GROWTH HORMONE THERAPY

Line(s) of Business: HMO; PPO; QUEST Integration

Original Effective Date: 05/21/1999
Current Effective Date: 06/01/2019

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, ISS, SGA, NS, PWS</td>
</tr>
<tr>
<td>Nutropin/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>Zomacton™</td>
<td>somatropin</td>
<td>Pediatric GHD, adult GHD, TS, ISS, SGA, SHOXD</td>
</tr>
<tr>
<td>Zorbvte®</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. EXCLUSIONS
Somatropin is not covered for in-vitro fertilization use.

C. REQUIRED DOCUMENTATION

- Initial therapy
  - 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)
  o X-ray evidence of open growth plates in members over 12 years of age
  o For adult GH deficiency, documentation of peak GH level after GH stimulation testing
• Continuation of therapy
  o For pediatric disorders, documentation (eg, chart notes, medical records) indicating height and growth velocity
  o For pediatric disorders, x-ray evidence of open growth plates in members over 12 years of age

D. 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
      iii. A minimum of one year of growth data is required with measurements at least six months apart and performed by an endocrinologist; or
      iv. 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
      v. 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: Levadopa 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.
E. CONTINUATION OF THERAPY

1. No previous authorization/precertification:
   All members (including new members or members currently receiving treatment without prior authorization) must meet criteria for initial approval in section C.

2. Reauthorization:
   a. Adult GH deficiency:
      Authorization of an additional 12 months may be granted to adult members requesting authorization for continuation of therapy who met initial criteria and were previously authorized by HMSA/CVS.
   b. Pediatric GH deficiency patients, ISS, familial short stature, SGA, Turner syndrome, Noonan syndrome, Prader-Willis syndrome, SHOX deficiency and pediatric chronic kidney disease:
      Authorization of an additional 12 months may be granted to patients with pediatric GH deficiency, ISS, familial short stature, SGA, Turner syndrome, Noonan syndrome, Prader-Willis syndrome, SHOX deficiency and pediatric chronic kidney disease requesting authorization for continuation of therapy who meet the following criteria and were previously authorized by HMSA/CVS:
      i. Growth velocity ≥ 2 cm per year while on GH therapy; and
      ii. X-ray evidence of open growth plates in members over 12 years of age; and
      iii. 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); and
      iv. Children previously treated with GH therapy 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. ADMINISTRATIVE GUIDELINES

Precertification is required. Please refer to the HMSA medical policy web site for the fax form.

G. 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 Turner’s syndrome Noonan’s syndrome Prader-Willi syndrome Chronic Renal Insufficiency Adult GHD</td>
<td>Up to 12 months</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 per year; and</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 for gender (150 centimeters for girls, 165 centimeters for boys).</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>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>
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<tr>
<td>AIDS wasting</td>
<td></td>
</tr>
</tbody>
</table>

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

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

**I. 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/CVS’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

**J. REFERENCES**

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
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<tr>
<td>10/01/2015</td>
<td>Original CVS/HMSA effective date</td>
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<tr>
<td>12/13/2016</td>
<td>Annual review</td>
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<tr>
<td>12/30/2016</td>
<td>Revision effective date</td>
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<tr>
<td>08/2017</td>
<td>Annual Review</td>
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<td>03/01/2018</td>
<td>Revision effective date</td>
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<td>08/2018</td>
<td>Annual review</td>
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<tr>
<td>04/01/2019</td>
<td>Revision effective date</td>
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<tr>
<td>12/2018</td>
<td>Added IVF exclusion</td>
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<tr>
<td>06/01/2019</td>
<td>Revision effective date</td>
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