Definition: Human growth hormone (hGH, somatotropin) is secreted by the anterior pituitary. Most of its anabolic effects are mediated by insulin-like growth factor-I (IGF-I, somatomedin C), which is synthesized in the liver and other tissues in response to growth hormone stimulation. Growth hormone stimulates linear growth in children and influences metabolism of carbohydrates, fats, minerals, and proteins. Somatropin is produced by recombinant DNA technology and has the same amino acid sequence as naturally occurring hGH (a single polypeptide chain of 191 amino acids).

BASIC FORMULARY

Preferred Products as part of Preferred Drug Step Therapy:
Genotropin® (all forms), Humatrope®, Norditropin® (all forms)

Non-preferred Products as part of Preferred Drug Step Therapy:
Nutropin® (all forms), Omnitrope®, Saizen®, Zomacton

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Preferred Products:
Omnitrope

Non-Preferred Products:
Genotropin, Humatrope, Norditropin, Nutropin/Nutropin AQ, Saizen, Zomacton

Policy Statement
Prior authorization is recommended for prescription benefit coverage of somatropin and mecasermin. All approvals are provided for 1 year in duration unless otherwise noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with somatropin/mecasermin as well as the monitoring required for adverse events and long-term
efficacy, initial approval requires somatropin/mecasermin to be prescribed by or in consultation with a physician who specializes in the condition being treated. Criteria for patients who are continuing on somatropin/mecasermin are provided. Human growth hormone is FDA-approved for treatment of a limited number of conditions. The FDA has not approved the use of human growth hormone as therapy for anti-aging, longevity, cosmetic or performance enhancement. Federal law prohibits the dispensing of human growth hormone for non-approved purposes. Drugs in this policy may be subject to the Growth Hormone Preferred Specialty Management. Serostim, Zortive, and Increlex are not subject the Preferred Specialty Management Policy.

**RECOMMENDED AUTHORIZATION CRITERIA**
Coverage of growth hormones is recommended in those who meet the following criteria:

**Food and Drug Administration (FDA)-Approved Indications**

1. Coverage is provided for **pediatric growth hormone deficiency** in the presence of the following (Genotropin, Humatrope, Norditropin, Nutropin/Nutropin AQ, Saizen, Zomacton, Omnitrope):
   a) patient’s height must be below the third percentile for their age and gender related height;
   OR
   b) growth velocity subnormal 2 standard deviations from the age related mean; OR
   c) delayed skeletal maturation 2 standard deviations below the age/gender related mean;
   AND
   d) epiphyses must be confirmed as open in patients 10 years of age; AND
   e) growth hormone deficiency confirmed by any 2 provocative stimulation tests OR by insulin growth factor-1 (IGF-1) a.k.a. somatomedin C, and IGF binding protein-3 (IGFBP-3) levels; OR
   f) If none of the coverage points related to height (i.e., height below the third percentile for age and gender related height, growth velocity >2 standard deviations from the bone age related mean, or skeletal maturation >2 standard deviations below the age/gender related mean) are met, coverage is provided if growth hormone deficiency has been confirmed by 2 provocative stimulation tests; AND low IGF-1 AND IGF-BP3.

   For continuation of therapy, a growth response of 4.5 cm/yr (pre-pubertal growth phase) or 2.5 cm/yr (post-pubertal) must occur.

2. Coverage is provided for (Genotropin, Humatrope, Norditropin, Nutropin/Nutropin AQ, Saizen, Zomacton, Omnitrope):
   - pediatric growth failure due to chronic renal failure (in situations where the patient has not undergone a renal transplant) (provocative tests not required)
   - growth failure in children born small for gestational age (SGA) who fail to manifest catch up growth by age 2 defined as birth weight, birth length, or both that are more than 2 standard deviations below mean normal values following adjustment for age and gender (provocative tests not required).
   - pediatric growth failure due to Turner’s syndrome (provocative tests not required)
   - treatment of short stature associated with of Prader-Willi syndrome (provocative tests not required)
   - treatment of short stature associated with Noonan Syndrome (provocative tests not required)
3. Coverage is provided for adult growth hormone deficiency in the presence of (Genotropin, Humatrope, Norditropin, Nutropin/Nutropin AQ, Saizen, Zomacton, Omnitrope):
   a) a negative response to growth hormone stimulation test when the adult growth hormone deficiency is due to childhood onset growth hormone deficiency, pituitary or hypothalamic disease, surgery or radiation therapy, trauma; OR
   b) three pituitary hormone deficiencies and baseline serum IGF-I levels below the age- and sex-appropriate reference range when the adult growth hormone deficiency is due to irreversible hypothalamic-pituitary structural lesions or panhypopituitarism

4. Short Stature Homeobox-Containing Gene (SHOX) Deficiency in Children or Adolescents (Genotropin, Humatrope, Norditroprin, Nutropin/Nutropin AQ, Saizen, Zomacton, Omnitrope): Coverage is provided in the presence of the following:
   a) patient has SHOX deficiency demonstrated by chromosome analysis; AND
   b) epiphyses are open; AND
   c) patient has been evaluated by an endocrinologist; AND
   d) the patient’s baseline height is less than the 3rd percentile for age and gender.

For continuation of therapy, patient’s height has increased by greater than or equal to 2.5 cm/yr in the most recent year; AND the epiphyses are open.

5. Coverage is provided for Serostim® for the treatment of HIV Infection with Wasting or Cachexia in the presence of the following:
   a) patient is 18 years of age; AND
   b) wasting syndrome is not attributable to other causes such as; depression, MAC, chronic infectious diarrhea, or malignancy (Kaposi’s sarcoma limited to the skin or mucous membranes is covered); AND
   c) confirmation of wasting syndrome (e.g., unintentional weight loss of 10% of body weight or 90% or less than their lower ideal body weight); AND
   d) in situations where optimal antiretroviral therapy has been attempted

6. Coverage is provided for Increlex® in the treatment of growth failure in children with severe primary IGF-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone in the presence of the following:
   a) patient’s height standard deviation score must be ≤ -3.0 at baseline; AND
   b) the basal IGF-1 score must be below the lower limits of normal for the reporting lab; AND
   c) the patient must have normal or elevated growth hormone (except for patients with growth hormone gene deletion); AND
   d) epiphyses must be confirmed as open in patients 10 years of age; AND
   e) diagnosis made by an endocrinologist; AND
   f) not used concurrently with growth hormones or corticosteroids

7. Coverage is provided for Zorbtive® and Genotropin, Humatrope, Norditroprin, Nutropin/Nutropin AQ, Saizen, Zomacton, Omnitrope: for the treatment of Short Bowel Syndrome in Adults. Approve for 4 weeks if following criteria are met:
a) patient is receiving nutritional support  
b) patient is over 18 years of age

**Approval Duration**: Dependent on criteria above or details below. 365 days (1 year) if not specified.

**Growth Hormone**:

- *Pediatric human growth hormone deficiency, growth failure in children SGA, growth failure due to Turner’s syndrome, Noonan Syndrome or chronic renal failure*; benefit approved for 12 months and is renewable in the presence of open epiphyses and a growth response of 4.5 cm/yr (prepubertal growth rate) or 2.5 cm/yr (post-pubertal growth rate).
- *Prader-Willi Syndrome*; benefit approved for 12 months and is renewable in the presence of an increase in lean body mass (or decrease in fat mass).
- *Adult growth hormone deficiency*; benefit approved for 12 months and is renewable in the presence of clinical benefit (e.g., increase in total lean body mass, increase in IGF-1 and IGFBP-3 levels, or increase in exercise capacity).
- *Short bowel syndrome*; benefit approved for 1 month initially and is renewable for 1 month in situations where the patient is deriving clinical benefit (e.g., the patient is experiencing a decrease in intravenous nutrition requirements).
- *AIDS related cachexia (Serostim only)*; benefit approved for 3 months and is renewable in the presence of weight stabilization or increase.

**Increlex®**:

- Growth failure in children with severe primary IGF-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone: benefit approved for 12 months and is renewable in the presence of open epiphyses and a growth response of 4.5 cm/yr (prepubertal growth) or 2.5 cm/yr (post-pubertal growth).

**Conditions Not Recommended for Approval**

Coverage of Genotropin, Humatrope, Norditropin, Nutropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Tev-Tropin, Zorbtive and Increlex is recommended in circumstances that are listed in the Recommended Authorization Criteria (FDA-Approved Indications). Note: This is not an exhaustive list of Conditions Not Recommended for Approval.

1. **Non-Growth Hormone Deficient Short Stature (Idiopathic Short Stature) in Children or Adolescents**. Somatropin is indicated for the long-term treatment of idiopathic short stature (non-growth hormone deficient short stature) which is defined by a height SDS > 2.25 below the mean for age, sex, and population group that is associated with growth rates that are unlikely to permit attainment of adult height in the normal range and where diagnostic evaluation has excluded other causes of short stature, including GHD. The use of growth hormone to treat non-growth hormone deficient children with short stature who are otherwise healthy (idiopathic, familial, or constitutional delay of growth and puberty [CDGP]) has been controversial. Patients with CDGP and familial short stature may have heights that are more than 2 SDS below the mean and are growth hormone sufficient. The American Academy of Pediatrics (AAP) concluded that therapy with growth hormone is medically and ethically acceptable for "children whose extreme short stature keeps them from participating in basic
activities of daily living and who have a condition for which the efficacy of growth hormone therapy has been demonstrated.” The mean increase in adult height in children with idiopathic short stature that is attributed to somatropin therapy (average duration 4 to 7 years) is 3.5 to 7.5 cm. In controlled trials, in children with idiopathic short stature who were not growth hormone deficient, somatropin therapy was effective in increasing final adult height greater than pretreatment predicted adult height. No specific studies have been conducted in pediatric patients with familial short stature.

2. **Constitutional Delay of Growth and Puberty (CDGP).** These children have delayed skeletal maturation and pubertal development. Administering somatropin does not increase adult height (which is usually normal). Short-term androgen therapy accelerates growth and the rate of pubertal advancement in boys.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

**References**

- Humatrope® for injection [prescribing information]. Indianapolis, IN: Eli Lilly and Company; April 2015.
- Nutropin® for injection [prescribing information]. South San Francisco, CA: Genentech, Inc; April 2012.
- Increlex® injection [prescribing information]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc. (manufactured by Hospira, Incorporated; McPhersen, KS); May 2014.