GROWTH HORMONE THERAPY

Line(s) of Business: HMO; PPO; QUEST Integration
Original Effective Date: 05/21/1999
Current Effective Date: 10/01/2015

POLICY
A. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Table 1. Growth Hormone Products

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
<th>FDA Approved Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotropin</td>
<td>somatropin</td>
<td>Pediatric GHD, adult GHD, TS, ISS, SGA, PWS</td>
</tr>
<tr>
<td>Humatrope</td>
<td>somatropin</td>
<td>Pediatric GHD, adult GHD, TS, ISS, SGA, SHOXD</td>
</tr>
<tr>
<td>Norditropin</td>
<td>somatropin</td>
<td>Pediatric GHD, adult GHD, TS, SGA, NS</td>
</tr>
<tr>
<td>Nutropin/AQ</td>
<td>somatropin</td>
<td>Pediatric GHD, adult GHD, TS, ISS, CKD</td>
</tr>
<tr>
<td>Omnitrope</td>
<td>somatropin</td>
<td>Pediatric GHD, adult GHD, TS, ISS, SGA, PWS</td>
</tr>
<tr>
<td>Saizen</td>
<td>somatropin</td>
<td>Pediatric GHD, adult GHD</td>
</tr>
<tr>
<td>Serostim</td>
<td>somatropin</td>
<td>HIV wasting or cachexia</td>
</tr>
<tr>
<td>Tev-Tropin</td>
<td>somatropin</td>
<td>Pediatric GHD</td>
</tr>
<tr>
<td>Zomacton</td>
<td>somatropin</td>
<td>Pediatric GHD</td>
</tr>
<tr>
<td>Zorbtime</td>
<td>somatropin</td>
<td>SBS</td>
</tr>
</tbody>
</table>

Abbreviations: CKD = chronic kidney disease; GHD = growth hormone deficiency; HIV = human immunodeficiency virus; ISS = idiopathic short stature; NS = Noonan syndrome; PWS = Prader-Willi syndrome; SBS = short bowel syndrome; SGA = small for gestational age; SHOXD = short stature homeobox-containing gene deficiency; TS = Turner syndrome.

B. REQUIRED DOCUMENTATION
- Documentation containing biochemical evidence of GH deficiency:
  - GH levels in response to GH stimulation tests
  - Insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-3 (IGFBP-3) levels (if applicable)
  - Random GH level associated with neonatal hypoglycemia (if applicable)
- Documentation (eg, chart notes, medical records) indicating height and growth velocity:
  - Growth data with either of the following may be required: a) at least 2 heights measured by an endocrinologist at least 6 months apart (minimum of 1 year), or b) at least 4 heights measured by a primary care physician at least 6 months apart (minimum of 2 years)
- X-ray evidence of open growth plates in members over 12 years of age
• For adult GH deficiency, documentation of peak GH level after GH stimulation testing

C. CRITERIA FOR APPROVAL
Initial therapy with GH is covered (subject to Limitations/Exclusions and Administrative Guidelines) for one of the following indications. Refer to Table 2 on page 5 for a summary of approval durations.

1. **Children with growth hormone deficiency (GHD)**
   Authorization for 12 months may be granted when the following biochemical and auxologic criteria are met (a. and b.):
   a. Biochemical Criteria
      i. Documentation of abnormal responses to two GH stimulation tests defined as less than 10 nanograms per milliliter (ng/mL) or as otherwise determined by the testing lab; or
      ii. At least one GH stimulation test response less than 15 ng/ml, and both IGF-1 & IGFBP-3 levels below normal for age and gender; or
      iii. One GH stimulation test response below 10 ng/ml with defined CNS pathology, history of cranial irradiation or genetic conditions associated with GHD; or
      iv. Two or more documented pituitary hormone deficiencies other than GH; or
      v. Abnormally low GH level documented in association with neonatal hypoglycemia
   b. Auxologic Criteria
      i. Height equal to or less than two standard deviations below the mean for age and gender; or
      ii. Height equal to or less than one standard deviation below the mean and growth velocity less than one standard deviation below the mean for age and gender measured in accordance with C.1.b.ii.; and
      1) A minimum of one year of growth data is required with measurements at least six months apart and performed by an endocrinologist; or
      2) Patient must have four or more height determinations measured at least six months apart, by the patient’s primary care physician, over a period of at least two years. Results must show a consistent growth pattern; and
      iii. X-ray evidence of open growth plates in patients over 12 years of age.

2. **Children with idiopathic short stature, familial short stature, or small for gestational age infants with failure of catch-up growth by the age of two**
   Authorization for 12 months may be granted when the following criteria are met:
   a. Auxologic Criteria
      i. Height less than or equal to 2.25 standard deviations below the mean for age and gender; and
      ii. Growth velocity equal to or less than one standard deviation below the mean for age and gender measured in accordance with C.1.b.ii.; and
      iii. X-ray evidence of open growth plates in patients over 12 years of age.

3. **Turner syndrome, Noonan syndrome, Prader-Willi syndrome, and SHOX deficiency**
   Authorization for 12 months may be granted when the following criteria are met:
   a. Height below the tenth percentile for age; and
   b. X-ray evidence of open growth plates in patients over 12 years of age
4. **Pediatric chronic kidney disease**  
Authorization for 12 months may be granted when the following criteria are met:  
   a. Creatinine clearance less than or equal to 75 mL/min per 1.73 m² or serum creatinine greater than 3.0 mg/dl, or dialysis dependent; and  
   b. X-ray evidence of open growth plates in patients over 12 years of age

5. **Adults with evidence of GH deficiency**  
Authorization for 12 months may be granted when the following criteria are met:  
   a. Irreversible hypothalamic/pituitary structural lesions or ablation: no further testing needed  
   b. Defect in GH synthesis: no further testing needed  
   c. GH deficiency diagnosed during childhood, circumstances other than 5.a. or 5.b. Only about 25% of children with GH deficiency will be found to have GH deficiency as adults. Therefore, once adult height has been achieved, patients should be retested for GH deficiency after at least a one month break in GH therapy to determine if continuing replacement is necessary in accordance with one of the following criteria:  
      i. Three or more pituitary hormone deficiencies and IGF-1 level below the laboratory range of normal: no further testing necessary;  
      ii. Peak GH level in response to insulin tolerance test less than or equal to 5.0 ng/ml and IGF-1 level below laboratory's range of normal;  
      iii. Peak GH level in response to glucagon stimulation test less than or equal to 3.0 ng/ml and IGF-1 level below laboratory's range of normal;  
      iv. Peak GH level in response to arginine stimulation test less than or equal to 0.4 ng/ml and IGF-1 level below laboratory's range of normal.  

   Note: Levodopa and clonidine stimulation tests are not acceptable for documenting persistence of GH deficiency into adulthood.

6. **Acquired immune deficiency syndrome (AIDS) wasting**  
Authorization for 12 months total may be granted when the following criteria are met:  
   a. Greater than 10 percent of baseline weight loss that cannot be explained by a concurrent illness other than HIV infection; and  
   b. Simultaneous treatment with antiviral agents.

7. **Short bowel syndrome**  
Authorization for 4 weeks total may be granted when the following criteria are met:  
   a. Receiving specialized nutritional support; and  
   b. Optimal management of short bowel syndrome

8. **Treatment of burns**  
Authorization for 12 months total may be granted when the following criteria are met:  
   a. Extensive 3rd-degree burns; and  
   b. Burns greater than or equal to 40 percent total body surface area.
D. CONTINUATION OF THERAPY

Continuation of therapy is covered (subject to Limitations/Exclusions and Administrative Guidelines) when the continuation criteria listed below are met. Refer to Table 3 on page 5 for a summary of approval durations.

1. Pediatric GH deficiency, ISS, familial short stature, SGA, Turner syndrome, Noonan syndrome, Prader-Willi syndrome, SHOX deficiency, and pediatric chronic kidney disease

Authorization for 12 months may be granted for members who are continuing with GH therapy when the following criteria are met:
   a. GH therapy was previously authorized by HMSA and initial criteria were met; and
   b. Growth velocity ≥ 2 cm per year while on GH therapy; and
   c. X-ray evidence of open growth plates in members over 12 years of age; and
   d. Current height less than 59 inches (4’11”) for a girl or less than 65 inches (5’5”) for a boy (i.e., less than 5th percentile of normal adult height for gender)

2. Adult GH deficiency

Authorization for 12 months may be granted for members continuing with GH therapy when previously authorized by HMSA and initial criteria were met.

E. ADMINISTRATIVE GUIDELINES

1. Prior authorization is required.
2. Children approved for GH therapy under previous HMSA policies will be approved for continuation of therapy in accordance with current continuation criteria.
3. Children receiving GH therapy without previous HMSA authorization will be considered for continuation of therapy in accordance with current initiation criteria (per clinical data prior to initiation of therapy) and current continuation criteria (per current clinical data).
4. Children previously treated with GHT but who have had treatment subsequently discontinued will be considered for re-initiation of therapy in accordance with current initial treatment criteria (per current clinical data) and continuation criteria except growth velocity (per current clinical data).

F. APPROVAL DURATION

Table 2. Initial Authorization Periods

<table>
<thead>
<tr>
<th>Indication</th>
<th>Initial Authorization Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric short stature</td>
<td>Up to 12 months</td>
</tr>
<tr>
<td>Turner’s syndrome</td>
<td></td>
</tr>
<tr>
<td>Noonan’s syndrome</td>
<td></td>
</tr>
<tr>
<td>Prader-Willi syndrome</td>
<td></td>
</tr>
<tr>
<td>Chronic Renal Insufficiency</td>
<td></td>
</tr>
<tr>
<td>Adult GHD</td>
<td></td>
</tr>
<tr>
<td>Burn patients</td>
<td>Up to 12 months</td>
</tr>
<tr>
<td>Short bowel syndrome</td>
<td>Four weeks</td>
</tr>
<tr>
<td>AIDS wasting</td>
<td>Up to 12 months</td>
</tr>
</tbody>
</table>

AIDS = acquired immune deficiency syndrome, GHD = growth hormone deficiency.
Table 3. Continuation of Therapy Authorization Periods

<table>
<thead>
<tr>
<th>Indication</th>
<th>Continuation of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHD</td>
<td>Approved in 12 month increments with current documentation of:</td>
</tr>
<tr>
<td>Pediatric short stature</td>
<td>• Growth velocity greater than or equal to two centimeters</td>
</tr>
<tr>
<td>Turner’s syndrome</td>
<td>• Open growth plates in children over 12 years of age; and</td>
</tr>
<tr>
<td>Noonan’s syndrome</td>
<td>• Height less than fifth percentile of normal adult height</td>
</tr>
<tr>
<td>Prader-Willi syndrome</td>
<td>for gender (150 centimeters for girls, 165 centimeters for</td>
</tr>
<tr>
<td>Chronic Renal Insufficiency</td>
<td>boys).</td>
</tr>
<tr>
<td>Adult GHD</td>
<td>Can be approved in 12 month increments</td>
</tr>
<tr>
<td>Short bowel syndrome</td>
<td>No further authorization shall be given</td>
</tr>
<tr>
<td>Burn patients</td>
<td></td>
</tr>
<tr>
<td>AIDS wasting</td>
<td></td>
</tr>
</tbody>
</table>

AIDS = acquired immune deficiency syndrome, GHD = growth hormone deficiency.

G. DOSAGE AND ADMINISTRATION
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

H. IMPORTANT REMINDER
The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that CVS/caremark reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

I. REFERENCES