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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

<table>
<thead>
<tr>
<th>Drug Name: Adcetris (brentuximab vedotin)</th>
</tr>
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</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hodgkin Lymphoma (HL)</th>
</tr>
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<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

### 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
Product Name: Adcetris

<table>
<thead>
<tr>
<th>Diagnosis</th>
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</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Systemic Anaplastic Large Cell Lymphoma (sALCL)</th>
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</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Systemic Anaplastic Large Cell Lymphoma (sALCL)</th>
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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.
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

<table>
<thead>
<tr>
<th>Drug Name: Afinitor (everolimus)</th>
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</table>

**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)**

**Indications**

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

2. Criteria

Product Name: Afinitor

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</table>

Approval Criteria

1. Diagnosis of progressive neuroendocrine tumors of pancreatic origin

2. Disease is one of the following:
   - Unresectable, locally advanced
   - Metastatic

3. Prescribed by or in consultation with an oncologist
### Advanced Neuroendocrine Tumors of Pancreatic Origin (PNET)

<table>
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<tr>
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**Approval Criteria**

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

**Product Name:** Afinitor

<table>
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<tr>
<th>Diagnosis</th>
<th>Advanced Renal Cell Carcinoma</th>
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</table>

**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
Prescribed by or in consultation with an oncologist

**Product Name:** Afinitor

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Advanced Renal Cell Carcinoma</th>
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**Approval Criteria**

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

**Product Name:** Afinitor

<table>
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<th>Diagnosis</th>
<th>Renal Angiomyolipoma with Tuberous Sclerosis Complex (TSC)</th>
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<td>Guideline Type</td>
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</table>

**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

<table>
<thead>
<tr>
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<th>Renal Angiomyolipoma with Tuberous Sclerosis Complex (TSC)</th>
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**Approval Criteria**

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

**Product Name:** Afinitor, Afinitor Disperz

<table>
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<th>Diagnosis</th>
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<td>Guideline Type</td>
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</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Subependymal Giant Cell Astrocytoma</th>
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**Approval Criteria**

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

**Product Name:** Afinitor

<table>
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<tr>
<th>Diagnosis</th>
<th>Breast cancer</th>
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**Approval Criteria**

1 Diagnosis of hormone receptor positive, HER-2 negative advanced breast cancer
2 History of failure, contraindication, or intolerance to one of the following:

- Femara (letrozole)
- Arimidex (anastrozole)

3 Used in combination with Aromasin (exemestane)

4 Prescribed by or in consultation with an oncologist

**Product Name:** Afinitor

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**Approval Criteria**

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

**Product Name:** Afinitor
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<tr>
<th>Diagnosis</th>
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**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
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

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Drug Name: Intron A (interferon alfa-2b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Hairy Cell Leukemia</td>
</tr>
<tr>
<td>Indicated for the treatment of patients 18 years of age or older with hairy cell leukemia.</td>
</tr>
<tr>
<td>Malignant Melanoma</td>
</tr>
<tr>
<td>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</td>
</tr>
</tbody>
</table>
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, low tumor 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 thyroid-stimulating 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/mm³ • Platelets - adults greater than or equal to 100,000/mm³, pediatrics greater than or equal to 150,000/mm³. 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

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<tr>
<td>Approval Length</td>
<td>48 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<td>48 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**Approval Criteria**

1. Diagnosis of chronic hepatitis C
Patients without decompensated liver disease†

For patients who have not previously been treated with interferon

One of the following:

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

<table>
<thead>
<tr>
<th>Notes</th>
<th>†Defined as Child-Pugh Class B or C</th>
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</table>

**Product Name:** Pegasys or PegIntron

<table>
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<th>Diagnosis</th>
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<tbody>
<tr>
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<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Hepatitis C</th>
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<tbody>
<tr>
<td>Approval Length</td>
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<td>Reauthorization</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Condylomata acuminata</th>
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<tr>
<td>Approval Length</td>
<td>6 Week</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

Approval Criteria

1. Diagnosis of condylomata acuminata (genital or perianal)

**Product Name:** Intron A

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Diagnoses other than hepatitis and condylomata acuminata</th>
</tr>
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<tbody>
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<td>12 Month</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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. 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAT deficiency</td>
<td>A chronic, hereditary, usually fatal, autosomal recessive</td>
</tr>
</tbody>
</table>
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


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

<table>
<thead>
<tr>
<th>Drug Name: Ampyra (dalfampridine)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

#### 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
Approval Criteria

1. Physician confirmation that the patient’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

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.

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**2. Criteria**
**Product Name:** Keytruda or Opdivo

<table>
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<th>Melanoma</th>
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<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Melanoma</th>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
</tbody>
</table>
Guideline Type | Prior Authorization
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### Approval Criteria

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

**Product Name:** Keytruda

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-Small Cell Lung Cancer (NSCLC)</th>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
</tbody>
</table>

**Guideline Type** | Prior Authorization
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### 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-Small Cell Lung Cancer (NSCLC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Opdivo

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-Small Cell Lung Cancer (NSCLC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-Small Cell Lung Cancer (NSCLC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Renal Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Classical Hodgkin Lymphoma (cHL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Head and Neck Squamous Cell Carcinoma (HNSCC), Recurrent or Metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

3 References
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

<table>
<thead>
<tr>
<th>Drug Name: Apokyn (apomorphine HCl injection)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIAS1 gene:</td>
<td>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]</td>
</tr>
<tr>
<td>Chronic Infantile Neurologic Cutaneous and Articular Syndrome:</td>
<td>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</td>
</tr>
</tbody>
</table>
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]

<table>
<thead>
<tr>
<th>Cryopyrin-Associated Periodic Syndromes (CAPS):</th>
<th>A group of rare, autosomal dominantly inherited autoinflammatory conditions comprising of Familial-Cold Autoinflammatory 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]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial Cold Autoinflammatory Syndrome:</td>
<td>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]</td>
</tr>
<tr>
<td>Muckle-Wells Syndrome:</td>
<td>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. [4, 5]</td>
</tr>
</tbody>
</table>

### 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-1β 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. 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Refractory Chronic Lymphocytic Leukemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 months [D]</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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)
   - Ritu (rituximab)
   - Treanda (bendamustine)
   - Gazyva (obinutuzumab)

   **AND**
3 Prescribed by or in consultation with a hematologist/oncologist

**Product Name:** Arzerra

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Previously Untreated Chronic Lymphocytic Leukemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [C]</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
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


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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>6 months [2, A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>6 months [2, A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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**

   2. Per clinical consult with rheumatologist, April 29, 2011.
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
# Criteria

**Product Name:** Blincyto

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Weeks [1, A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### Approval Criteria

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

2. Prescribed by or in consultation with a hematologist/oncologist

**Product Name:** Blincyto

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>18 Weeks [1, A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

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

<table>
<thead>
<tr>
<th>Drug Name:</th>
<th>Bosulif (bosutinib)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

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

3 References

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Neuromuscular and Autonomic Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<p>| Diagnosis | Neuromuscular and Autonomic Disorders |</p>
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>3 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Confirmed improvement in symptoms with initial Botox treatment

\[
\text{AND}
\]

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

**Product Name:** Botox

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hyperhidrosis, axillary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Time</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of primary axillary hyperhidrosis [G]

\[
\text{AND}
\]

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hyperhidrosis, axillary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Time</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Migraine headache, chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Urinary incontinence associated with a neurologic condition OR Overactive bladder with symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Urinary incontinence associated with a neurologic condition OR Overactive bladder with symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
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<tr>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic anal fissure (Off-Label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic anal fissure (Off-Label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic back pain [D] (Off-Label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 treatment session (series of injections) [L]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Achalasia (Off-Label)</th>
</tr>
</thead>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Achalasia (Off-Label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month [C]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>---------------------</td>
<td>-----------------</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

\[\text{AND}\]

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

**Product Name:** Botox

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>All other diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>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.</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

      \[\text{AND}\]
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 injury (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 overactivity (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, fesoterodine, 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


34. Per clinical consultation with neurologist, January 7, 2011.


41. Per clinical consultation with neurologist, July 20, 2015.
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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Months [A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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 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
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

<table>
<thead>
<tr>
<th>Drug Name: Cayston (aztreonam for inhalation solution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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


**Prior Authorization Guideline**

GL-17344 Cimzia (certolizumab pegol)

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>16 Week</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Ocrevus (abatacept)] [1]

AND

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

Product Name: Cimzia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Crohn's disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Documentation of positive clinical response to Cimzia therapy
Product Name: Cimzia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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), Ocrenza (abatacept)] [1]

AND

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

Product Name: Cimzia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
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<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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), Ocrevus (abatacept)] [1]

AND

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

Product Name: Cimzia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Psoriatic Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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), Orenzia (abatacept)] [1]

AND

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

**Product Name:** Cimzia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Psoriatic Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Orenzia (abatacept)] [1]

AND

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ankylosing Spondylitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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), Oremia (abatacept)] [1]

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

**Product Name:** Cimzia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ankylosing Spondylitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Oncia (abatacept)] [1]

   **AND**

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

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

<table>
<thead>
<tr>
<th>Drug Name: Neulasta (pegfilgrastim, G-CSF)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Febrile Neutropenia (FN), Prophylaxis</td>
</tr>
<tr>
<td>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.</td>
</tr>
</tbody>
</table>

| 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/mm³ 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bone Marrow/Stem Cell Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months or duration of therapy</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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]
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>AML Induction or Consolidation Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months or duration of therapy [C]</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>AML Induction or Consolidation Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months or duration of therapy [C]</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Neutropenia Associated with Cancer Chemotherapy - Dose Dense Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months or duration of therapy</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)
1.2 Patient is receiving a dose-dense chemotherapy regimen for which the incidence of FN is unknown

AND

2 Prescribed by or in consultation with a hematologist/oncologist

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Primary Prophylaxis of Chemotherapy-Induced Febrile Neutropenia (FN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months or duration of therapy</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Secondary Prophylaxis of Febrile Neutropenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months or duration of therapy</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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, 1]

   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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Severe Chronic Neutropenia (SCN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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]
2 Prescribed by or in consultation with a hematologist/oncologist

**Product Name:** Leukine, Neupogen, or Zarxio

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>HIV-Related Neutropenia (Off-label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 months [11, 15, H]</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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


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
2. Criteria

Product Name: Cometriq

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Medullary Thyroid Cancer (MTC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>11 months [A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Medullary Thyroid Cancer (MTC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>11 months [A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Cometriq

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-Small Cell Lung Cancer (NSCLC) (off-label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>11 months [A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

   AND

3 Prescribed by or in consultation with an oncologist/hematologist

**Product Name:** Cometriq

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-Small Cell Lung Cancer (NSCLC) (off-label)</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
<td>11 months [A]</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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
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

<table>
<thead>
<tr>
<th>Drug Name: Cotellic (cobimetinib)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td><strong>Melanoma</strong></td>
</tr>
</tbody>
</table>

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*

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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]
**Product Name:** Cotellic®

<table>
<thead>
<tr>
<th>Approval Length</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
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<tr>
<th>Approval Criteria</th>
</tr>
</thead>
</table>

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]
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

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

<table>
<thead>
<tr>
<th>Drug Name: Cystaran (cysteamine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Corneal cystine crystal accumulation</td>
</tr>
</tbody>
</table>
Indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis.
2. Criteria

Product Name: Cystaran

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

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*

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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*

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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.
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Hepatitis C - Genotype 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

**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

<table>
<thead>
<tr>
<th>Drug Name: Darzalex (daratumumab)</th>
</tr>
</thead>
</table>

**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*

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
<table>
<thead>
<tr>
<th>Notes</th>
<th>*Product may be excluded depending on the plan.</th>
</tr>
</thead>
</table>

**Product Name:** Darzalex*

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

<table>
<thead>
<tr>
<th>Notes</th>
<th>*Product may be excluded depending on the plan.</th>
</tr>
</thead>
</table>

### 3. References

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

<table>
<thead>
<tr>
<th>Drug Name: Dysport (abobotulinum toxin type A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>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-naive and previously treated patients.</td>
</tr>
<tr>
<td>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</td>
</tr>
</tbody>
</table>
to primarily improve or otherwise modify the member’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.

<table>
<thead>
<tr>
<th>2. Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product Name:</strong> Dysport</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
</tr>
<tr>
<td><strong>Approval Length</strong></td>
</tr>
<tr>
<td><strong>Therapy Stage</strong></td>
</tr>
<tr>
<td><strong>Guideline Type</strong></td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Upper or lower limb spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Upper or lower limb spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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. 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 studied 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>6 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of HIV-associated lipodystrophy

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

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
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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>6 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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. Indications

**Drug Name:** Elaprase (idursulfase) [1]

**Indications**

**Hunter Syndrome**

It 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)

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>5 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of Hunter syndrome (Mucopolysaccharidosis II, MPS II)

3. Definitions

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elaprase (idursulfase)</td>
<td>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.</td>
</tr>
<tr>
<td>Hunter syndrome</td>
<td>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</td>
</tr>
<tr>
<td><strong>Treatment of Hunter syndrome</strong></td>
<td>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.</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>Hunter Syndrome (Mucopolysaccharidosis II, MPS II)</strong></td>
<td>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]</td>
</tr>
</tbody>
</table>

### 4. References

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

<table>
<thead>
<tr>
<th>Drug Name: Empliciti (elotuzumab)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Multiple myeloma</td>
</tr>
</tbody>
</table>

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*

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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*

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<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**Notes**

*Product may be excluded depending on the plan.

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**3. References**

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

<table>
<thead>
<tr>
<th>Drug Name: Enbrel (etanercept)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Rheumatoid Arthritis (RA)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [1,4]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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), Orenzia (abatacept)] [1,5]

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

<table>
<thead>
<tr>
<th>Product Name: Enbrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>Approval Length</td>
</tr>
<tr>
<td>Therapy Stage</td>
</tr>
<tr>
<td>Guideline Type</td>
</tr>
</tbody>
</table>

**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), Ocrevus (abatacept)] [1,5]

   AND

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

<table>
<thead>
<tr>
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<tr>
<td>Diagnosis</td>
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<td>Approval Length</td>
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<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Therapy Stage</td>
</tr>
<tr>
<td>Guideline Type</td>
</tr>
</tbody>
</table>

**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), Ocrenica (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Polyarticular Juvenile Idiopathic Arthritis (JIA)</th>
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</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Psoriatic Arthritis (PsA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Psoriatic Arthritis (PsA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Plaque Psoriasis</th>
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<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Ocrevus (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Plaque Psoriasis</th>
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</tr>
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</tbody>
</table>

**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), Ocrevus (abatacept)] [1,5]
### Product Name: Enbrel

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ankylosing Spondylitis (AS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
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<tr>
<th>Diagnosis</th>
<th>Ankylosing Spondylitis (AS)</th>
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<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
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</tbody>
</table>
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), Ocrevus (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


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

<table>
<thead>
<tr>
<th>Drug Name: Aranesp (darbepoetin alfa)</th>
</tr>
</thead>
</table>

**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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia Due to Chronic Kidney Disease (CKD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia Due to Chronic Kidney Disease (CKD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia due to CKD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Diagnosis of chronic kidney disease (CKD)
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]

<table>
<thead>
<tr>
<th>Notes</th>
<th>†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.</th>
</tr>
</thead>
</table>

**Product Name:** Procrit

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia in HIV-infected patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

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

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*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia in HIV-infected patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<td>Guideline Type</td>
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<td>----------------</td>
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</tr>
<tr>
<td>Approval Criteria</td>
<td></td>
</tr>
</tbody>
</table>

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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia in cancer patients on chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 month [C]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

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

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

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

<table>
<thead>
<tr>
<th>Notes</th>
<th>†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.</th>
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</table>

**Product Name**: Epogen*

<table>
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<th>Diagnosis</th>
<th>Anemia in cancer patients on chemotherapy</th>
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<tr>
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</table>

**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
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia in cancer patients on chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month [C]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Preoperative use for reduction of allogeneic blood transfusion in patients undergoing surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 month [3]</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1 Patient is scheduled to undergo elective, non-cardiac, non-vascular surgery
2 Hemoglobin (Hgb) is greater than 10 to less than or equal to 13 g/dL

3 Patient is at high risk for perioperative transfusions

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

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

<table>
<thead>
<tr>
<th>Notes</th>
<th>†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.</th>
</tr>
</thead>
</table>

**Product Name:** Aranesp* or Procrit

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia in Myelodysplastic Syndrome (MDS) patients [off-label] [4-6, 28]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months [I]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia in MDS patients (off-label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Notes</th>
<th>*Product may be excluded depending on the plan.</th>
</tr>
</thead>
</table>

**Product Name:** Procrit

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia in HCV-infected patients due to ribavirin in combination with interferon or peg-interferon [off-label] [28]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia in HCV-infected patients due to ribavirin in combination with interferon or peg-interferon [off-label] [6]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Diagnosis of hepatitis C viral (HCV) infection [18, 28]
2 Verification of iron evaluation for adequate iron stores † [2]

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

4 Verification of both of the following:

4.1 Patient is receiving ribavirin [28]

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

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

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anemia due to HCV therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Months or if patient has demonstrated response to therapy, authorization will be issued for the full course of ribavirin therapy.</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Erythropoietin Stimulating Agents - Off-Label Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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


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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

3. Fabry Disease Disease Monograph. Genzyme Corporation, 2001
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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month [1,A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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)]
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

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Firmagon (degarelix)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
</tbody>
</table>

Advanced Prostate Cancer

Indicated for treatment of patients with advanced prostate cancer.
## 2. Criteria

**Product Name:** Firmagon

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### Approval Criteria

1. Diagnosis of advanced prostate cancer  

   AND

2. Prescribed by or in consultation with an oncologist

**Product Name:** Firmagon

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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. 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>6 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

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

<table>
<thead>
<tr>
<th>Drug Name: Cerezyme (imiglucerase for injection)</th>
</tr>
</thead>
</table>

Indications

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

<table>
<thead>
<tr>
<th>Drug Name: Elelyso (taliglucerase alfa) for injection</th>
</tr>
</thead>
</table>
### 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Patient is 18 years of age or older

   AND

2. Diagnosis of Type 1 Gaucher disease
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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Lymphocytic Leukemia (CLL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
Prescribed by or in consultation with a hematologist/oncologist

**Product Name:** Gazyva

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Lymphocytic Leukemia (CLL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Gazyva

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Follicular Lymphoma (FL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Follicular Lymphoma (FL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Geodon (ziprasidone mesylate) injection (intramuscular)</th>
</tr>
</thead>
</table>

Indications

Acute agitation [1]

It 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>3 Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Non-Preferred</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Description</th>
</tr>
</thead>
</table>

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 40 mg/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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geodon® Injection:</td>
<td>20 mg/mL as powder for injection</td>
</tr>
</tbody>
</table>

5. Background

Clinical Practice Guidelines

American Psychiatric Association [2]

Table 1. Acute phase treatment of schizophrenia

<table>
<thead>
<tr>
<th>Patient Profile</th>
<th>Consider Medication from</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
</tr>
<tr>
<td>First episode</td>
<td></td>
</tr>
<tr>
<td>Persistent suicidal ideation or behavior</td>
<td></td>
</tr>
<tr>
<td>Persistent hostility and aggressive behavior</td>
<td></td>
</tr>
<tr>
<td>Tardive dyskinesia</td>
<td></td>
</tr>
<tr>
<td>History of sensitivity to extrapyramidal side effects</td>
<td></td>
</tr>
<tr>
<td>History of sensitivity to prolactin elevation</td>
<td>Risperdal)</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>X (except Risperdal)</td>
<td></td>
</tr>
<tr>
<td>History of sensitivity to weight gain, hyperglycemia, or hyperlipidemia</td>
<td>X (Geodon or Abilify)</td>
</tr>
</tbody>
</table>

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


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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Gleevec (imatinib mesylate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td><strong>Chronic myelogenous/myeloid leukemia (CML)</strong></td>
</tr>
</tbody>
</table>

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-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα 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)

2. Patient is found to be Philadelphia chromosome positive or BCR-ABL positive as detected by bone marrow cytogenetics, FISH or PCR

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Myelodysplastic Disease (MDS)/Myeloproliferative Disease (MPD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Aggressive Systemic Mastocytosis (ASM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hypereosinophilic Syndrome (HES) and/or Chronic Eosinophilic Leukemia (CEL)</th>
</tr>
</thead>
</table>
### Approval Criteria

1. Diagnosis of at least one of the following:
   - Hypereosinophilic syndrome (HES)
   - Chronic eosinophilic leukemia (CEL)
   
2. Prescribed by or in consultation with a hematologist/oncologist

**Product Name:** Brand Gleevec, Generic imatinib

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Dermatofibrosarcoma Protuberans (DFSP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Gastrointestinal Stromal Tumors (GIST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
3 Prescribed by or in consultation with an oncologist

**Product Name:** Brand Gleevec, Generic imatinib

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>All diagnoses listed above</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**3. References**

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

<table>
<thead>
<tr>
<th>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)</th>
</tr>
</thead>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Endometriosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1. Diagnosis of endometriosis

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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Endometriosis [10, 18, 20]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Uterine Leiomyomata (Fibroids) - For the reduction of the size of fibroids [off-label]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>4 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Uterine Leiomyomata (Fibroids) - Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Central Precocious Puberty (CPP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
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
6. Prescribed by or in consultation with a pediatric endocrinologist

**Product Name:** Generic leuprolide acetate, Lupron Depot-Ped, Supprelin LA

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</tr>
</tbody>
</table>

**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*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Treatment of Infertility [off-label]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>2 Month [A] (or per plan benefit design)</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Prostate Cancer</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

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)
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Prostate Cancer</th>
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<tbody>
<tr>
<td>Approval Length</td>
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</tbody>
</table>

**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

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</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Lupaneta Pack

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Endometriosis</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
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<tr>
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<td>Initial Authorization</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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

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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.
17. American College of Obstetricians and Gynecologists (ACOG). Management of endometriosis. Available at:


25. Lupron Depot (22.5 mg, 30 mg, 45 mg) Prescribing Information. AbbVie Inc., June 2014.


1. Indications

**Drug Name:** Genotropin, Humatrope, Norditropin, Nutropin/Nutropin AQ/Nutropin AQ NuSpin, Omnitrope, Saizen, and Zomacton

**Indications**

**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.

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**2. Criteria**

**Product Name:** Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pediatric Growth Hormone Deficiency (GHD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pediatric Growth Hormone Deficiency (GHD)</th>
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**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
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</table>

**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
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

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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
3 Prescribed by or in consultation with an endocrinologist

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Prader-Willi Syndrome [off-label]</th>
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<tbody>
<tr>
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</tbody>
</table>

Approval Criteria

1 Diagnosis of Prader-Willi Syndrome [10, 11]

AND
### 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
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

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**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)
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]

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**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]
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

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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
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]

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**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]

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AND
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- 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

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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]

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Approval Criteria

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1.1.1 Turner Syndrome (Gonadal Dysgenesis)

AND

1.1.2 Documentation of both of the following:

- Patient is female
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OR

1.2  Both of the following:

1.2.1 Nooonan Syndrome

AND

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• Patient is male
• Bone age < 16 years

OR

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• 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)

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**Product Name:** Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen [off-label]

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**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]

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   - 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
History of failure or intolerance to all of the following: [B]

- Norditropin (somatropin)
- Nutropin AQ/Nutropin AQ NuSpin (somatropin)
- Saizen (somatropin)

**Product Name:** Nordicropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

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<th>Short-Stature Homeobox (SHOX) Gene Deficiency [off-label]</th>
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**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]

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**Approval Criteria**

1 Diagnosis of pediatric growth failure with short stature homeobox (SHOX) gene deficiency as confirmed by genetic testing [2]

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2 Documentation of one of the following: [28]
2.1 Both of the following:
- Patient is male
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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

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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
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   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]

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4. History of failure or intolerance to all of the following: [B]
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   - 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 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
**Product Name:** Genotropin, Humatrope, Omnitrope, or Zomacton

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**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**

**Notes**

NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.
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)

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| Product Name: Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen [off-label] |

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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

NOTE: Documentation of previous height, current height and goal expected adult height will be required for renewal.
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

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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

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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 [anastrozole], Femara [letrozole])
• 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]

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AND

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2.1 Both of the following:

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- Insulin tolerance test (ITT)
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AND

2.1.2 One of the following peak GH values:

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- 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 [letrozole])
• Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate].
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**Product Name:** Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen

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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 [anastrozole], Femara [letrozole])
•  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]

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</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
2.2.2 Both of the following:

- Not used in combination with aromatase inhibitors (e.g., Arimidex [anastrozole], Femara [letrozole])
- 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)

<table>
<thead>
<tr>
<th>Notes</th>
<th>Use the following criteria for child- and adult-onset with pituitary disease; use Isolated GHD in Adult criteria for patients without pituitary disease.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Name:</td>
<td>Norditropin, Nutropin AQ, Nutropin AQ NuSpin, or Saizen</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Transition Phase Adolescent Patients</td>
</tr>
</tbody>
</table>
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

3.1.2.3 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Transition Phase Adolescent Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<td>Guideline Type</td>
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**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**
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:

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- 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Transition Phase Adolescent Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Transition Phase Adolescent Patients</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
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<td>Prior Authorization</td>
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</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Human Immunodeficiency Virus (HIV)-Associated Cachexia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
</tbody>
</table>
Guideline Type | Prior Authorization

Approved 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Human Immunodeficiency Virus (HIV)-Associated Cachexia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 months [D]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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: Zorbive

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Short Bowel Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>4 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Isolated Growth Hormone Deficiency in Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
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</table>

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 [anastrozole], Femara [letrozole])
- Not used in combination with androgens (e.g., Delatestryl [testosterone enanthate], Depo-Testosterone [testosterone cypionate])

AND
Prescribed by or in consultation with an endocrinologist

**Product Name:** Genotropin, Humatrope, Omnitrope, or Zomacton [off-label]

<table>
<thead>
<tr>
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**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 [anastrozole], Femara [letrozole])
   - 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
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

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</table>

**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 [anastrozole], Femara [letrozole])
- 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]

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<th>Diagnosis</th>
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</table>

**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 [anastrozole], Femara [letrozole])
   - 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
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

2. Humatrope Prescribing Information. Lilly, April 2015.
7. Serostim Prescribing Information. Serono, June 2014.
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

<table>
<thead>
<tr>
<th>Drug Name: H.P. Acthar Gel (repository corticotropin injection)</th>
</tr>
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</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Infantile Spasms (West Syndrome)</th>
</tr>
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<tr>
<td>Approval Length</td>
<td>4 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Multiple Sclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Opsoclonus-Myoclonus Syndrome (off-label)</th>
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<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of opsoclonus-myoclonus syndrome

AND

2. Prescribed by or in consultation with a neurologist

**Product Name:** H.P. Acthar Gel

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Other FDA-Approved Indications</th>
</tr>
</thead>
</table>
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

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

<table>
<thead>
<tr>
<th>Drug Name: Halaven (eribulin mesylate)</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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 consultation with an oncologist

**Product Name**: Halaven

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</table>

**Approval Criteria**

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

**Product Name**: Halaven

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Liposarcoma</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1 Diagnosis of liposarcoma
2 Disease is one of the following:
   - Unresectable
   - Metastatic

3 Previous treatment with one anthracycline-containing regimen

4 Prescribed by or in consultation with an oncologist

**Product Name:** Halaven

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Liposarcoma</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</table>

**Approval Criteria**

1 Patient does not show evidence of progressive disease while on Halaven therapy
3. References

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Adjuvant or Neoadjuvant Breast Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Metastatic Breast Cancer</th>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1 Diagnosis of HER2-overexpressing of breast cancer [A]

AND

2 Disease is metastatic
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)

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

5 Prescribed by or in consultation with an oncologist

**Product Name:** Herceptin

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Metastatic Breast Cancer</th>
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<tbody>
<tr>
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<td>Guideline Type</td>
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</table>

**Approval Criteria**
1. Patient does not show evidence of progressive disease while on Herceptin therapy.

**Product Name:** Herceptin

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Metastatic Gastric Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Metastatic Gastric Cancer</th>
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<tbody>
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</table>

**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 HER2 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 gastroesophageal 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


Prior Authorization Guideline

GL-30121 Hetlizox (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: Hetlizox (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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>6 Month</th>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**
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. Indications

<table>
<thead>
<tr>
<th>Drug Name: Humira (adalimumab)</th>
</tr>
</thead>
</table>

**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
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 Crohn’s disease (CD) Indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn’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 Crohn’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 Crohn’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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
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<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<td>Therapy Stage</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Juvenile Idiopathic Arthritis (JIA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
</tbody>
</table>
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), Ocrevus (abatacept)] [1, 6]

   AND

5. Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz
### Product Name: Humira

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Juvenile Idiopathic Arthritis (JIA)</th>
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<tbody>
<tr>
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</table>

#### 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), Ocrelizumab (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Psoriatic Arthritis (PsA)</th>
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<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months [15]</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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</table>
### 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), Oremcia (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), Ocrevus (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]
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
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<tbody>
<tr>
<td>Therapy Stage</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Ocrevus (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Plaque Psoriasis [1, 5]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
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<tr>
<td>Therapy Stage</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**Approval Criteria**

1. Documentation of positive clinical response to Humira therapy
   
   \[\text{AND}\]

2. Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orenzia (abatacept)] [1, 6]
   
   \[\text{AND}\]

3. Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]
   
   \[\text{AND}\]

4. Patient is not receiving Humira in combination with a phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)] [1, 6]
Diagnosis | Ankylosing Spondylitis
---|---
Approval Length | 12 Month
Therapy Stage | Initial Authorization
Guideline Type | Prior Authorization

**Approval Criteria**

1. Diagnosis of active ankylosing spondylitis

2. Prescribed by or in consultation with a rheumatologist

3. History of failure, contraindication, or intolerance to two NSAIDs [20, 30]

4. Patient is not receiving Humira in combination with a biologic DMARD [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]
5 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

Product Name: Humira

<table>
<thead>
<tr>
<th>Diagnosis</th>
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</thead>
<tbody>
<tr>
<td>Approval Length</td>
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</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Crohn’s disease [1-4]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>---------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of moderately to severely active Crohn’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), Ocrevus (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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), Ocrevus (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Week</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hidradenitis Suppurativa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

**Product Name:** Humira

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hidradenitis Suppurativa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Ocrenica (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

2. Uveitis is classified as one of the following:
   - intermediate
   - posterior
   - panuveitis

3. Prescribed by or in consultation with one of the following:
   - ophthalmologist
   - rheumatologist

4. Patient is not receiving Humira in combination with a biologic DMARD [eg, Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept)] [1, 6]
5 Patient is not receiving Humira in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1, 6]

**Product Name:** Humira

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Uveitis (UV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Oncia (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

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:


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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>3 Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>3 Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
</tbody>
</table>
### Approval Criteria

<table>
<thead>
<tr>
<th>Guideline Type</th>
<th>Prior Authorization</th>
</tr>
</thead>
</table>

**Product Name:** Synvisc-One

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>1 Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of OA of the knee

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>1 Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>1 Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>1 Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Documentation of improvement in pain with previous course of treatment
2  At least 6 months have elapsed since last injection of the prior treatment cycle [9]

**Product Name:** Genvisc 850, Hyalgan, Supartz, Supartz FX

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>5 Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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]
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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>5 Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>3 or 4 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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**
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>3 or 4 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>2 Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>2 Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Makena (hydroxyprogesterone caproate injection)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td><strong>Reduce Risk of Preterm birth</strong> 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.</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Reduce Risk of Preterm birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>21 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Amenorrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>4 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**
1 Diagnosis of primary or secondary amenorrhea

AND

2 Amenorrhea is due to hormonal imbalance in the absence of organic pathology (e.g., 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Production of secretory endometrium and desquamation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Used for production of secretory endometrium and desquamation

AND

2 Patient is not pregnant
### Product Name: hydroxyprogesterone caproate injection

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Test for endogenous estrogen production</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>2 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Used for the testing of endogenous estrogen production

   **AND**

2. Patient is not pregnant

Notes: This product and its criteria do NOT apply to brand Makena.

### Product Name: hydroxyprogesterone caproate injection

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Adenocarcinoma of uterine corpus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of Stage III or IV adenocarcinoma of the uterine corpus

Notes: 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**

2. **Patient is not pregnant**

Note: This product and its criteria do NOT apply to brand Makena.
3. References

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.
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

<table>
<thead>
<tr>
<th>Drug Name: Ibrance (palbociclib)</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of breast cancer

2. Disease is one of the following: [2,3]
   - Locally advanced
   - Metastatic

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)]
Prescribed by or in consultation with an oncologist

Product Name: Ibrance

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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.


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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Myelogenous Leukemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Myelogenous Leukemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Iclusig

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acute Lymphoblastic Leukemia</th>
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<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acute Lymphoblastic Leukemia</th>
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</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Esbriet (pirfenidone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Idiopathic pulmonary fibrosis</td>
</tr>
<tr>
<td>Indicated for the treatment of idiopathic pulmonary fibrosis (IPF).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Name: Ofev (nintedanib)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
</tbody>
</table>
Idiopathic pulmonary fibrosis
Indicated for the treatment of idiopathic pulmonary fibrosis (IPF)

2. Criteria

Product Name: Esbriet, Ofev

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1 Documentation of positive clinical response to Esbriet or Ofev therapy

3. References
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

<table>
<thead>
<tr>
<th>Drug Name: Ilaris (canakinumab injection)</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cryopyrin-Associated Periodic Syndromes (CAPS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

**Product Name:** Ilaris

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Systemic Juvenile Idiopathic Arthritis (SJIA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

**Product Name:** Ilaris

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>All diagnoses listed above</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<tr>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryopyrin-Associated Periodic Syndromes (CAPS):</td>
<td>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]</td>
</tr>
<tr>
<td>Familial Cold Autoinflammatory Syndrome (FCAS):</td>
<td>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]</td>
</tr>
<tr>
<td>Muckle-Wells Syndrome (MWS):</td>
<td>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]</td>
</tr>
</tbody>
</table>

5 . References

1. Ilaris Prescribing Information. Novartis Pharmaceuticals Corporation, October, 2014

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
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.

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma: Indicated for the treatment of patients with Waldenström's macroglobulinemia (WM).

## 2. Criteria

**Product Name:** Imbruvica

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mantle Cell Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mantle Cell Lymphoma</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Imbruvica

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**Approval Criteria**

1 Diagnosis of one of the following:

- chronic lymphocytic leukemia
- small lymphocytic lymphoma

and
**Approval Criteria**

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

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**Product Name: Imbruvica**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<tr>
<td>Therapy Stage</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
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**Approval Criteria**

1. Diagnosis of Waldenström's Macroglobulinemia

   and

2. Prescribed by or in consultation with a hematologist/oncologist
**Product Name:** Imbruvica

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Waldenstrom's Macroglobulinemia</th>
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<tbody>
<tr>
<td>Approval Length</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</table>

**Approval Criteria**

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

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### 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.

### References

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 $50 \times 10^9 \text{ /L}$ [105]

**Product Name:** Intravenous immune globulins (IVIG)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Kawasaki Disease (KD) [5, 19-21]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1  Diagnosis of Kawasaki Disease [5]

**Product Name:** Intravenous immune globulins (IVIG)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>B-cell Chronic Lymphocytic Leukemia (CLL) [5,22-26]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [27-32, 67, 70, C, H]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [27-32, 67, 70, C, H]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hepatitis A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Course of therapy</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Measles (Rubeola)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Course of therapy</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. For use in susceptible individuals exposed to measles fewer than 6 days previously [69]
2. Patient is not receiving measles vaccine at the same time [69]

**Product Name:** Gamastan S/D

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Varicella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Course of therapy</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. For passive immunization against varicella [69]

2. Patient is immunosuppressed [69]

3. Varicella Zoster Immune Globulin (Human) vaccine is not available

**Product Name:** Gamastan S/D

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rubella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Course of therapy</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
<tr>
<td>----------------</td>
<td>---------------------</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bone Marrow Transplantation (off-label) [33-36]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>HIV(off-label) [47-79, 95]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
</tbody>
</table>
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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Multifocal Motor Neuropathy (off-label) [42-46]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
</tbody>
</table>
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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Multifocal Motor Neuropathy (off-label) [42-46]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Relapsing-Remitting Multiple Sclerosis (off-label) [62-64]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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,
Product Name: Intravenous immune globulin (IVIG)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Relapsing-Remitting Multiple Sclerosis (off-label) [62-64]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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]
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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Myasthenia Gravis Exacerbation (off-label) [57-60]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Stiff Person Syndrome (off-label) [65]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Stiff Person Syndrome (off-label) [65]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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)

<p>| Diagnosis                      | Dermatomyositis and Polymyositis (off-label) [37-41, 75, 77] |</p>
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Dermatomyositis and Polymyositis (off-label) [37-41, 75, 77]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Guillain-Barre Syndrome (off-label) [50-52]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of Guillain-Barre Syndrome

2. Patients with severe disease requiring aid to walk [52, E]

3. Onset of neuropathic symptoms within the last four weeks [52, E]

**Product Name:** Intravenous immune globulin (IVIG)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Guillain-Barre Syndrome (off-label) [50-52]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Lambert-Eaton Myasthenic Syndrome (off-label) [53]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Lambert-Eaton Myasthenic Syndrome (off-label) [53]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
</tbody>
</table>
## Details

<table>
<thead>
<tr>
<th>Therapy Stage</th>
<th>Reauthorization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### Approval Criteria

1. Documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect

**Product Name:** Cytogam

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Prophylaxis for CMV Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>16 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Varicella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Dose</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

3. Carimune NF Prescribing Information. CSL Behring LLC. September 2013.


68. Vivaglobin Prescribing Information. CSL Behring LLC. April 2010.
73. Hizentra Prescribing Information. CSL Behring LLC. January 2015.
74. Privigen Prescribing Information. CSL Behring LLC. November 2013.
78. Flebogamma 5% DIF Prescribing Information. Instituto Grifols. August 2014.
84. Octagam 5% Prescribing Information. Octapharma USA Inc. September 2009.
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.
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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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.

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Crohn's Disease or Fistulizing Crohn's Disease [A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Ocrevus (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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>24 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Ocrevus (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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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]
<table>
<thead>
<tr>
<th>Product Name: Remicade, Inflectra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
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<tr>
<td>Approval Length</td>
</tr>
<tr>
<td>Therapy Stage</td>
</tr>
<tr>
<td>Guideline Type</td>
</tr>
</tbody>
</table>

**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), Ocrevia (abatacept), Kineret (anakinra), Cimzia (certolizumab)]

   **AND**

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

<table>
<thead>
<tr>
<th>Product Name: Remicade, Inflectra</th>
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</thead>
<tbody>
<tr>
<td>Diagnosis</td>
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<tr>
<td>Approval Length</td>
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</tbody>
</table>
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), Ocrevus (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), Oencia (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 | 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), Orenzia (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Psoriatic Arthritis (PsA)</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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), Ocrevus (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Plaque Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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), Ocrevus (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Plaque Psoriasis</th>
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</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sarcoidosis [Off-label] [13,14]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

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), Ocrevus (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sarcoidosis [Off-label] [2, 13,14]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Orenicia (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 Crohn’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 Crohn’s disease < 6 years of age. Long term (greater than one year) safety and efficacy of Remicade in pediatric Crohn’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


490


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

<table>
<thead>
<tr>
<th>Drug Name: Nulojix (belatacept)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td><strong>Prophylaxis of organ rejection in organ transplant</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
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

<table>
<thead>
<tr>
<th>Guideline Type</th>
<th>Non Formulary</th>
</tr>
</thead>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Inlyta (axitinib)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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.
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

<table>
<thead>
<tr>
<th>Drug Name: Istodax (romidepsin)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cutaneous T-cell lymphoma (CTCL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [7, A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Peripheral T-cell lymphoma (PTCL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [7, A]</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Peripheral T-cell lymphoma (PTCL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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 difitox), 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, epidirubicin) alternating with methotrexate, HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with methotrexate 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.
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Myelofibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Months [1, A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. One of the following diagnoses: [1]
   - Primary myelofibrosis
   - Post-polycythemia vera myelofibrosis
   - Post-essential thrombocytopenia myelofibrosis

   **AND**

2. Prescribed by or in consultation with a hematologist/oncologist

**Product Name:** Jakafi

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Polycythemia Vera</th>
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</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>8 Months [1, B]</td>
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<td>-------------------------------------------</td>
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<tr>
<td><strong>Approval Criteria</strong></td>
<td></td>
</tr>
<tr>
<td>1  Diagnosis of polycythemia vera [1]</td>
<td></td>
</tr>
<tr>
<td><strong>AND</strong></td>
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</tr>
<tr>
<td>2  History of failure, contraindication, or intolerance to hydroxyurea [1]</td>
<td></td>
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<tr>
<td><strong>AND</strong></td>
<td></td>
</tr>
<tr>
<td>3  Prescribed by or in consultation with a hematologist/oncologist</td>
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<tr>
<td><strong>Product Name:</strong></td>
<td><strong>Jakafi</strong></td>
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<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>All indications listed above</th>
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<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization (for patients with clinical response)</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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<tr>
<td><strong>Approval Criteria</strong></td>
<td></td>
</tr>
<tr>
<td>1  Documentation of positive clinical response to Jakafi therapy (e.g., spleen volume reduction, symptom improvement, hematocrit control)</td>
<td></td>
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<td><strong>Product Name:</strong> Jakafi</td>
<td></td>
</tr>
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<td>Diagnosis</td>
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<tr>
<td>Approval Length</td>
<td>2 Month*</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization (for patients with no clinical response)</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria
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

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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..
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

<table>
<thead>
<tr>
<th>Drug Name: Kadcyla (ado-trastuzumab emtansine)</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
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</tr>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
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<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</table>

**Approval Criteria**

1. Patient does not show evidence of progressive disease

**3. References**

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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 hypercholesterolemia [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

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

<table>
<thead>
<tr>
<th>Drug Name: Keveyis (dichlorphenamide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.</td>
</tr>
</tbody>
</table>

Indicated for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants.
2. Criteria

Product Name: Keveyis

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>3 Months [A]</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Drug Name: Kineret (anakinra)</th>
</tr>
</thead>
</table>

**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]

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<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Neonatal-Onset Multisystem Inflammatory Disease (NOMID) [1, C]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Neonatal-Onset Multisystem Inflammatory Disease (NOMID) [1, C]</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
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</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Systemic Juvenile Idiopathic Arthritis (SJIA) (off-label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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]
5 Patient is not receiving Kineret in combination with a Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [1,15,A,B]

**Product Name:** Kineret

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Systemic Juvenile Idiopathic Arthritis (SJIA) (off-label)</th>
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<tbody>
<tr>
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<td>Prior Authorization</td>
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</tbody>
</table>

**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


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

<table>
<thead>
<tr>
<th>Drug Name: Krystexxa (pegloticase)</th>
</tr>
</thead>
</table>

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

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<thead>
<tr>
<th>Approval Length</th>
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<tbody>
<tr>
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<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Months [C]</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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. References

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

<table>
<thead>
<tr>
<th>Drug Name: Kuvan (sapropterin dihydrochloride)</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>2 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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</table>
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. 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 months [E]</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<td>Guideline Type</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 months [D]</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<td>Guideline Type</td>
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</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name:</th>
<th>Lenvima (lenvatinib)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
<td></td>
</tr>
<tr>
<td>Differentiated Thyroid Carcinoma</td>
<td>Indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).</td>
</tr>
<tr>
<td>Renal Cell Carcinoma (RCC)</td>
<td>Indicated in combination with everolimus for the treatment of patients with advanced RCC following one prior anti-angiogenic therapy.</td>
</tr>
</tbody>
</table>
2. Criteria

Product Name: Lenvima

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Differentiated thyroid cancer (DTC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
4 Disease is refractory to radioactive iodine treatment

5 Prescribed by or in consultation with an oncologist

Product Name: Lenvima

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Renal Cell Carcinoma (RCC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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. 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

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Drug Name: Lumizyme (alg glucosidase alfa)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Pompe Disease</td>
</tr>
<tr>
<td>Indicated for patients with Pompe disease [acid alpha-glucosidase (GAA) deficiency].</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Name: Myozyme (alg glucosidase alfa)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>5 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Lynparza (olaparib)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>gBRCA-mutated advanced ovarian cancer</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of advanced ovarian cancer

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]

3. History of failure, contraindication, or intolerance to three or more prior lines of chemotherapy (e.g., paclitaxel with cisplatin)
Prescribed by or in consultation with an oncologist

**Product Name:** Lynparza

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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. 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**3. References**

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Multiple Sclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Months [5-6, A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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]
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Multiple Sclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Months [5-6, A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>---------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Prostate Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Months [5-6, A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of advanced hormone-refractory (castration-resistant) prostate cancer
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/mm³

**Product Name:** Mitoxantrone

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Prostate Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Months [5-6, A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acute Non-Lymphocytic Leukemia (ANLL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Months [5-6, A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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.
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

<table>
<thead>
<tr>
<th>Drug Name: Mozobil (plerixafor injection)</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>1 course of therapy (up to four days of therapy). [2, 3, 4, 5, A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Zaxio (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

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. Because 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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*

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
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 "relapsing forms of MS" disease course that is characterized by the occurrence of relapses. [12] The effectiveness of IFNβ 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. 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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**

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

<table>
<thead>
<tr>
<th>Drug Name: Myobloc (rimabotulinumtoxin B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Cervical Dystonia (CD)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cervical Dystonia (also known as spasmodic torticollis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Months for a single dose (up to 10,000 units) [1]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### Approval Criteria

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

**Product Name:** Myobloc

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cervical Dystonia (also known as spasmodic torticollis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Months for a single dose (up to 10,000 units) [1]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myobloc - Recommended Initial Dose:</td>
<td>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.</td>
</tr>
</tbody>
</table>

4. References

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1. Diagnosis of Mucopolysaccharidosis VI (MPS VI, Maroteaux-Lamy Syndrome)

3. References

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

<table>
<thead>
<tr>
<th>Drug Name: Neumega (oprelvekin)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>3 week intervals for up to six cycles post-chemotherapy [C]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia:</td>
<td>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 &lt; 75,000 cells/microliter; Grade 3: 25,000 to &lt; 50,000 cells/microliter; Grade 4: &lt; 25,000 cells/microliter</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Nexavar (sorafenib)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Renal Cell Carcinoma</td>
</tr>
<tr>
<td>Indicated for the treatment of patients with advanced renal cell carcinoma (RCC).</td>
</tr>
<tr>
<td>Hepatocellular Carcinoma</td>
</tr>
<tr>
<td>Indicated for the treatment of patients with unresectable hepatocellular carcinoma (HCC).</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Renal cell carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months [B]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Renal cell carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months [B]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**Product Name: Nexavar**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hepatocellular carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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
### Product Name: Nexavar

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hepatocellular carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

#### Approval Criteria

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

### Product Name: Nexavar

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Thyroid Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

#### 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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Thyroid Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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**


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**

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
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<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
Product Name: Ninlaro*

<table>
<thead>
<tr>
<th>Approval Length</th>
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</tr>
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<tbody>
<tr>
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</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Nplate (romiplostim)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Chronic Idiopathic Thrombocytopenic Purpura (ITP)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
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</tbody>
</table>

Approval Criteria

1 Patient’s platelet count has increased to a level sufficient to avoid clinically important bleeding

3. References


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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
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<tr>
<td>Guideline Type</td>
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</tbody>
</table>

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

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<td>Guideline Type</td>
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</table>

**Approval Criteria**

1. Documentation of positive clinical response (e.g., 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) [e.g., greater than or equal to 880 mcg fluticasone propionate equivalent/day]
       - Additional asthma controller medication [e.g., leukotriene receptor antagonist, long-acting beta-2 agonist (LABA), theophylline]

   OR

   2.2 One maximally-dosed combination ICS/LABA product [e.g., 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. 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).

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### 2. Criteria

**Product Name:** Orencia SC or Orencia IV

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<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
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<td><strong>Guideline Type</strong></td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

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<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
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<tr>
<td>Approval Length</td>
<td>24 Month</td>
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</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Juvenile Idiopathic Arthritis (JIA)</th>
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<tbody>
<tr>
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</tbody>
</table>

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

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<thead>
<tr>
<th>Diagnosis</th>
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<td>Guideline Type</td>
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</tbody>
</table>

**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. 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

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<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Approval Length</td>
<td>6 Months [A]</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

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 rosvastatin 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

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<thead>
<tr>
<th>Diagnosis</th>
<th>Primary Hyperlipidemia</th>
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<tbody>
<tr>
<td>Approval Length</td>
<td>6 Months [A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
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</tbody>
</table>
## 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]

   - 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
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)
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

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<td>Guideline Type</td>
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</tbody>
</table>

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)
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
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) 

\[ \text{and} \]

9. Not used in combination with another proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor 

**Product Name:** Repatha 

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Homozygous Familial Hypercholesterolemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Patient continues to receive statin at the maximally tolerated dose (unless patient has documented inability to take statins) 

\[ \text{and} \]

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) 

\[ \text{and} \]
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)

<table>
<thead>
<tr>
<th>Age, years</th>
<th>First-degree relative LDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-19</td>
<td>$\text{â‰¥ 155}$</td>
</tr>
<tr>
<td>20-29</td>
<td>$\text{â‰¥ 170}$</td>
</tr>
<tr>
<td>30-39</td>
<td>$\text{â‰¥ 190}$</td>
</tr>
<tr>
<td>â‰¥ 40</td>
<td>$\text{â‰¥ 205}$</td>
</tr>
</tbody>
</table>
First-degree relative with tendon xanthoma and/or corneal arcus (score: 2)

Children aged < 18 years with LDL-C ≥ 155 mg/dL (score: 2)

ii. Group 2: Personal clinical history

Premature CHD (male < 55 years of age; female < 60 years of age) (score: 2)

Premature cerebrovascular or peripheral vascular disease (male < 55 years of age; female < 60 years of age) (score: 1)

iii. Group 3: Physical exam

Tendon xanthoma (score: 6)

Corneal arcus in subject manifesting before 45 years of age (score: 4)

iv. Group 4: LDL-C level

> 325 mg/dL (> 8.5 mmol/L) (score: 8)

251-325 mg/dL (6.5-8.4 mmol/L) (score: 5)

191-250 mg/dL (5.0-6.4 mmol/L) (score: 3)

155-190 mg/dL (4.0-4.9 mmol/L) (score: 1)

v. Group 5: Genetic testing

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 4–12 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
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 ≥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

2. Repatha Prescribing Information. Amgen Inc. August 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

<table>
<thead>
<tr>
<th>Drug Name: Perjeta (pertuzumab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Metastatic Breast Cancer (first-line therapy)</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Metastatic breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Metastatic breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
<tr>
<td>----------------</td>
<td>---------------------</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Perjeta

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Early Stage, Locally-Advanced, or Inflammatory Breast Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month* [B]</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**References**

1. Pomalyst Prescribing Information, Celgene Corporation, Summit, NJ. May 2014.
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

2. Criteria

Product Name: Portrazza

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>6 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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**

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

<table>
<thead>
<tr>
<th>Drug Name: Procysbi (cysteamine bitartrate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Nephropathic cystinosis</td>
</tr>
</tbody>
</table>

Indicated for the management of nephropathic cystinosis in adults and children ages 2 years and older.
2. Criteria

**Product Name:** Procysbi

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of nephropathic cystinosis

2. Diagnosis is confirmed by elevated leukocyte cystine levels (LCL) or genetic analysis of the CTNS gene [A, 2, 3]

3. History of failure or intolerance to Cystagon (immediate-release cysteamine bitartrate)

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

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

<table>
<thead>
<tr>
<th>Drug Name:</th>
<th>Prolia (denosumab)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
<td>Treatment of postmenopausal women with osteoporosis at high risk for fracture</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bone loss in men receiving androgen deprivation therapy for nonmetastatic prostate cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [D]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bone loss in men receiving androgen deprivation therapy for nonmetastatic prostate cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [D]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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)
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bone loss in women receiving adjuvant aromatase inhibitor therapy for breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [D]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bone loss in women receiving adjuvant aromatase inhibitor therapy for breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Prevention of postmenopausal osteoporosis [off-label]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Prevention of postmenopausal osteoporosis [off-label]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
<tr>
<td>-----------------------</td>
<td>---------------------</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Patient is benefiting from therapy (e.g., improved or stabilized BMD, no new fractures, improved biochemical markers, etc.)

**Product Name: Prolia**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Postmenopausal women with osteoporosis at a high risk for fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Postmenopausal women with osteoporosis at a high risk for fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Patient is benefiting from therapy (e.g., improved or stabilized BMD, no new fractures, improved biochemical markers, etc.)
**Product Name:** Prolia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Increase bone mass in men at high risk for fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Increase bone mass in men at high risk for fracture</th>
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</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone mineral density (BMD) [3]</td>
<td>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.</td>
</tr>
<tr>
<td>Dual x-ray absorptiometry (DXA) [3]</td>
<td>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.</td>
</tr>
<tr>
<td>Fracture [3]</td>
<td>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.</td>
</tr>
<tr>
<td>Osteopenia [3]</td>
<td>The designation for bone density between 1.0 and 2.5 standard deviations below the mean for young normal adults</td>
</tr>
<tr>
<td>Term</td>
<td>Description</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Osteoporosis [3]</td>
<td>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).</td>
</tr>
<tr>
<td>Quantitative computed tomography (QCT) [3]</td>
<td>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).</td>
</tr>
<tr>
<td>Quantitative ultrasound densitometry (QUS) [3]</td>
<td>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.</td>
</tr>
<tr>
<td>Resorption [3]</td>
<td>The loss of substance (in this case, bone) through physiological or pathological means.</td>
</tr>
<tr>
<td>Risk factors [3]</td>
<td>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.</td>
</tr>
<tr>
<td>Severe or “established” osteoporosis [3]</td>
<td>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.</td>
</tr>
</tbody>
</table>
In describing bone mineral density, the number of standard deviations above or below the mean for young normal adults of the same sex.

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. 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.

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.

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.

6. References

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

<table>
<thead>
<tr>
<th>Drug Name: Promacta (eltrombopag)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Idiopathic Thrombocytopenic Purpura (ITP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Hepatitis C-Associated Thrombocytopenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>9 weeks [A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Diagnosis of chronic hepatitis C
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Hepatitis C-Associated Thrombocytopenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Severe Aplastic Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>16 weeks [B]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Severe Aplastic Anemia</th>
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<tbody>
<tr>
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<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<td>Guideline Type</td>
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</table>

Approval Criteria
**Product Name:** Promacta

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Idiopathic Thrombocytopenic Purpura (ITP)</th>
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<tbody>
<tr>
<td>Approval Length</td>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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.
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 (epoprostol 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 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: 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pulmonary Arterial Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pulmonary Arterial Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pulmonary Arterial Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Thromboembolic Pulmonary Hypertension (CTEPH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>All indications listed above</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1 Documentation of positive clinical response to therapy

**Product Name:** Revatio oral suspension

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pulmonary Arterial Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pulmonary Arterial Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pulmonary Arterial Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary arterial hypertension (PAH)</td>
<td>Is characterized by a progressive increase in pulmonary vascular resistance leading to right ventricular failure and death. [2]</td>
</tr>
</tbody>
</table>

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
- 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, fatigue, chest pain, or presyncope.
- Class IV: Patients with pulmonary hypertension who have a cy孫 medication limitations.
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.
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.


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

<table>
<thead>
<tr>
<th>Drug Name: Pulmozyme (dornase alpha) Inhalation Solution</th>
</tr>
</thead>
</table>

**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*

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1. Diagnosis of cystic fibrosis (CF)

Notes

*Prior Authorization may not apply depending on the plan

Product Name: Pulmozyme*

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
3. References

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

<table>
<thead>
<tr>
<th>Drug Name: Ravicti (glycerol phenylbutyrate)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Drug Name: Relistor (methylnaltrexone bromide)</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>4 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>4 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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.
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Myelodysplastic Syndromes (MDS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Multiple Myeloma (MM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mantle Cell Lymphoma (MCL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Myelodysplastic Syndromes, Multiple Myeloma, Mantle Cell Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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. 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

**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 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), Orenica (abatacept), Kineret (anakinra)] [19]

AND

6 Not received in combination with a janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [19]

**Product Name:** Rituxan

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Month</td>
</tr>
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<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1 Documentation of positive clinical response to Rituxan therapy
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]

2. At least 16 weeks have elapsed since last course of therapy [1,B]

3. Not received in combination with a biologic DMARD [e.g., Enbrel (etanercept), Oncia (abatacept), Kineret (anakinra)] [19]

4. Not received in combination with a janus kinase inhibitor [e.g., Xeljanz (tofacitinib)] [19]
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-Hodgkin’s Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Immune or Idiopathic Thrombocytopenic Purpura [17-18] (Off-Label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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 $50 \times 10^9 / L$ [29]

**Product Name:** Rituxan

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Other Indications</th>
</tr>
</thead>
</table>

740
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

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 months [A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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


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

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<thead>
<tr>
<th>Diagnosis</th>
<th>Acromegaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acromegaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Carcinoid Tumors, for Symptomatic Treatment of Diarrhea or Flushing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Carcinoid Tumors, for Symptomatic Treatment of Diarrhea or Flushing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

Approval Criteria

1. Documentation of an improvement in the number of diarrhea and flushing episodes

Product Name: Brand Sandostatin, Generic octreotide, or Sandostatin LAR

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Vasoactive Intestinal Peptide Tumors, for Symptomatic Treatment of Diarrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Vasoactive Intestinal Peptide Tumors, for Symptomatic Treatment of Diarrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Documentation of an improvement in the number of diarrhea episodes

3 References
# 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

<table>
<thead>
<tr>
<th>Drug Name: Selzentry (maraviroc)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>CCR5-tropic HIV-1</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Drug Name: Signifor LAR (pasireotide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Acromegaly</td>
</tr>
<tr>
<td>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.</td>
</tr>
</tbody>
</table>

| 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acromegaly</th>
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</thead>
<tbody>
<tr>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acromegaly</th>
</tr>
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<tbody>
<tr>
<td>Approval Length</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Approval Length</td>
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<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cushing’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Drug Name: Simponi (golimumab) - for subcutaneous use</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Indications</th>
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</thead>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
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<tr>
<td>Therapy Stage</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Ocrevus (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Psoriatic Arthritis (PsA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
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<td>Prior Authorization</td>
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</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Psoriatic Arthritis (PsA)</th>
</tr>
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<tbody>
<tr>
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</tbody>
</table>
Approval Criteria

1  Documentation of positive clinical response to Simponi therapy

\[ \text{AND} \]

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

\[ \text{AND} \]

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

Product Name: Simponi

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ankylosing Spondylitis (AS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1  Diagnosis of active ankylosing spondylitis

\[ \text{AND} \]
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ankylosing Spondylitis (AS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ulcerative Colitis (UC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>10 Week</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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), Orenzia (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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ulcerative Colitis (UC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>24 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>---------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Orecnia (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

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

<table>
<thead>
<tr>
<th>Drug Name: Soliris (eculizumab)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Paroxysmal Nocturnal Hemoglobinuria (PNH), Atypical Hemolytic Uremic Syndrome (aHUS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Paroxysmal Nocturnal Hemoglobinuria (PNH), Atypical Hemolytic Uremic Syndrome (aHUS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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


# 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acromegaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1. Diagnosis of acromegaly

   AND

2. One of the following:

   2.1 Inadequate response to one of the following:

   • Surgery
   • Radiotherapy

   OR


<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acromegaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NET)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NET)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

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

3. References

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Documentation of positive clinical response to Somavert therapy (such as biochemical control; decrease or normalization of IGF-1 levels)

**3. References**


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

<table>
<thead>
<tr>
<th>Drug Name: Sprycel (dasatinib)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Newly diagnosed Chronic Myelogenous Leukemia</td>
</tr>
<tr>
<td>Resistant or intolerant Chronic Myelogenous Leukemia</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acute Lymphoblastic Leukemia/Acute Lymphoblastic Lymphoma (ALL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Acute Lymphoblastic Leukemia/Acute Lymphoblastic Lymphoma (ALL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
</tbody>
</table>
Therapy Stage | Reauthorization
---|---
Guideline Type | Prior Authorization

**Approval Criteria**

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

**Product Name:** Sprycel

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Myelogenous/Myeloid Leukemia (CML)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Myelogenous/Myeloid Leukemia (CML)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Stivarga (regorafenib)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
<td></td>
</tr>
<tr>
<td>Metastatic Colorectal Cancer (mCRC)</td>
<td>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.</td>
</tr>
<tr>
<td>Gastrointestinal STromal Tumor (GIST)</td>
<td></td>
</tr>
</tbody>
</table>

794
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Metastatic Colorectal Cancer (mCRC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Metastatic Colorectal Cancer (mCRC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stivarga</td>
<td>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).</td>
</tr>
</tbody>
</table>

4 . Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stivarga</td>
<td>40 mg regorafenib tablets</td>
</tr>
</tbody>
</table>

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
6. References

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

<table>
<thead>
<tr>
<th>Drug Name: Strensiq (asfotase alfa)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of perinatal/infantile or juvenile-onset hypophosphatasia (HPP) [A-C]  

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of perinatal/infantile or juvenile-onset hypophosphatasia (HPP) [A-C]  

2. Prescribed by or in consultation with a specialist experienced in the treatment of inborn errors of metabolism [A]
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

Available at: http://www.clinicalendocrinologynews.com

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.

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.

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.

1. Indications

<table>
<thead>
<tr>
<th>Drug Name: Sutent (sunitinib)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Advanced pancreatic neuroendocrine tumors (pNET)</td>
</tr>
<tr>
<td>Indicated for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable locally advanced or metastatic disease.</td>
</tr>
<tr>
<td>Gastrointestinal stromal tumor (GIST)</td>
</tr>
<tr>
<td>Indicated for the treatment of gastrointestinal stromal tumor after disease progression on or</td>
</tr>
</tbody>
</table>
intolerance to imatinib mesylate.

**Renal cell carcinoma (RCC)**
Indicated for the treatment of advanced renal cell carcinoma.

## 2. Criteria

**Product Name:** Sutent

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Gastrointestinal Stromal Tumor (GIST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Gastrointestinal Stromal Tumor (GIST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Sutent

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pancreatic Neuroendocrine Tumors (pNET)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pancreatic Neuroendocrine Tumors (pNET)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Sutent

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Renal Cell Carcinoma (RCC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of advanced/metastatic renal cell carcinoma (RCC)

   AND
Prescribed by or in consultation with an oncologist

**Product Name:** Sutent

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Renal Cell Carcinoma (RCC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**References**

1. Indications

<table>
<thead>
<tr>
<th>Drug Name: Sylatron (peginterferon alfa-2b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Melanoma</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**
1. Patient does not show evidence of progressive disease while on Sylatron therapy

3. References

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Premature Infants (without other indications)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>5 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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]
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Lung Disease of Prematurity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>5 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hemodynamically Significant Congenital Heart Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>5 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pulmonary Abnormality or Neuromuscular Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>5 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Immunocompromised Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>5 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

- Pediatric pulmonologist
- Infectious disease specialist
- Pediatric intensivist

5 Used for the prevention of serious lower respiratory tract disease caused by RSV during the RSV season for the patient's geographic region

<table>
<thead>
<tr>
<th>Notes</th>
<th>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]</th>
</tr>
</thead>
</table>

**Product Name:** Synagis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Children with Cystic Fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>5 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1 Diagnosis of cystic fibrosis [2]
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 coarctation 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

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

<table>
<thead>
<tr>
<th>Drug Name: Synribo (omacetaxine mepesuccinate)</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Patient has not experienced disease progression

---

### 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]

---

### References

1. Synribo [Package Insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc. April, 2014
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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
Prescribed by or in consultation with an oncologist

**Product Name:** Tafinlar

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**References**

**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**

<table>
<thead>
<tr>
<th>Drug Name: Tagrisso (osimertinib)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td><strong>Non-small cell lung cancer</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
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</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

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</tr>
</tbody>
</table>

**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 signs 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


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

<table>
<thead>
<tr>
<th>Drug Name: Tarceva (erlotinib)</th>
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<tbody>
<tr>
<td><strong>Indications</strong></td>
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</table>

<table>
<thead>
<tr>
<th>Non-Small Cell Lung Cancer (NSCLC)</th>
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</thead>
<tbody>
<tr>
<td>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</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-Small Cell Lung Cancer (NSCLC)</th>
</tr>
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<tbody>
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</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Non-Small Cell Lung Cancer (NSCLC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</tbody>
</table>
Approval Criteria

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

Product Name: Tarceva

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pancreatic Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
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</table>

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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pancreatic Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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</tbody>
</table>

**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**

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

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<thead>
<tr>
<th>Approval Length</th>
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<tbody>
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</table>

**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

<table>
<thead>
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</tbody>
</table>

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

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

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</tbody>
</table>

**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 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 [2]

Product Name: Tasigna

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</table>

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

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

<table>
<thead>
<tr>
<th>Drug Name: Temodar (temozolomide)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Glioblastoma Multiforme</th>
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<tbody>
<tr>
<td>Approval Length</td>
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</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
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<td>Guideline Type</td>
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</tbody>
</table>

**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
3 Prescribed by or in consultation with an oncologist

**Product Name:** Brand Temodar, Generic temozolomide

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Glioblastoma Multiforme</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Brand Temodar, Generic temozolomide

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anaplastic Astrocytoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
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</tbody>
</table>

**Approval Criteria**

1. Diagnosis of anaplastic astrocytoma

AND
Patient's condition has progressed on a drug regimen containing nitrosourea and procarbazine

AND

Prescribed by or in consultation with an oncologist

**Product Name:** Brand Temodar, Generic temozolomide

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<th>Diagnosis</th>
<th>Anaplastic Astrocytoma</th>
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</tbody>
</table>

**Approval Criteria**

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

**References**

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.
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®

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Male hypogonadism</th>
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<tbody>
<tr>
<td>Approval Length</td>
<td>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]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
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<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</table>

**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^

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Gender Identity Disorder (off-label) [8]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>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]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Inoperable breast cancer in women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>1 Year</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Diagnosis of breast cancer

AND

2 Breast cancer is inoperable

AND

3 Used for palliative treatment

AND
<table>
<thead>
<tr>
<th>4</th>
<th>Female patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notes</td>
<td><em>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]</em></td>
</tr>
</tbody>
</table>

**Product Name:** Generic testosterone enanthate*, Testopel*, Testosterone implant pellets*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Delayed puberty [A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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 testosterone 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 Society (AGS) Beers Criteria list of inappropriate medications in older adults (greater than or equal to 65 years old). [11]

4. References

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

<table>
<thead>
<tr>
<th>Drug Name: Thalomid (thalidomide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Erythema Nodosum Leprosum (ENL)</td>
</tr>
</tbody>
</table>

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


2. Criteria

Product Name: Thalomid

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Erythema Nodosum Leprosum (ENL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [1, 40]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1. Diagnosis of moderate to severe erythema nodosum leprosum (ENL) with cutaneous manifestations [1]

Product Name: Thalomid

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Erythema Nodosum Leprosum (ENL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [1, 40]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>-----------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Documentation of positive clinical response to Thalomid therapy

**Product Name:** Thalomid

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Multiple Myeloma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 months [1, 4]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

---

### References

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:


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

<table>
<thead>
<tr>
<th>Drug Name: Thyrogen (thyrotropin alfa for injection)</th>
</tr>
</thead>
</table>

**Indications**

**Thyroid cancer**

Indicated for: 1. Use as an adjunctive diagnostic tool for serum thyroglobulin (Tg) testing with or without radiiodine imaging in the follow-up of patients with well-differentiated thyroid cancer. 2. Use as an adjunctive treatment for radiiodine 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>1 course of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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]
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

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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), Arimidex (anastrozole)]

   AND
3 Prescribed by or in consultation with an oncologist

**Product Name:** Tykerb

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Patient does not show evidence of progressive disease

### References

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.

**Crohn’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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Multiple Sclerosis (MS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Crohn’s Disease (CD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Months [E]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)
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)

4 History of inadequate response or intolerance to a tumor necrosis factor (TNF)-inhibitor (e.g., Cimzia [certolizumab pegol], Humira [adalimumab], Remicade [infliximab])

5 Not used in combination with an immunosuppressant (e.g., 6-MP, azathioprine, cyclosporine, or methotrexate) [B, D]

6 Not used in combination with a TNF-inhibitor (e.g., Enbrel [etanercept], Humira [adalimumab], or Remicade [infliximab]) [B, D]

**Product Name:** Tysabri

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Crohn’s Disease (CD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>---------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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 monotherapy 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 Crohn'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


**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

<table>
<thead>
<tr>
<th>Drug Name: Valchlor (mechlorethamine gel)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Mycosis fungoides-type cutaneous T-cell lymphoma (MF-CTCL)</td>
</tr>
<tr>
<td>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.</td>
</tr>
</tbody>
</table>
2. Criteria

**Product Name:** Valchlor

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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)

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.]

3. Prescribed by or in consultation with an oncologist or dermatologist

**Product Name:** Valchlor

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
Approval Criteria

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

3. References

**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

<table>
<thead>
<tr>
<th>Drug Name: Velcade (bortezomib)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Multiple Myeloma</td>
</tr>
<tr>
<td>Indicated for the treatment of patients with multiple myeloma</td>
</tr>
<tr>
<td>Mantle Cell Lymphoma</td>
</tr>
<tr>
<td>Indicated for the treatment of patients with mantle cell lymphoma</td>
</tr>
</tbody>
</table>
2. Criteria

**Product Name:** Velcade

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Multiple Myeloma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of multiple myeloma [1,5]

   AND

2. Prescribed by or in consultation with a hematologist/oncologist

**Product Name:** Velcade

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mantle Cell Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of mantle cell lymphoma [1,3,4,6]
2 Prescribed by or in consultation with a hematologist/oncologist

3. References

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

<table>
<thead>
<tr>
<th>Drug Name: Vimizim (elosulfase alfa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Mucopolysaccharidosis type IVA</td>
</tr>
<tr>
<td>Indicated for patients with Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome).</td>
</tr>
</tbody>
</table>
2. Criteria

**Product Name:** Vimizim

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome)

3. References

**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

<table>
<thead>
<tr>
<th>Drug Name: Votrient (pazopanib)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td><strong>Renal Cell Carcinoma (RCC)</strong></td>
</tr>
<tr>
<td>Indicated for the treatment of patients with advanced RCC.</td>
</tr>
<tr>
<td><strong>Soft tissue sarcoma (STS)</strong></td>
</tr>
<tr>
<td>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</td>
</tr>
</tbody>
</table>
patients with adipocytic STS or gastrointestinal stromal tumors has not been demonstrated.

2. Criteria

**Product Name:** Votrient

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Renal Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Renal Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

**Product Name:** Votrient

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Soft tissue sarcoma (STS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<p>| Diagnosis                | Soft tissue sarcoma (STS) |</p>
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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**


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.

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

<table>
<thead>
<tr>
<th>Drug Name: Xalkori (crizotinib)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
<tr>
<td>Non-small cell lung cancer (NSCLC)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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 (crizotinib) 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


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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chorea associated with Huntington's disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months [C]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chorea associated with Huntington’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
**Approval Criteria**

1. Documentation of positive clinical response to therapy

**Product Name:** Brand Xenazine, Generic tetrabenazine

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Tardive dyskinesia (Off-label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months [C]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Tardive dyskinesia (Off-label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Documentation of positive clinical response to therapy

**Product Name:** Brand Xenazine, Generic tetrabenazine

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Tourette’s syndrome (Off-label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 Months [C]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Tourette’s syndrome (Off-label)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

It 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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cervical Dystonia (also known as spasmodic torticollis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months (for 1 dose) [A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

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

Product Name: Xeomin (incobotulinumtoxinA)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cervical Dystonia (also known as spasmodic torticollis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months (for 1 dose) [A]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
</tbody>
</table>
### 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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Blepharospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months (for 1 dose) [1, B]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
</tbody>
</table>

### 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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Blepharospasm</th>
</tr>
</thead>
</table>
**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)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Upper Limb Spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months (for 1 dose) [1, 6]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of upper limb spasticity [1]

**Product Name:** Xeomin (incobotulinumtoxinA)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Upper Limb Spasticity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months (for 1 dose) [1, 6, D]</td>
</tr>
</tbody>
</table>
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.
**Prior Authorization Guideline**

GL-17444 Xgeva (denosumab)

**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**

<table>
<thead>
<tr>
<th>Drug Name: Xgeva (denosumab)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Bone metastasis from solid tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month [B]</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Giant cell tumor of bone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month [C]</td>
</tr>
<tr>
<td>-----------------</td>
<td>------------</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Giant cell tumor of bone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
</tbody>
</table>
**Guideline Type** | Prior Authorization
--- | ---

### Approval Criteria

1. Patient does not show evidence of progressive disease while on Xgeva therapy [C]

**Product Name:** Xgeva

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hypercalcemia of malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>2 Month [D]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>Therapy Stage</th>
<th>Guideline Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Month [D]</td>
<td>Reauthorization</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

#### Approval Criteria

1. Documentation of positive clinical response to Xgeva therapy

#### 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]

#### References


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

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>Dupuytren’s contracture</td>
</tr>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Peyronie’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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
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. 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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Allergic Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 months [B]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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]
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Idiopathic Urticaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>3 months [E]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Allergic Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 months [B]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Idiopathic Urticaria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>6 months [B]</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Patient’s disease status has been re-evaluated since the last authorization to confirm the patient’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


4. Per clinical consult with asthma specialist, January 6, 2011.


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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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**

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Narcolepsy with Cataplexy (Narcolepsy Type 1) [2, 3, A-D]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

\[ \text{AND} \]

3 Symptoms of excessive daytime sleepiness (e.g., irrepresible need to sleep or daytime lapses into sleep) are present

\[ \text{AND} \]

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Narcolepsy without Cataplexy (Narcolepsy Type 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
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</table>

**Approval Criteria**

1 Documentation demonstrating a reduction in symptoms of excessive daytime sleepiness associated with Xyrem therapy
3. Background

<table>
<thead>
<tr>
<th>Benefit/Coverage/Program Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity Limit</td>
</tr>
</tbody>
</table>

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 irrepessible 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 irrepessible 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

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

<table>
<thead>
<tr>
<th>Drug Name: Yervoy (ipilimumab)</th>
</tr>
</thead>
</table>

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
2. Criteria

Product Name: Yervoy

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Unresectable or Metastatic Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>4 doses or up to 16 weeks from the first dose, whichever occurs first [A]</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cutaneous Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months</td>
</tr>
<tr>
<td>-----------------</td>
<td>-----------</td>
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<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Diagnosis of cutaneous melanoma

   \[\text{AND}\]

2. Disease with pathologic involvement of regional lymph nodes of more than 1 mm

   \[\text{AND}\]

3. Patient has undergone resection, including total lymphadenectomy

   \[\text{AND}\]

4. Prescribed by or in consultation with an oncologist

**Product Name:** Yervoy

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cutaneous Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Months</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
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<td>Guideline Type</td>
<td>Prior Authorization</td>
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<td>---------------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>Approval Criteria</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Patient does not show evidence of progressive disease while on Yervoy therapy</td>
</tr>
</tbody>
</table>

### 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. 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

1. Patient does not show evidence of progressive disease

---

## 3. References

1. Zaltrap Prescribing Information. Sanofi Aventis, March, 2016
# 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

<table>
<thead>
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<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td><strong>Melanoma</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month [B]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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 (e.g., 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month [B]</th>
</tr>
</thead>
</table>
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**

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Hepatitis C - Genotype 1a: treatment-naïve or PegIFN/RBV-experienced or PegIFN/RBV/protease inhibitor-experienced without baseline NS5A polymorphisms*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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-naïve

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
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]
**NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.

**Product Name:** Zepatier

**Diagnosis:**
Chronic Hepatitis C - Genotype 1a: treatment-naive 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
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-naïve 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-naïve

   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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Hepatitis C - Genotype 4: Treatment-naive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

1 Submission of medical records (eg, chart notes, laboratory values) documenting a diagnosis of genotype 4
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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Hepatitis C - Genotype 4: PegIFN/RBV-experienced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>16 Week</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
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)]
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

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

<table>
<thead>
<tr>
<th>Drug Name: Zolinza (vorinostat)</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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
<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Drug Name: Zortress (everolimus)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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

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

<table>
<thead>
<tr>
<th>Drug Name: Zydelig (idelalisib)</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Chronic Lymphocytic Leukemia (CLL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Small Lymphocytic Lymphoma (SLL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Follicular Lymphoma (FL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
</tr>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**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]
3 Prescribed by or in consultation with an oncologist/hematologist

**Product Name:** Zydelig

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>All diagnoses listed above</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Length</td>
<td>12 Month</td>
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<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

**Approval Criteria**

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

3. **References**

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

<table>
<thead>
<tr>
<th>Drug Name: Zykadia (ceritinib)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
</tr>
<tr>
<td>Non-small cell lung cancer (NSCLC)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

Approval Criteria

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

3. References

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Initial Authorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Approval Length</th>
<th>12 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy Stage</td>
<td>Reauthorization</td>
</tr>
<tr>
<td>Guideline Type</td>
<td>Prior Authorization</td>
</tr>
</tbody>
</table>
Approval Criteria

1. Patient does not show evidence of progressive disease

3. References