GROWTH HORMONE AND RELATED THERAPIES
Pharmacy Coverage Policy

P&T Review Date: 11/19/2014
UMC Revision Date: 10/23/2014
Reviewer Initials: CYB
Effective Date: 02/15/2015

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>GPI</th>
<th>Drug Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotropin</td>
<td>somatropin</td>
<td>3010002000****</td>
<td>Growth hormone and related therapy</td>
</tr>
<tr>
<td>Humatrope</td>
<td>somatropin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norditropin</td>
<td>somatropin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutropin/Nutropin AQ</td>
<td>somatropin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omnitrope</td>
<td>somatropin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saizen</td>
<td>somatropin</td>
<td>301000201021**</td>
<td></td>
</tr>
<tr>
<td>Serostim</td>
<td>somatropin</td>
<td>301000201021**</td>
<td></td>
</tr>
<tr>
<td>Tev-Tropin</td>
<td>somatropin</td>
<td>3010002000****</td>
<td></td>
</tr>
<tr>
<td>Zorbtive</td>
<td>somatropin</td>
<td>301000201021**</td>
<td></td>
</tr>
</tbody>
</table>

CRITERIA FOR COVERAGE/NONCOVERAGE

GROWTH HORMONE (somatropin) will be considered for coverage under the pharmacy benefit program when the following criteria are met:

FOR GENOTROPIN, HUMATROPE, NORDITROPIN, NUTROPIN/NUTROPIN AQ, OMNITROPE, SAIZEN, SEROSTIM, AND TEV-TROPIN
- Patient does not have any of the following contraindications:
  - Acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure
  - Active malignancy
  - Active proliferative or severe non-proliferative diabetic retinopathy

AND
- Patient has tried and had an inadequate response or intolerance to Norditropin or Nutropin/Nutropin AQ (for Genotropin, Humatrope, Omnitrope, Saizen, and Tev-Tropin only)

Pediatric Patients (less than 18 years of age)
- The prescription is written by or in consultation with a pediatric endocrinologist

AND
- The patient’s epiphyses are open

AND
- The patient has one of the following set of criteria:

Growth hormone deficiency (GHD)
- Patient has a diagnosis of growth hormone deficiency AND one of the following:
  - Height more than 3 SD below the mean for same age and sex
  - Height more than 2 SD below the mean for same age and sex AND decreased growth velocity more than 1 SD below the mean for same age and sex
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- Growth velocity (GV) measured 2 SD below the mean over one year or 1.5 SD below the mean sustained over two years for same age and sex

AND
- Other causes of growth failure have been ruled out (e.g., hypothyroidism, chronic systemic disease, skeletal disorders, malnutrition)

AND
- The patient has had an inadequate response to two (2) pharmacological GH stimulation tests (peak level below 10 ng/mL)
  OR
- The patient has had an inadequate response to at least one (1) pharmacological GH stimulation test (peak level below 10 ng/mL) for patient with defined CNS pathology, multiple pituitary hormone deficiencies, history of irradiation, or proven genetic cause

Note: acceptable tests include: arginine, clonidine, glucagon, insulin levodopa)

Small for gestational age (SGA)
- The patient has a diagnosis of small for gestational age (SGA) AND
- The patient is 2 years of age or older AND
- The patient’s birth weight or length was at least 2 SD below the mean for gestational age AND
- The patient failed to manifest catch up growth by 2 years of age, defined as height at least 2 SD below the mean for same age and sex

Growth failure due to chronic renal insufficiency
- The patient has a diagnosis of chronic renal insufficiency AND
- The patient’s nutritional status has been optimized and metabolic abnormalities have been corrected AND
- Patient has not had a kidney transplant AND
- Patient’s height is less than the 3rd percentile OR a GV measured over 1 year greater than 2 SD below the mean for same age and sex

Growth failure due to Prader-Willi syndrome
- The patient has a diagnosis of Prader-Willi syndrome confirmed by appropriate genetic testing AND
- The patient does not have any of the following exclusions to therapy: severe obesity, history of upper airway obstruction or sleep apnea, or severe respiratory impairment AND
- Height is more than 2 SD below the mean for same age and sex

Growth failure due to Turner's syndrome
- The patient has a diagnosis of Turner's syndrome confirmed by chromosome analysis AND
- The patient has a height less than the 5th percentile for same age and sex

Short Stature Homeobox-containing Gene (SHOX) Deficiency or Noonan Syndrome
- The patient has a diagnosis of SHOX or Noonan syndrome AND one of the following:
  - Height more than 3 SD below the mean for same age and sex
  - Height more than 2 SD below the mean for same age and sex AND decreased growth velocity more than 1 SD below the mean for same age and sex
  - Growth velocity (GV) measured 2 SD below the mean over one year or 1.5 SD below the mean sustained over two years for same age and sex
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Adult Patients (18 years of age or older)
- The prescription is written by or in consultation with an endocrinologist AND
- Patient completed linear growth as defined by growth rate of less than 2 cm/year AND
- GH treatment has been discontinued for at least one month (if previously treated with somatropin for GHD in childhood)

AND
- Patient has one of the following diagnosis:
  o Patient has a diagnosis of childhood or adult-onset GHD confirmed or reconfirmed by an inadequate response to TWO standard GH stimulation tests (assay type must be provided):
    — At least one test must be the insulin tolerance test (ITT) with documented blood glucose nadir of less than 40 mg/dL (less than 2.2mmol/L) OR
    — If ITT is contraindicated (which must be documented), then other stimulation tests include: arginine plus GHRH (preferred, if available), glucagon, or arginine

Subnormal GH Peak Measurements Based on Stimulation Test

<table>
<thead>
<tr>
<th>GH Stimulation Test</th>
<th>Peak GH level</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT</td>
<td>5 ng/mL or less</td>
<td>N/A</td>
</tr>
<tr>
<td>Arginine+GHRH</td>
<td>11 ng/mL or less</td>
<td>Less than 25 kg/m²</td>
</tr>
<tr>
<td></td>
<td>8 ng/mL or less</td>
<td>≥ 25 and &lt;30 kg/m²</td>
</tr>
<tr>
<td></td>
<td>4 ng/mL or less</td>
<td>30 kg/m² or greater</td>
</tr>
<tr>
<td>Glucagon</td>
<td>3 ng/mL or less</td>
<td>N/A</td>
</tr>
<tr>
<td>Arginine</td>
<td>0.4 ng/mL or less</td>
<td>N/A</td>
</tr>
</tbody>
</table>

ITT= insulin tolerance test; GHRH=growth hormone releasing hormone

- GHD with at least one additional pituitary hormone deficiency confirmed by a subnormal response to at least one GH stimulation test (ITT is test of choice unless contraindicated, which must be documented [see above for peak GH level requirements])
- GHD with panhypopituitarism (three or more documented pituitary hormone deficiencies) and low IGF-1 level
- GHD with irreversible hypothalamic-pituitary structural lesions as a result of tumors, surgery or radiation of the pituitary or hypothalamus region AND a subnormal IGF-1 (after at least one month off of GH therapy in patients previous receiving GH therapy)

AND
- Patient has objective evidence of complications from GHD, which can include any of the following:
  o Low bone density as measured by BMD T-score
  o Increased visceral fat mass measured by CT
  o Cardiovascular complications (e.g., elevated blood pressure, elevated C-reactive protein, low HDL, elevated LDL or total cholesterol, increased intima-media thickness, or reduced left ventricular mass or left ventricular end diastolic volume)

SEROSTIM
- Patient does not have any of the following contraindications:
  o Acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure
  o Active malignancy
  o Active proliferative or severe non-proliferative diabetic retinopathy

AND
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- The medication is prescribed by or in consultation with an infectious disease specialist
- Patient has a diagnosis of AIDS-wasting syndrome or cachexia (defined as unintentional weight loss ≥10% of baseline weight) AND
- Patient has tried and had an inadequate response or intolerance to dronabinol or megestrol AND
- Patient is currently receiving treatment with antiretrovirals

ZORBTIVE
- Patient does not have any of the following contraindications:
  - Acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure
  - Active malignancy

AND
- The medication is prescribed by or in consultation with a gastroenterologist
- Patient has a diagnosis of short bowel syndrome AND
- Patient is receiving specialized nutritional support (i.e. parenteral nutrition)

Authorization Duration and Renewal Criteria
Initial and renewal authorization will be approved for the duration specified in the table below.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Initial Approval</th>
<th>Renewal Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHD and growth failure in pediatric patients</td>
<td>6 months</td>
<td>6 months</td>
</tr>
<tr>
<td>GHD in adult patients</td>
<td>12 months</td>
<td>12 months</td>
</tr>
<tr>
<td>AIDS-wasting syndrome or cachexia (for Serostim)</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Short bowel syndrome (for Zorbtive)</td>
<td>4 weeks</td>
<td>N/A</td>
</tr>
</tbody>
</table>

FOR ALL GROWTH HORMONES (EXCEPT ZORBTIVE)
- Patient does not have any of the following contraindications:
  - Acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure
  - Active malignancy
  - Active proliferative or severe non-proliferative diabetic retinopathy

AND
- Patient has been established on therapy for the last 3 months AND Patient is adherent to therapy (for Genotropin, Humatrope, Omnitrope, Saizen, and Tev-Tropin)

AND

Pediatric Patients (less than 18 years of age)
- The medication is prescribed by or in consultation with a pediatric endocrinologist
- Patient’s epiphyses are open OR
- Final adult height has not been reached as determined by the 5th percentile of adult height OR
- Linear growth velocity is greater than 2 cm/year

Adult Patients (18 years of age or older)
- The medication is prescribed by or in consultation with an endocrinologist AND
- Patient has experienced an improvement of normalization of IGF-1 levels (not a requirement for adults with panhypopituitarism)
- Patient has experienced an objective improvement since starting therapy (e.g., improvement in body composition, dyslipidemia, bone mineral density, or quality of life)
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**SEROSTIM**
- Medication is prescribed by or in consultation with an infectious disease specialist AND
- Patient is currently receiving treatment with antiretrovirals
- Patient has experienced an increase in body weight and/or improvement in lean body mass AND
- Wasting is still evident

Somatropin is considered experimental/investigational for conditions not listed in this coverage policy section.