects compared to antidepressants. [7]
E. Generally modafinil or armodafinil is given first for excessive daytime sleepiness without cataplexy (narcolepsy type 2), followed by on-demand stimulants, then by Xyrem. There are no head-to-head trials with Xyrem, but anecdotal and clinical practice reports find that patients receive a similar response as with modafinil/armodafinil, but not as good as stimulants for excessive daytime sleepiness. [7]

5 . References

1. Xyrem Prescribing Information. Jazz Pharmaceuticals, Inc. April 2015.
2. Morgenthaler TI, Kapur VK, Brown TM, Swick TJ, Alessi C, Aurora N, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin: An American Academy of Sleep Medicine report. Sleep. 2007;30(12):1705-1711.
3. Wise MS, Arand DL, Auger RR, et al. Treatment of narcolepsy and other hypersomnias of central origin: An American Academy of Sleep Medicine report. Sleep. 2007; 30(12):1712-1727.
4. American Academy of Sleep Medicine. International Classification of Sleep Disorders: Diagnostic and Coding Manual. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.
5. Sateia MJ. International classification of sleep disorders - third edition: highlights and modifications. CHEST. 2014; 146(5):1287-94.
6. Scammell TE. Clinical features and diagnosis of narcolepsy. UpToDate Website. June 2015. www.uptodate.com. Accessed July 20, 2015.
7. Per clinical consultation with neurologist/sleep specialist. October 9, 2012 (confirmed on March 20, 2015).

Prior Authorization Guideline

GL-15020 Yervoy (ipilimumab)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/24/2016

Technician Note :

P&T Approval Date: 7/12/2011 P&T Revision Date: 5/19/2016 **Effective 6/15/2016**

1 . Indications

Drug Name: Yervoy (ipilimumab)

Indications

Unresectable or Metastatic Melanoma

Indicated for the treatment of unresectable or metastatic melanoma.

Adjuvant Treatment of Melanoma

Indicated for the adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete

resection, including total lymphadenectomy.

2 . Criteria

Product Name: Yervoy

Diagnosis	Unresectable or Metastatic Melanoma
Approval Length	4 doses or up to 16 weeks from the first dose, whichever occurs first [A]
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of melanoma

AND

2 Disease is one of the following:

- Unresectable
- Metastatic

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Yervoy

Diagnosis	Cutaneous Melanoma

Approval Length	12 Months
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cutaneous melanoma

AND

2 Disease with pathologic involvement of regional lymph nodes of more than 1 mm

AND

3 Patient has undergone resection, including total lymphadenectomy

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Yervoy

Diagnosis	Cutaneous Melanoma
Approval Length	12 Months
Therapy Stage	Reauthorization

Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Yervoy therapy

3 . Endnotes

A. The recommended dose of Yervoy for unresectable or metastatic melanoma is 3 mg/kg intravenously every 3 weeks for a maximum of 4 doses; doses may be delayed due to toxicity, but all doses must be administered within 16 weeks of the initial dose. [1]

4 . References

1. Yervoy Prescribing Information. Bristol-Myers Squibb Company. October 2015.
2. Hodi FS, O'day SJ, McDermott DF, Weber RW, et al. Improved survival with ipilimumab in patients with metastatic melanoma. NEJM 2010;363:711-723.
3. Korn EL, Liu P, Lee SJ, et al. Meta-Analysis of Phase II Cooperative Group Trials in Metastatic Stage IV Melanoma to Determine Progression-Free and Overall Survival Benchmarks for Future Phase II Trials. J Clin Oncol 2008; 26:527-534.
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines on Melanoma_v.2.2016. Available at: www.nccn.com. Accessed March 3, 2016.
5. The Surveillance, Epidemiology and End Results (SEER) Program. Available at http://seer.cancer.gov/statfacts/html/melan.html Accessed on December 9, 2010.
6. Wolchok JD, Neyns B, Linette G, et al. Ipilimumab monotherapy in patients with pretreated advanced melanoma: a randomized, double blind, multicenter, Phase 2, dose-ranging study. Lancet Oncol 2010;11:155-164.
7. Yervoy Product Dossier. AMCP Formulary Submission. In the treatment of unresectable or metastatic melanoma. Bristol-Myers Squibb Company. April 2011.
8. American Joint Committee on Cancer. Staging Resources. Available at: http://www.cancerstaging.org/staging/. Accessed May 24, 2013.

Prior Authorization Guideline

GL-17143 Zaltrap (ziv-aflibercept)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 11/13/2012; P&T revision date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Zaltrap (ziv-aflibercept)

Indications

Metastatic Colorectal Cancer (mCRC)

In combination with 5-fluorouracil, leucovorin, irinotecan-(FOLFIRI), indicated for patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

2 . Criteria

Product Name: Zaltrap

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of metastatic colon and/or rectal cancer

AND

2 Used in combination with 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) regimen

AND

3 Patient has disease that is resistant to or has progressed following an oxaliplatin-containing regimen [e.g., 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX)]

AND

4 Prescribed by or in consultation with an oncologist

Product Name: Zaltrap

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease

3 . References

1. Zaltrap Prescribing Information. Sanofi Aventis, March, 2016
2. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Colorectal Cancer Version 1.2013. Accessed October 3, 2012

Prior Authorization Guideline

GL-15730 Zelboraf (vemurafenib)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 3/31/2016

Technician Note :

P&T Approval Date: 2/21/2012; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Zelboraf (vemurafenib)

Indications

Melanoma

Indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test. It is not recommended for use in patients with wild-type BRAF melanoma.

2 . Criteria

Product Name: Zelboraf

Approval Length	12 Month [B]
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 One of the following diagnoses: [2, 4, C]

- Unresectable melanoma
- Metastatic melanoma

AND

2 Cancer is BRAF V600 mutant type as detected by an FDA-approved test (eg, cobas 4600 BRAF V600 Mutation Test) or performed at a facility approved by Clinical Laboratory Improvement Amendments (CLIA)

AND

3 Prescribed by or in consultation with an oncologist

Product Name: Zelboraf

Approval Length	12 Month [B]

Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Zelboraf therapy

3 . Endnotes

A. Per medical oncologist consultant: Physicians routinely follow-up and assess patient response to the drug every 1-2 months; the majority of these patients fail treatment within the first 6 months. The authorization process forces an honest assessment since it is easier to continue treating for an additional month than to have a hard discussion about treatment failure. [3]
B. In the pivotal trial (Trial 1) evaluating treatment naive patients who received vemurafenib, the median follow-up was 6.2 months and the median progression free survival (PFS) was 5.3 months (95% CI, 4.9 - 6.6). In the pivotal trial (Trial 2) evaluating vemurafenib in patients who received prior systemic therapy, the best overall response rate was 52% (95% CI, 43 - 61%), the median time to response was 1.4 months, and the median duration of response was 6.5 months (95% CI, 5.6 - not reached). [1] According to the NCCN melanoma guidelines, vemurafenib is associated with a 40-50% response rate in patients with a V600 mutated BRAF gene; however, the median duration of response is only 5 - 6 months. [2]
C. The NCCN Drugs and Biologics Compendium recommends use of vemurafenib as a preferred single agent in patients with V600 mutation of the BRAF gene for (category 1): • unresectable stage III in-transit metastases • local/satellite and/or in-transit unresectable recurrence • incompletely resected or unresectable nodal recurrence • recurrent or metastatic disease. [4]

4 . References

1. Zelboraf Prescribing Information. Genentech USA, Inc., April 2012.

2. National Comprehensive Cancer Network, Practice Guidelines in Oncology – Melanoma v.2.2013. Available at http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf. Accessed June 4, 2013.
3. Per clinical consultation with oncologist, December 8, 2011.
4. National Comprehensive Cancer Network, Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed June 4, 2013.

Prior Authorization Guideline

GL-31684 Zepatier (elbasvir-grazoprevir)

Formulary OptumRx SP

Formulary Note

Approval Date 8/26/2016

Revision Date 8/26/2016

Technician Note :

P&T Approval Date: 11/18/2015; P&T Revision Date: 6/22/2016

1 . Indications

Drug Name: Zepatier (elbasvir and grazoprevir)

Indications

Chronic Hepatitis C Indicated with or without ribavirin for the treatment of chronic hepatitis C virus (HCV) genotypes 1 or 4 infection in adults.

2 . Criteria

Product Name: Zepatier

Diagnosis	Chronic Hepatitis C - Genotype 1a: treatment-naÃ¯ve or PegIFN/RBV-experienced or PegIFN/RBV/protease inhibitor-experienced without baseline NS5A polymorphisms*
Approval Length	12 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (eg, chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1a

AND

2 One of the following:

2.1 Patient is treatment-naive

OR

2.2 Patient has prior failure to peginterferon alfa plus ribavirin treatment

OR

2.3 Both of the following:

- Patient has prior failure to treatment with peginterferon alfa plus ribavirin plus a HCV NS3/4A protease inhibitor (eg, boceprevir, simeprevir, or telaprevir)
- Used in combination with ribavirin

AND

3 Both of the following: [1, A]

3.1 Patient has been tested for the presence of NS5A resistance-associated polymorphisms

AND

3.2 Patient is without baseline NS5A resistance-associated polymorphisms (ie, polymorphisms at amino acid positions 28, 30, 31, or 93)

AND

4 Prescribed by or in consultation with one of the following:

- Hepatologist
- Gastroenterologist
- Infectious disease specialist
- HIV specialist certified through the American Academy of HIV Medicine

AND

5 Patient is not receiving Zepatier in combination with another HCV direct acting antiviral agent [eg, Sovaldi (sofosbuvir), Olysio (simeprevir)]

AND

6 Patient does not have moderate to severe hepatic impairment (eg, Child-Pugh Class B or C) [1, C]

Notes	**NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.

Product Name: Zepatier

Diagnosis	Chronic Hepatitis C - Genotype 1a: treatment-naÃ¯ve or PegIFN/RBV-experienced or PegIFN/RBV/protease inhibitor-experienced with baseline NS5A polymorphisms*
Approval Length	16 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (eg, chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1a

AND

2 One of the following:

- Patient is treatment-naive
- Patient has prior failure to peginterferon alfa plus ribavirin treatment
- Patient has prior failure to treatment with peginterferon alfa plus ribavirin plus a HCV NS3/4A protease inhibitor (eg, boceprevir, simeprevir, or telaprevir)

AND

3 Both of the following: [1, A]

3.1 Patient has been tested for the presence of NS5A resistance-associated polymorphisms

AND

3.2 Patient has baseline NS5A resistance-associated polymorphisms (ie, polymorphisms at amino acid positions 28, 30, 31, or 93)

AND

4 Used in combination with ribavirin

AND

5 Prescribed by or in consultation with one of the following:

- Hepatologist
- Gastroenterologist
- Infectious disease specialist
- HIV specialist certified through the American Academy of HIV Medicine

AND

6 Patient is not receiving Zepatier in combination with another HCV direct acting antiviral agent [eg, Sovaldi (sofosbuvir), Olysio (simeprevir)]

AND

7 Patient does not have moderate to severe hepatic impairment (eg, Child-Pugh Class B or C) [1, C]

Notes	*NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.

Product Name: Zepatier

Diagnosis	Chronic Hepatitis C - Genotype 1b: treatment-naÃ¯ve or PegIFN/RBV-experienced or PegIFN/RBV/protease inhibitor-experienced
Approval Length	12 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (eg, chart notes, laboratory values) documenting diagnosis of chronic hepatitis C genotype 1b

AND

2 One of the following:

2.1 Patient is treatment-naive

OR

2.2 Patient has prior failure to peginterferon alfa plus ribavirin treatment

OR

2.3 Both of the following:

- Patient has prior failure to treatment with peginterferon alfa plus ribavirin plus a HCV NS3/4A protease inhibitor (eg, boceprevir, simeprevir, or telaprevir)
- Used in combination with ribavirin

AND

3 Prescribed by or in consultation with one of the following:

- Hepatologist
- Gastroenterologist
- Infectious disease specialist
- HIV specialist certified through the American Academy of HIV Medicine

AND

4 Patient is not receiving Zepatier in combination with another HCV direct acting antiviral agent [eg, Sovaldi (sofosbuvir), Olysio (simeprevir)]

AND

5 Patient does not have moderate to severe hepatic impairment (eg, Child-Pugh Class B or C) [1, C]

Product Name: Zepatier

Diagnosis	Chronic Hepatitis C - Genotype 4: Treatment-naive
Approval Length	12 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (eg, chart notes, laboratory values) documenting a diagnosis of genotype 4

AND

2 Patient is treatment-naive

AND

3 Prescribed by or in consultation with one of the following:

- Hepatologist
- Gastroenterologist
- Infectious disease specialist
- HIV specialist certified through the American Academy of HIV Medicine

AND

4 Patient is not receiving Zepatier in combination with another HCV direct acting antiviral agent [eg, Sovaldi (sofosbuvir), Olysio (simeprevir)]

AND

5 Patient does not have moderate to severe hepatic impairment (eg, Child-Pugh Class B or C) [1, C]

Product Name: Zepatier

Diagnosis	Chronic Hepatitis C - Genotype 4: PegIFN/RBV-experienced
Approval Length	16 Week
Guideline Type	Prior Authorization

Approval Criteria

1 Submission of medical records (eg, chart notes, laboratory values) documenting a diagnosis of genotype 4

AND

2 Patient has prior failure to peginterferon alfa plus ribavirin treatment

AND

3 Used in combination with ribavirin

AND

4 Prescribed by or in consultation with one of the following:

- Hepatologist
- Gastroenterologist
- Infectious disease specialist
- HIV specialist certified through the American Academy of HIV Medicine

AND

5 Patient is not receiving Zepatier in combination with another HCV direct acting antiviral agent [eg, Sovaldi (sofosbuvir), Olysio (simeprevir)]

AND

6 Patient does not have moderate to severe hepatic impairment (eg, Child-Pugh Class B or C) [1, C]

3 . Endnotes

A. Testing patients with HCV genotype 1a infection for the presence of virus with NS5A resistance-associated polymorphisms is recommended prior to initiation of treatment with Zepatier to determine dosage regimen and duration. In subjects receiving Zepatier for 12 weeks, sustained virologic response (SVR12) rates were lower in genotype 1a-infected patients with one or more baseline NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93. [1]
B. Zepatier is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C) due to the expected significantly increased grazoprevir plasma concentration and the increased risk of alanine aminotransferase (ALT) elevations. [1]

4 . References

1. Zepatier Prescribing Information, Merck Sharp & Dohme Corp, 2016.

Prior Authorization Guideline

GL-17351 Zolinza (vorinostat)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/23/2016

Technician Note :

P&T Approval Date: 2/20/2007; P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Zolinza (vorinostat)

Indications

Cutaneous T-cell Lymphoma

Indicated for treatment of cutaneous manifestations in patients with cutaneous T-cell lymphoma (CTCL) who have progressive, persistent or recurrent disease on or following two systemic therapies.

2 . Criteria

Product Name: Zolinza

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of cutaneous T-cell lymphoma

AND

2 One of the following:

2.1 Patient has progressive, persistent or recurrent disease on or following 2 systemic therapies (e.g., extracorporeal photopheresis [ECP], systemic retinoids, interferons) [A]

OR

2.2 History of contraindication or intolerance to other systemic therapies [A]

AND

3 Prescribed by or in consultation with a hematologist/oncologist

Product Name: Zolinza

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Zolinza therapy

3 . Endnotes

A. Examples of systemic therapies include (but are not limited to): [4] • Campath (alemtuzumab) • Cytoxan (cyclophosphamide) • Doxil (pegylated doxorubicin) • Extracorporeal photochemotherapy • Folotyn (pralatrexate) • Gemzar (gemcitabine) • Interferon-alpha • Leukeran (chlorambucil) • Nipent (pentostatin) • Ontak (denileukin diftitox) • Targretin (bexarotene) • Temodar (temozolamide) • Toposar (etoposide) • Trexall (methotrexate) • Velcade (bortezomib)

4 . References

1. Zolinza Prescribing Information. Merck & Co, Inc., October 2010.
2. National Cancer Institute. Mycosis fungoides and the Sezary Syndrome (PDQ) Treatment. Available at: http://www.nci.nih.gov/cancertopics/pdq/treatment/mycosisfungoides/HealthProfessional. Accessed January 2, 2007.
3. Whittaker SJ, Marsden JR, Spittle M, Jones RR. Joint British Association of Dermatologists and U.K. Cutaneous Lymphoma Group guidelines for the management of primary cutaneous T-cell lymphomas. Br J Dermatol. 2003;149:1095-1107.
4. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in OncologyTM Non-Hodgkin's Lymphomas (Version 4.2011). Available at: http://www.nccn.org/professionals/physician_gls/PDF/nhl.pdf. Accessed September 16, 2011.

Prior Authorization Guideline

GL-17147 Zortress (everolimus)

Formulary OptumRx SP

Formulary Note

Approval Date 3/21/2013

Revision Date 5/25/2016

Technician Note :

P&T Approval Date: 2/7/2005; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Zortress (everolimus)

Indications

Prophylaxis of organ rejection in kidney transplantation

Indicated for the prophylaxis of organ rejection in adult patients at low-moderate immunologic risk receiving a kidney transplant. Zortress is to be administered in combination with basiliximab induction and concurrently with reduced doses of cyclosporine and corticosteroids. Therapeutic drug monitoring of everolimus and cyclosporine is recommended for all patients receiving these products. Limitations of use: The safety and efficacy of Zortress has not been established in the following populations: Kidney transplant patients at high immunologic risk, recipients of

transplanted organs other than kidney and liver, and pediatric patients (<18 years).

Prophylaxis of organ rejection in liver transplantation

Indicated for the prophylaxis of allograft rejection in adult patients receiving a liver transplant. Zortress is to be administered no earlier than 30 days post-transplant concurrently in combination with reduced doses of tacrolimus and with corticosteroids. Therapeutic drug monitoring of everolimus and tacrolimus is recommended for all patients receiving these products. Limitations of use: The safety and efficacy of Zortress has not been established in the following populations: Kidney transplant patients at high immunologic risk, recipients of transplanted organs other than kidney and liver, and pediatric patients (<18 years).

2 . Criteria

Product Name: Zortress

Approval Length	60 Month
Guideline Type	Prior Authorization

Approval Criteria

1 Patient is 18 years of age or older

AND

2 Prescriber is experienced in immunosuppressive therapy and management of transplant patients

AND

3 One of the following:

3.1 All of the following:

3.1.1 The medication is being used for prevention of kidney transplant organ rejection

AND

3.1.2 The patient is at low-to-moderate immunologic risk

AND

3.1.3 The patient is prescribed concurrent therapy with reduced doses of cyclosporine and corticosteroids

OR

3.2 All of the following:

3.2.1 The medication is being used for prevention of liver transplant organ rejection

AND

3.2.2 Thirty (30) or more days have passed since the transplant procedure

AND

3.2.3 The patient is prescribed concurrent therapy with reduced doses of tacrolimus and corticosteroids

3 . References

1. Zortress Prescribing Information. Novartis Pharmaceuticals Corporation. January 2015.

Prior Authorization Guideline

GL-17140 Zydelig (idelalisib)

Formulary OptumRx SP

Formulary Note

Approval Date 10/14/2014

Revision Date 5/26/2016

Technician Note :

P&T Approval Date: 10/14/2014; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Zydelig (idelalisib)

Indications

Relapsed Chronic Lymphocytic Leukemia

Indicated, in combination with rituximab, for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL) for whom rituximab alone would be considered appropriate therapy due to other co-morbidities.

Relapsed Follicular B-cell non-Hodgkin Lymphoma

Indicated for the treatment of patients with relapsed follicular B-cell non-Hodgkin lymphoma (FL) who have received at least two prior systemic therapies. Accelerated approval was granted for this indication based on Overall Response Rate [see Clinical Studies (14.2)]. An improvement in patient survival or disease related symptoms has not been established. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

Relapsed Small Lymphocytic Lymphoma

Indicated for the treatment of patients with relapsed small lymphocytic lymphoma (SLL) who have received at least two prior systemic therapies. Accelerated approval was granted for this indication based on Overall Response Rate [see Clinical Studies (14.3)]. An improvement in patient survival or disease related symptoms has not been established. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

2 . Criteria

Product Name: Zydelig

Diagnosis	Chronic Lymphocytic Leukemia (CLL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Chronic Lymphocytic Leukemia (CLL) [2]

AND

2 Patient has relapsed on at least one prior therapy (e.g., purine analogues [fludarabine, pentostatin, cladribine], alkylating agents [chlorambucil, cyclophosphamide], or monoclonal

antibodies [rituximab])

AND

3 Used in combination with Rituxan (rituximab)* [2]

AND

4 Patient is a candidate for Rituxan (rituximab) monotherapy due to presence of other comorbidities (e.g., coronary artery disease, peripheral vascular disease, diabetes mellitus, pulmonary disease [COPD], etc.)

AND

5 Prescribed by or in consultation with an oncologist/hematologist

Notes	*This drug may require prior authorization.

Product Name: Zydelig

Diagnosis	Small Lymphocytic Lymphoma (SLL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of Small Lymphocytic Lymphoma (SLL) [2]

AND

2 Patient has relapsed on at least two prior systemic therapies(e.g., rituximab, alkylating agents [cyclophosphamide, chlorambucil], anthracyclines [doxorubicin, daunorubicin], purine analogs [fludarabine]) [2]

AND

3 Prescribed by or in consultation with an oncologist/hematologist

Product Name: Zydelig

Diagnosis	Follicular Lymphoma (FL)
Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of follicular B-cell non-Hodgkin lymphoma (FL) [2]

AND

2 Patient has relapsed on at least two prior systemic therapies (e.g., rituximab, alkylating agents [cyclophosphamide, chlorambucil], anthracyclines [doxorubicin, daunorubicin], purine analogs [fludarabine]) [2]

AND

3 Prescribed by or in consultation with an oncologist/hematologist

Product Name: Zydelig

Diagnosis	All diagnoses listed above
Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Zydelig therapy

3 . References

1. Zydelig Prescribing Information. Gilead Sciences, Inc., July 2014.
2. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium: Cometriq Available at: http://www.nccn.org/professionals/drug_compendium/MatrixGenerator/AgentList.aspx?aid=395. Accessed November 30, 2015.

Prior Authorization Guideline

GL-17352 Zykadia (ceritinib)

Formulary OptumRx SP

Formulary Note

Approval Date 7/8/2014

Revision Date 5/31/2016

Technician Note :

P&T Approval Date: 7/8/2014; P&T Revision Date: 2/25/2016. **Effective 7/1/2016**

1 . Indications

Drug Name: Zykadia (ceritinib)

Indications

Non-small cell lung cancer (NSCLC)

Indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic NSCLC who have progressed on or are intolerant to crizotinib. This indication is approved under accelerated approval based on tumor response rate and duration of response. An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

2 . Criteria

Product Name: Zykadia

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of non-small cell lung cancer (NSCLC) [2, 3]

AND

2 One of the following: [2, 3]

- Disease is metastatic
- Disease is recurrent

AND

3 Tumor is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test or Clinical Laboratory Improvement Amendments-approved facility [2, 3]

AND

4 History of failure or intolerance to Xalkori (crizotinib)* [2, 3] **AND** **5** Prescribed by or in consultation with an oncologist

Notes	*This drug may require prior authorization.

Product Name: Zykadia

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease while on Zykadia therapy

3 . References

1. Zykadia Prescribing Information. Novartis Pharmaceuticals Corp, April 2014.
2. The NCCN Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed May 26, 2015.

3. National Comprehensive Cancer Network (NCCN) Non-small cell lung cancer guideline. v.6.2015. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed May 26, 2015.

Prior Authorization Guideline

GL-16811 Zytiga (abiraterone acetate)

Formulary OptumRx SP

Formulary Note

Approval Date 7/11/2013

Revision Date 5/27/2016

Technician Note :

P&T Approval Date: 7/9/2013 P&T Revision Date: 2/25/2016 **Effective 7/1/2016**

1 . Indications

Drug Name: Zytiga (abiraterone acetate)

Indications

Metastatic castration-resistant prostate cancer (mCRPC)

In combination with prednisone, indicated for the treatment of patients with metastatic castration-resistant prostate cancer.

2 . Criteria

Product Name: Zytiga

Approval Length	12 Month
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 Diagnosis of metastatic castration-resistant (chemical or surgical) prostate cancer

AND

2 Used in combination with prednisone

AND

3 Prescribed by or in consultation with one of the following:

- Oncologist
- Urologist

Product Name: Zytiga

Approval Length	12 Month
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 Patient does not show evidence of progressive disease

3 . References

1. Zytiga Prescribing Information. Janssen Biotech Inc., May 2015
2. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Prostate Cancer. v.2.2013. Available at: http://www.nccn.org/professionals/physician_gls/PDF/prostate.pdf. Accessed May 30, 2013.