This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace, FocusRx and KeyRx formularies.

This is a FlexRx standard and GenRx standard prior authorization program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

### FDA APPROVED INDICATIONS AND DOSAGE

<table>
<thead>
<tr>
<th>Agent</th>
<th>CHILD GHD</th>
<th>ADULT GHD</th>
<th>CKD</th>
<th>PWS</th>
<th>TS</th>
<th>SGA</th>
<th>ISS</th>
<th>SHOX</th>
<th>HIV</th>
<th>NS</th>
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<tr>
<td>Genotropin® (mg/kg/week)</td>
<td>✓ 0.16-0.24</td>
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<td>✓ Up to 0.48</td>
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| **Zorbtive®**  
(Sc: mg/kg/day) | may increase up to 0.0125 mg/kg/day | ✓*  
(0.1 (max 8 mg daily)) |

GHD = growth hormone deficiency; CKD = chronic kidney disease; PWS = Prader-Willi syndrome; TS = Turner syndrome; SGA = small for gestational age; ISS = idiopathic short stature; SHOX = SHOX deficiency; HIV = HIV patients with wasting or cachexia; NS = Noonan syndrome; SBS = short bowel syndrome

* Consideration should be taken for obese patients and/or geriatric patients using a weight-based dosing regimen.

Somatropin products can use a non-weight based dosing regimen: A starting dose of approximately 0.2 mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1-2 months by increments of approximately 0.1-0.2 mg/day, according to individual patient requirements based on the clinical response and serum insulin-like growth factor 1 (IGF-1) concentrations.

* Administration for more than 4 weeks has not been adequately studied.

- Most of the effect of Serostim on work output and lean body mass was apparent after 12 weeks of treatment. The effect was maintained during an additional 12 weeks of therapy. There are no safety or efficacy data available from controlled studies in which patients were treated with Serostim continuously for more than 48 weeks.

**CLINICAL RATIONALE**

**Growth Hormone Deficiency in Children and Adults**

Growth hormone deficiency (GHD) can be divided into congenital and acquired forms. The single most important clinical manifestation of GHD is growth failure, and careful documentation of height velocity is critical to making the correct diagnosis. Patients with congenital GHD have only a slightly reduced birth length and may not immediately show growth failure. Neonatal morbidity may include hypoglycemia. Children with acquired GHD present with severe growth failure, delayed bone age, and increased weight:height ratios. Causes of acquired GHD include intracranial tumors involving the hypothalamic-pituitary region, cranial irradiation, and head trauma.

Clinical presentation, diagnosis, and treatment of GHD in children and adolescents, as described by the 2016 Pediatric Endocrine Society Guidelines for Growth Hormone and Insulin-Like Growth Factor-1 (IGF-1) Treatment in Children and Adolescents, the 2019 Growth Hormone Research Society (GRS) Guidelines for the Diagnosis, Genetics, and Therapy of Short Stature Children, the 2000 Growth Hormone Research Society (GRS) Consensus Guidelines for the Diagnosis and Treatment of Growth Hormone (GH) Deficiency in Childhood and Adolescence, and UpToDate, is stated as follows:

- A more comprehensive evaluation is warranted in children with one or more of the following:
  - Height-for-age curve that has deviated downward across two major height percentile curves (e.g., from above the 25th percentile to below the 10th percentile)
  - Age 2-4 years: height velocity (HV) less than 5.5 cm/year (<2.2 inches/year)
  - Age 4-6 years: HV less than 5 cm/year (<2 inches/year)
  - Age 6 years to puberty:
    - HV less than 4 cm/year for boys (<1.6 inches/year)
    - HV less than 4.5 cm/year for girls (<1.8 inches/year)
  - Decrease in height standard deviation (SD) of more than 0.5 over one year in children over 2 years of age
  - Height velocity more than 2 SD below the mean over one year, or more than 1.5 SD sustained over 2 years
  - Height more than 1.5 SD below the midparental height

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Effective: 12/01/2020
• Height greater than 2 SD below the mean for age and sex\textsuperscript{12,14}  
• Severe short stature (e.g., height \leq -2.5 standard deviations [SD], i.e., 0.6\textsuperscript{th} percentile), or less severe short stature combined with growth failure\textsuperscript{10,12,13}  
• Features that raise concerns for hypothalamic-pituitary dysfunction, either congenital or acquired, with decelerating growth, even if the child’s height is within the normal range\textsuperscript{10}  
• Evidence for deficits in other hypothalamic-pituitary hormones, either congenital or acquired\textsuperscript{10}  

Once the decision to evaluate a short child has been made, a variety of different tests can be performed. Assessment of pituitary GH production is difficult because GH secretion is pulsatile. Between normal pulses of GH secretion, serum GH levels are often low, below the limits of sensitivity of most conventional assays. Because of these issues, the diagnosis of GHD is made with a combination of clinical assessment and auxology, levels of insulin-like growth factor I (IGF-I) and insulin-like growth factor binding protein 3 (IGFBP-3), and GH stimulation (provocation) tests.\textsuperscript{10,12,13}  

The IGF-I, IGFBP-3, and bone age testing results may be interpreted as follows:  
  • Moderately or severely reduced: IGF-I and IGFBP-3 < -2 SD with delayed bone age; possibility of GHD should be explored by provocative testing in most cases\textsuperscript{10,13}  
  • Somewhat low: IGF-I and IGFBP-3 between 0 and -2 SD; decision about whether to perform provocative testing depends on other factors\textsuperscript{10}  
  • Clearly normal: IGF-I and IGFBP-3 SD \geq 0; no further testing required\textsuperscript{10}  
  • If the IGF-I and IGFBP-3 are discordant, IGF-I takes precedence except for infants and young children, in whom IGFBP-3 should guide the decision about further testing.\textsuperscript{10,12}  

Provocative (stimulation) GH testing is indicated for most patients to confirm GHD, however, because this testing has limitations, it should not be the sole diagnostic criterion.\textsuperscript{10,11} In general, two different tests should be used for provocative GH testing. For those with known pathology of the central nervous system, history of irradiation, other pituitary hormone defects (e.g., multiple pituitary hormone deficiency [MPHD]), or a genetic defect, one test is sufficient.\textsuperscript{10,12,13}  

The use of GH provocative testing is not required for diagnosis of GHD in the following conditions:  
  • In patients possessing all of the following three conditions: auxological criteria, hypothalamic-pituitary defect (such as major congenital malformation [ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk], tumor or irradiation), and deficiency of at least one additional pituitary hormone\textsuperscript{10,11,12}  
  • In a newborn with hypoglycemia who does not attain a serum GH concentration above 5 mcg/L and has deficiency of at least one additional pituitary hormone and/ or congenital pituitary abnormality (ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk)\textsuperscript{10,11,12}  
  • Infant or young child with extreme short stature (e.g., height < -3 SD), normal nutrition, significantly reduced IGF-1 and IGFBP-3 (e.g., < -2 SD), and delayed bone age\textsuperscript{10}  
  • In newborns who present with hypoglycemia in the absence of a metabolic disorder, a serum growth hormone level of < 20 mcg/L suggests GHD. An IGFBP-3 measurement (e.g., < -2 SD) is of value for the diagnosis of GHD in infancy.\textsuperscript{13}  
  • When an alternative diagnosis for short stature is evident, such as Turner syndrome, Noonan syndrome, Prader-Willi syndrome (PWS), SHOX deficiency, chronic renal insufficiency, or in children born small for gestational age (SGA)\textsuperscript{12}  

Some guidelines acknowledge that a threshold test result distinguishing “normal” from GHD has not been well established.\textsuperscript{11,12} Most pediatric endocrinologists define a “normal” response by a serum GH concentration of > 10 mcg/L, but a cutoff of 7.5 mcg/L is often used for modern assays.\textsuperscript{10,12,13}  

Treatment of children with GHD is the following:  
  • Weight-based or body-surface-area dosing should be used.\textsuperscript{11,12,13,15}
Guidelines for patients transitioning from pediatric to adult care, as described by the 2016 Pediatric Endocrine Society Guidelines for Growth Hormone and Insulin-Like Growth Factor-1 (IGF-1) Treatment in Children and Adolescents\textsuperscript{11}, the 2000 Growth Hormone Research Society (GRS) Consensus Guidelines for the Diagnosis and Treatment of Growth Hormone (GH) Deficiency in Childhood and Adolescence\textsuperscript{13}, the 2019 American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology Guidelines for Management of Growth Hormone Deficiency in Adults and Patients Transitioning from Pediatric to Adult Care\textsuperscript{24}, the 2011 Endocrine Society Clinical Practice Guidelines for Evaluation and Treatment of Adult Growth Hormone Deficiency\textsuperscript{25}, and UpToDate\textsuperscript{27}, is stated as follows:

- Only a minority of children with childhood-onset GHD will remain deficient as adults and require ongoing GH therapy. The transition period is loosely defined as occurring from mid-to-late teens until 6-7 years after reaching near-adult height.\textsuperscript{27}
- For patients transitioning from pediatric to adult care:
  - Because the majority of isolated childhood-onset GHD patients will have normal results when tested as adults, it is important to repeat GH stimulation testing to determine if ongoing therapy is required.\textsuperscript{11,24,27}
  - Measurement of the serum IGF-1 concentration should be the initial test of the somatotropic axis if re-evaluation of the somatotropic axis is clinically indicated.\textsuperscript{11}
  - GH provocative testing should be performed to evaluate the function of the somatotropic axis in the transition period if indicated by a low IGF-I level.\textsuperscript{11,24,25}
  - Patients with multiple (≥ 3) pituitary hormone deficiencies regardless of etiology, or GHD with an established causal genetic mutation, or GHD with a specific pituitary/hypothalamic structural defect (except ectopic posterior pituitary), should be diagnosed with persistent GHD.\textsuperscript{11,13,24,27} GH treatment should be offered to individuals with persistent GHD in the transition period.\textsuperscript{11,24,25,27}

Clinical presentation, diagnosis, and treatment of GHD in adults, as described by the 2019 American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology Guidelines for Management of Growth Hormone Deficiency in Adults and Patients Transitioning from Pediatric to Adult Care\textsuperscript{24}, the 2011 Endocrine Society Clinical Practice Guidelines for Evaluation and Treatment of Adult Growth Hormone Deficiency\textsuperscript{25}, and UpToDate\textsuperscript{26}, is stated as follows:

- The diagnosis of adult GHD should be based on the combination of documented pituitary or hypothalamic disease, panhypopituitarism, and a subnormal serum IGF-1 concentration (lower than the gender- and age-specific lower limit of normal).\textsuperscript{26} GH levels decline with aging, whereas serum IGF-1 levels can be lowered by factors such as malnutrition and various comorbidities (e.g., diabetes, renal and/or hepatic disease). Stimulation (provocative) tests should only be performed based on the clinical context of each patient with a history suggestive of a reasonable clinical suspicion of GHD, and with the intent to initiate GH therapy if the diagnosis is confirmed.\textsuperscript{24}
- Diagnosis of adult GHD, without the need for stimulation/provocation tests, can be made in the following patient subtypes:
  - Patients with organic hypothalamic-pituitary disease (e.g., suprasellar mass with previous surgery and cranial irradiation) and presence of deficiencies in three or more pituitary axes (multiple pituitary hormone deficiency [MHPD]) together with subnormal serum IGF-1 levels (< -2 SD)\textsuperscript{24,25,26}
  - Patients with genetic defects affecting the hypothalamic-pituitary axes\textsuperscript{24,25}
  - Patients with hypothalamic-pituitary structural brain defects\textsuperscript{24,25}
- GH stimulation tests are needed to confirm diagnosis in the following patient subtypes:
In patients with ≤ 2 pituitary hormone deficiencies, subnormal IGF-1 levels alone are not sufficient to make a diagnosis of adult GHD; one GH stimulation test should be performed to confirm the diagnosis.24

In transition patients who have completed longitudinal growth:

- After at least one month of discontinuation of therapy, patients with childhood-onset GHD and subnormal serum IGF-1 levels should be retested for GHD with provocation tests.24,25
- Patients with idiopathic childhood-onset GHD with organic hypothalamic-pituitary disease should have at least one stimulation test performed.24

In the past, a level of serum GH ≤ 5 mcg/L on the insulin tolerance test was considered confirmation of GHD. However, experts increasingly report the disuse of this test and instead the glucagon-stimulation test (GST) and the macimorelin test should be utilized.24,26

**Idiopathic Short Stature**

Idiopathic short stature (ISS) refers to extreme short stature that does not have a diagnostic explanation. "Short stature" has been defined by the American Association of Clinical Endocrinologists as height more than two standard deviations (SD) below the mean for age and sex. GH is approved by the FDA for children with ISS whose current height is below -2.25 SD of the mean for age, and whose predicted adult height is unlikely to fall within the normal range. However, treatment of children with ISS with GH is controversial because of variable efficacy and high costs.16,17

**Growth Failure in Chronic Kidney Disease**

The goal of GH therapy in children with chronic kidney disease (CKD) is normalization of final height. GH therapy should be initiated when the following criteria have been met:16,19

- All other amenable risk factors for growth impairment have been addressed
- There is evidence of growth impairment, defined as HV for age < -1.88 SD OR a HV for age < 3rd percentile

**Short Bowel Syndrome**

Short bowel syndrome (SBS) is a malabsorption disorder caused by either the surgical removal of the small intestine or the loss of its absorptive function due to various diseases. In clinical studies, the administration of GH enhanced the transmucosal transport of water, electrolytes, and nutrients. Zorbtive is indicated for the treatment of SBS in adult patients receiving specialized nutritional support.3

**Growth Failure in Children Born Small for Gestational Age**

Low birth weight remains a major cause of morbidity and mortality in early infancy and childhood throughout the world. The International Societies of Pediatric Endocrinology and the Growth Hormone Research Society (GRS) 2007 Consensus Statement Guidelines on the Management of the Child Born Small for Gestational Age (SGA) recommend that SGA should be defined as a birth weight and/or birth length less than -2 SD below the population average. Approximately 90% of term SGA infants display sufficient catch-up growth to attain a height above -2 SD by the age of 2 years, whereas 10 percent remain short throughout childhood and adolescence.20-22 A child who reaches 24 months of age and fails to manifest catch-up growth (i.e., height remains less than 2 SD below the mean for age and gender) meets the indication to receive GH therapy.22,23

**HIV Patients with Wasting or Cachexia**

HIV/AIDS wasting syndrome is defined by the Centers for Disease Control and Prevention (CDC) as an involuntary weight loss of > 10% of body weight. The incidence of wasting has declined since the introduction of anti-retroviral therapy (ART), but many patients still meet the criteria for serious weight loss and wasting. Tissue wasting responds rapidly to ART, and the primary therapy for HIV wasting is ART.28,30 The diagnosis of HIV wasting requires one of the following:29

- 10% unintentional weight loss over 12 months
- 7.5% unintentional weight loss over 6 months
- > 5% unintentional weight loss over 4 months
- 5% body cell mass (BCM) loss within 6 months
- Body mass index (BMI) < 20 kg/m²
- In men: BCM < 35% of total body weight and BMI < 27 kg/m²
- In women: BCM < 23% of total body weight and BMI < 27 kg/m²

**Efficacy**
- Recombinant growth hormone products are considered clinically identical, with no evidence that one commercial product is different or more advantageous than another, apart from differences in how the GH product is stored, dosed, and administered by device. Therefore, one commercial GH product is not recommended over another because there are no prospective head-to-head trials comparing the clinical efficacy of one commercial product with another.

**References**


Growth Hormone Prior Authorization

**TARGET AGENTS**

**Preferred Agents**
Norditropin® FlexPro® (somatropin)

**Nonpreferred Agents**
Genotropin®, Genotropin® MiniQuick (somatropin)
Humatrope®, Humatropen® (somatropin)
Nutropin AQ® NuSpin® (somatropin)
Omnitrope® (somatropin)
Saizen®, saizenprep® (somatropin)
Serostim® (somatropin)
Zomacton® (somatropin)
Zortive® (somatropin)

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<th>Brand (generic)</th>
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PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Children – Initial Evaluation

Target Agent will be approved when ALL of the following are met:

1. The patient is a child (as defined by the prescriber)
   AND
2. The patient has ONE of the following diagnoses:
   a. The patient is a newborn (≤ 4 months of age) with hypoglycemia AND serum growth hormone (GH) concentration ≤ 5 mcg/L AND at least ONE of the following:
      i. Congenital pituitary abnormality (e.g., ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk)
         OR
      ii. Deficiency of at least one additional pituitary hormone
         OR
   b. The patient is a newborn (≤ 4 months of age) with hypoglycemia AND growth hormone (GH) concentration < 20 mcg/L AND BOTH of the following:
      i. The patient does not have a known metabolic disorder
         AND
      ii. The patient has a reduced IGFBP-3 level (e.g., < -2 SD)
         OR
   c. The patient has a diagnosis of Turner syndrome
   OR
   d. The patient has a diagnosis of Noonan syndrome
   OR
   e. The patient has a diagnosis of Prader-Willi syndrome
   OR
   f. The patient has a diagnosis of SHOX gene deficiency
   OR
   g. The patient has a diagnosis of short bowel syndrome (SBS) AND is receiving specialized nutritional support
   OR
   h. The patient has a diagnosis of panhypopituitarism or has deficiencies in at least 3 or more pituitary axes AND serum IGF-I levels below the age- and sex-appropriate reference range when off GH therapy
   OR
   i. The patient has a diagnosis of chronic renal insufficiency and BOTH of the following:

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<th>Multisource Code</th>
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**Saizen, saizenprep (somatropin)**

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<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 mg vial</td>
<td>30100020102120</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>8.8 mg vial and cartridge</td>
<td>30100020102130</td>
<td>M, N, O, or Y</td>
</tr>
</tbody>
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**Serostim (somatropin)**

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<th>Multisource Code</th>
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<tbody>
<tr>
<td>4 mg vial</td>
<td>30100020102118</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>5 mg vial</td>
<td>30100020102121</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>6 mg vial</td>
<td>30100020102125</td>
<td>M, N, O, or Y</td>
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**Zomacton (somatropin)**

<table>
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<th>GPI</th>
<th>Multisource Code</th>
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<tbody>
<tr>
<td>5 mg vial</td>
<td>30100020102121</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>10 mg vial</td>
<td>30100020102140</td>
<td>M, N, O, or Y</td>
</tr>
<tr>
<td>8.8 mg vial</td>
<td>30100020102132</td>
<td>M, N, O, or Y</td>
</tr>
</tbody>
</table>
- The patient’s height velocity (HV) for age is < -1.88 standard deviations (SD) OR HV for age is less than the third percentile
  AND
- Other etiologies for growth impairment have been addressed
  OR
- The patient has a diagnosis of small for gestational age (SGA) and ALL of the following:
  - The patient is 2 years of age or older
  AND
  - The patient has a documented birth weight and/or birth length that is 2 or more standard deviations (SD) below the mean for gestational age
  AND
  - At 24 months of age, the patient failed to manifest catch-up growth evidenced by a height that remains 2 or more standard deviations (SD) below the mean for age and gender
  OR
- The patient has a diagnosis of growth hormone deficiency (GHD), short stature, or other AND ONE of the following:
  - The patient has extreme short stature (e.g., height < -3 SD), normal nutrition, significantly reduced IGF-1 and IGFBP-3 (e.g., < -2 SD), and delayed bone age
  OR
  - BOTH of the following:
    1. The patient has ONE of the following:
      a. Height more than 2 SD below the mean for age and sex
      OR
      b. Height more than 1.5 SD below the midparental height
      OR
      c. A decrease in height SD of more than 0.5 over one year in children >2 years of age
      OR
      d. Height velocity (HV) more than 2 SD below the mean over one year or more than 1.5 SD sustained over two years
      OR
      e. Height-for-age curve that has deviated downward across two major height percentile curves (e.g., from above the 25th percentile to below the 10th percentile)
      OR
      f. Age 2-4 years: HV less than 5.5 cm/year (<2.2 inches/year)
      OR
      g. Age 4-6 years: HV less than 5 cm/year (<2 inches/year)
      OR
      h. Age 6 years to puberty AND ONE of the following:
        i. The patient is a boy and HV is less than 4 cm/year (< 1.6 inches/year)
        OR
        ii. The patient is a girl and HV is less than 4.5 cm/year (< 1.8 inches/year)
  AND
  2. One of the following:
    a. The patient has failed at least 2 GH stimulation tests (e.g., peak GH value of <10 mcg/L after stimulation, or otherwise considered abnormal as determined by testing lab)
    OR
b. The patient has failed at least 1 GH stimulation test (e.g., peak GH value of <10 mcg/L after stimulation, or otherwise considered abnormal as determined by testing lab) AND ONE of the following:
   i. Pathology of the central nervous system OR
   ii. History of irradiation OR
   iii. Other pituitary hormone defects (e.g., multiple pituitary hormone deficiency [MPHD]) OR
   iv. A genetic defect OR

c. The patient has a pituitary abnormality and a known deficit of at least one other pituitary hormone

AND

3. The patient does NOT have any FDA labeled contraindications to the requested agent AND

4. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., endocrinologist) or has consulted with a specialist in the area of the patient’s diagnosis AND

5. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication AND

6. If the client has preferred agent(s), then ONE of the following:
   a. The request is for a preferred agent OR
   b. The request is for a nonpreferred agent and ONE of the following:
      i. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to a preferred agent that is not expected to occur with the requested nonpreferred agent (medical record required) OR
      ii. The prescriber has provided information to support the efficacy of the requested nonpreferred agent over the preferred agent for the intended diagnosis (medical record required) OR
      iii. The patient’s medication history includes use of the preferred agent in the past 999 days OR
      iv. BOTH of the following:
         1. The prescriber has stated that the patient has tried the preferred agent AND
         2. The preferred agent was discontinued due to lack of effectiveness or an adverse event OR
      v. The patient is currently being treated with the requested agent as indicated by ALL of the following:
         1. A statement by the prescriber that the patient is currently taking the requested agent AND
         2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent AND
         3. The prescriber states that a change in therapy is expected to be ineffective or cause harm
vi. The prescriber has provided documentation that the preferred agent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: 4 weeks for SBS  
12 months for other indications

Children – Renewal Evaluation  
Target Agent will be approved when ALL of the following are met:  
1. The patient has been previously approved for therapy with GH through the plan’s prior authorization process  
   AND  
2. The patient is a child (as defined by the prescriber)  
   AND  
3. If the client has preferred agent(s), then ONE of the following:  
   a. The request is for a preferred agent  
   OR  
   b. The request is for a nonpreferred agent and ONE of the following:  
      i. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to a preferred agent that is not expected to occur with the requested nonpreferred agent (medical record required)  
      OR  
      ii. The prescriber has provided information to support the efficacy of the requested nonpreferred agent over the preferred agent for the intended diagnosis (medical record required)  
      OR  
      iii. The patient’s medication history includes use of the preferred agent in the past 999 days  
      OR  
      iv. BOTH of the following:  
         1. The prescriber has stated that the patient has tried the preferred agent  
         AND  
         2. The preferred agent was discontinued due to lack of effectiveness or an adverse event  
      OR  
      v. The patient is currently being treated with the requested agent as indicated by ALL of the following:  
         1. A statement by the prescriber that the patient is currently taking the requested agent  
         AND  
         2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent  
         AND  
         3. The prescriber states that a change in therapy is expected to be ineffective or cause harm  
      OR  
      vi. The prescriber has provided documentation that the preferred agent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm  
   AND
4. **ONE** of the following:
   a. The patient has a diagnosis of short bowel syndrome (SBS) **AND** has shown clinical benefit from treatment with growth hormone **OR**
   b. The patient has any other diagnosis **AND** ALL of the following:
      i. The patient does not have closed epiphyses **AND**
      ii. The patient’s height has increased or height velocity has improved since initiation or last GH approval

5. **The patient is being monitored for adverse effects of GH**

6. **The patient does NOT** have any FDA labeled contraindications to the requested agent **AND**

7. **The prescriber is a specialist in the area of the patient’s diagnosis (e.g., endocrinologist) or has consulted with a specialist in the area of the patient’s diagnosis**

8. **The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication**

**Length of Approval:** 4 weeks for SBS  
12 months for other indications

**Adults – Initial Evaluation**

**Target Agent** will be approved when **ALL** of the following are met:

1. **The patient is an adult** (as defined by the prescriber) **AND**

2. **The patient has ONE** of the following diagnoses:
   a. The patient has a diagnosis of AIDS wasting/cachexia **AND** **ALL** of the following:
      i. The patient is receiving antiretroviral therapy and GH concurrently **AND**
      ii. BOTH of the following:
         1. **ONE** of the following:
            a. The patient has had weight loss that meets **ONE** of the following:
               i. 10% unintentional weight loss over 12 months **OR**
               ii. 7.5% unintentional weight loss over 6 months **OR**
         2. The patient has a body cell mass (BCM) loss ≥5% within 6 months **OR**
         3. The patient is male and has BCM <35% of total body weight **AND** body mass index (BMI) < 27 kg/m² **OR**
         4. The patient is female and has BCM < 23% of total body weight **AND** BMI < 27 kg/m² **OR**
         5. The prescriber has provided information that the patient’s BCM < 35% or < 23% and BMI < 27 kg/m² are medically appropriate for diagnosing AIDS wasting/cachexia for the patient’s gender **OR**
         6. The patient’s BMI is < 20 kg/m² **AND**
   b. All other causes of weight loss have been ruled out **OR**
c. The patient has a diagnosis of short bowel syndrome (SBS) AND is receiving specialized nutritional support

   OR

d. The patient has a diagnosis of growth hormone deficiency (GHD) AND ONE of the following:

   i. The patient had a diagnosis of childhood-onset growth hormone deficiency AND has failed at least one growth hormone (GH) stimulation test as an adult

   OR

   ii. The patient has a low insulin-like growth factor-1 (IGF-1) level AND ONE of the following:

       1. Organic hypothalamic-pituitary disease

       OR

       2. Pituitary structural lesion or trauma

       OR

       3. The patient has panhypopituitarism or multiple (≥ 3) pituitary hormone deficiency

   OR

   iii. The patient has an established causal genetic mutation OR hypothalamic-pituitary structural defect other than ectopic posterior pituitary

   OR

   iv. The patient has failed at least two growth hormone (GH) stimulation tests as an adult

   OR

   v. The patient has failed at least one GH stimulation test as an adult AND the patient has an organic pituitary disease

   AND

   3. The patient does NOT have any FDA labeled contraindications to the requested agent

   AND

   4. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., endocrinologist) or the prescriber has consulted with a specialist in the area of the patient’s diagnosis

   AND

   5. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication

   AND

   6. If the client has preferred agent(s), then ONE of the following:

       a. The request is for a preferred agent

       OR

       b. If the request is for a nonpreferred agent, ONE of the following:

           i. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to a preferred agent that is not expected to occur with the requested nonpreferred agent (medical record required)

           OR

           ii. The prescriber has provided information to support the efficacy of the requested nonpreferred agent over the preferred agent for the intended diagnosis (medical record required)

           OR

           iii. The patient’s medication history includes use of the preferred agent in the past 999 days

           OR

           iv. BOTH of the following:

               1. The prescriber has stated that the patient has tried the preferred agent

               AND

               2. The preferred agent was discontinued due to lack of effectiveness or an adverse event
OR

v. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   1. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   3. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR

vi. The prescriber has provided documentation that the preferred agent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: 4 weeks for SBS;
12 weeks for AIDS wasting/cachexia;
12 months for other indications

Adults – Renewal Evaluation

Target Agent will be approved when ALL of the following are met:
1. The patient has been approved for therapy with GH previously through the plan’s prior authorization process
   AND
2. The patient is an adult (as defined by the prescriber)
   AND
3. If the client has preferred agent(s), then ONE of the following:
   a. The request is for a preferred agent
   OR
   b. The request is for a nonpreferred agent AND ONE of the following:
      i. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to a preferred agent that is not expected to occur with the requested nonpreferred agent (medical record required)
      OR
      ii. The prescriber has provided information to support the efficacy of the requested nonpreferred agent over the preferred agent for the intended diagnosis (medical record required)
      OR
      iii. The patient’s medication history includes use of the preferred agent in the past 999 days
      OR
      iv. BOTH of the following:
         1. The prescriber has stated that the patient has tried the preferred agent
         AND
         2. The preferred agent was discontinued due to lack of effectiveness or an adverse event
      OR
   v. The patient is currently being treated with the requested agent as indicated by ALL of the following:
1. A statement by the prescriber that the patient is currently taking the requested agent
   
   AND

2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   
   AND

3. The prescriber states that a change in therapy is expected to be ineffective or cause harm
   
   OR
   
   vi. The prescriber has provided documentation that the preferred agent cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm
   
   AND

4. ONE of the following:
   
   a. The patient has a diagnosis of short bowel syndrome (SBS) AND has shown clinical benefit from treatment with growth hormone
   
   OR
   
   b. The patient has a diagnosis of AIDS wasting/cachexia AND BOTH of the following:
      
      i. The patient continues to receive concurrent antiretroviral therapy
      
      AND
      
      ii. The patient shows evidence of benefit of GH treatment (weight increase or weight stabilization)
      
   OR
   
   c. The patient has any other diagnosis AND ALL of the following:
      
      i. The patient’s IGF-I level has been evaluated to confirm the appropriateness of the current dose
      
      AND
      
      ii. The patient has had benefits from GH therapy in any of the following response parameters; body composition, hip-to-waist ratio, cardiovascular health, bone mineral density, serum cholesterol, physical strength, or quality of life
      
   AND

5. The patient does NOT have any FDA labeled contraindications to the requested agent
   
   AND

6. The prescriber is a specialist in the area of the patient’s diagnosis (e.g., endocrinologist) or has consulted with a specialist in the area of the patient’s diagnosis
   
   AND

7. The requested quantity (dose) does not exceed the maximum FDA labeled dose for the requested indication
   
   AND

8. The patient is being monitored for adverse effects of GH

Length of Approval: 4 weeks for SBS;
12 weeks for AIDS wasting/cachexia;
12 months for other indications
<table>
<thead>
<tr>
<th>Agent</th>
<th>Contraindication(s)</th>
</tr>
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</table>
| Genotropin, Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Zomacton | - Acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure  
- Children with Prader-Willi syndrome who are severely obese, have a history of upper airway obstruction or sleep apnea, or have severe respiratory impairment  
- Active malignancy  
- Active proliferative or severe non-proliferative diabetic retinopathy  
- Children with closed epiphyses  
- Hypersensitivity to somatropin or diluents/excipients |
| Serostim                     | - Acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma or acute respiratory failure  
- Active malignancy  
- Active proliferative or severe non-proliferative diabetic retinopathy  
- Hypersensitivity to somatropin or diluent |
| Zorbtive                     | - Acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma or acute respiratory failure  
- Active neoplasia  
- Known hypersensitivity to growth hormone |