Human Growth Hormone
Drug Class Monograph

Line of Business: Medi-Cal
Effective Date: February 15, 2017
Revision Date: May 17, 2017

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutics Subcommittee.

Drugs: Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Saizen, Serostim, Zorbtive (Somatropin)

Policy/Criteria:

Human Growth Hormone may be considered medically necessary if the following conditions are met:

1. Use in one of the following indications:
   
   a. Children;
      
      • Congenital Growth Hormone Deficiency (GHD)*: short stature associated with lack of adequate endogenous growth hormone secretion;
      • Acquired GHD*: short stature associated with lack of adequate growth hormone due to tumors of the hypothalamic, pineal, and pituitary region and optic gliomas;
      • Chronic Kidney Disease (CKD)*: short stature associated with CKD before renal transplantation;
      • Turner Syndrome: short stature in patients with Turner Syndrome;
      • Prader-Willi Syndrome: short stature in patients with Prader-Willi Syndrome;
      • Small for Gestational Age (SGA): infants born SGA who have not caught up in height;
      • Noonan Syndrome: short stature in patients with Noonan Syndrome.

   * Growth Hormone Deficiency (GHD) and Chronic Kidney Disease (CKD) are CCS-covered diagnoses. All of the criteria above must be met for CCS coverage and must be prescribed by a CCS paneled pediatric endocrinologist (GHD) at a CCS approved endocrine center or physician from CCS authorized Renal Center (CKD).
b. Adults;
   - Pituitary disease from known causes including pituitary tumor, pituitary surgical damage, trauma, hypothalamic disease and reconfirmed childhood GHD;
   - AIDS-associated wasting;
   - Short bowel syndrome.

2. Growth hormone therapy is determined to be medically necessary, if the patient is evaluated by an endocrinologist (or another specialist if specified below) and one of the following criteria is met:
   
a. Child GHD;
      - Two provocative stimulation tests of growth hormone release with peak growth hormone level of less than 10 ng/mL AND;
      - Height greater than 2 SD below the mean or < 3% for age and gender.
   
b. Child Idiopathic Short Stature who pass GH stimulation tests;
      - >2.25 SD below the mean in height or > 2 SD below the midparental height percentile AND;
      - One of the following:
         - Growth velocity < 25th percentile for bone age;
         - Bone age > 2 SD below the mean for age;
         - Low serum insulin-like growth factor 1 (IGF-1) and/or insulin-like growth factor binding protein 3 (IGFBP3).
   
c. Chronic Kidney Disease;
      - Prescribed by endocrinologist or nephrologist or pediatrician AND;
      - Height greater than 2 SD below the mean or < 3% for age and gender AND;
      - Prior to renal transplantation.
   
d. Turner Syndrome;
      - Confirmed diagnosis AND;
      - Height greater than 2 SD below the mean or < 3% for age and gender.
   
e. Prader-Willi Syndrome;
      - Confirmed diagnosis by AND;
      - Height greater than 2 SD below the mean or < 3% for age and gender.
   
f. Small for Gestational Age (SGA) Children;
      - Birth weight below the 10th percentile for gestational age AND;
      - Height greater than 2 SD below the mean or < 3% for age and gender by age 2.
   
g. Noonan Syndrome;
      - Confirmed diagnosis AND;
      - Height greater than 2 SD below the mean or < 3% for age and gender.
   
h. Short bowel syndrome;
      - Confirmed diagnosis AND;
      - Prescribed by gastroenterologist AND;
      - Receiving parenteral nutrition (TPN dependent).
   
i. Adult GHD;
      - Two provocative stimulation tests of growth hormone release with peak growth hormone level of less than 5 ng/mL AND;
• Documented GHD associated with pituitary disease, irradiation, surgery, or trauma.

j. AIDS-associated wasting:
• Prescribed by endocrinologist or HIV specialist AND;
• Involuntary weight loss greater than 10% of normal baseline body weight or body mass index (BMI) less than 20 kg/m² without a concurrent condition other than HIV infection that may have contributed to the condition AND;
• Currently receiving antiviral agents AND;
• Failure or intolerance to appetite stimulants AND;
• Failure or contraindication to anabolic steroid treatment.

3. Monitoring:

a. Should be performed by a pediatric endocrinologist in partnership with the pediatrician or primary care physician and should be conducted on a 3 to 6 months basis;
b. Increase in height and change in height velocity should be assessed;
c. Monitoring of serum IGF-I (preferred for GHD) and IGFBP-3 levels (for short stature in children younger than 3 years);
d. Monitoring T₄ and TSH to detect hypothyroidism (can appear during GH therapy).

4. Therapy End Point:

a. Pediatric
• Treatment to continue until final height or epiphyseal closure has been documented;
• Bone age > 15 years (girls) and > 16 years (boys);
• Growth rate < 2.5 cm/year;
• Achievement of mid-parental adult height;
• Further treatment is generally futile if no increase in growth rate or serum IGF over baseline within the first 6-12 months in a compliant patient receiving an appropriate dose of GH.

b. Adult
• IGF-I level above normal;
• Decrease in LDL, increase in HDL, and a change in body composition;
• Decrease in body fat and an increase in bone density;
• If a patient shows no improvement when maximum dose is achieved, treatment should be discontinued.
Formulary Position:

Omnitrope vial is the preferred Growth Hormone product. However, the following growth hormone products will be covered for the corresponding FDA approved indication:

- **Norditropin** will be covered for Noonan Syndrome;
- **Serostim** will be covered for AIDS-associated wasting;
- **Zorbtive** will be covered for Short Bowel Syndrome;
- **Nutropin** will be covered for Chronic Kidney Disease.

References:

13. Humatrope® (Somatropin (rDNA origin)) [package insert]. Indianapolis, IN: Lilly USA, LLC; 2016.

<table>
<thead>
<tr>
<th>Date</th>
<th>Change</th>
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<tbody>
<tr>
<td>02/15/2017</td>
<td>• Revised criteria for Serostim: Trial and failure of anabolic steroid or medical justification (e.g. contraindication) why anabolic steroid cannot be used</td>
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<tr>
<td>05/17/2017</td>
<td>• Omnitrope vial is the non-formulary preferred growth hormone product</td>
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