

Growth Stimulating Drugs

To Initiate a Coverage Review, call 1 800 753-2851

Covered Medication

- Biosynthetic Human Growth Hormone: somatropin (*Humatrope*®, *Nutropin*®, *Serostim*®, *Saizen*®, *Norditropin*®, *Genotropin*®, *Tev Tropin*®, *Zorbtive*®, *Omnitrope*®, *Valtropin*®); somatrem (*Protropin*®); mecasermin (*Increlex*®)

Note: sermorelin (Geref® Diagnostic) is used for GH deficiency testing only and not for the treatment of GH deficiency.

What It Does and How It Is Used

- Growth hormone (GH) stimulates linear and skeletal growth, increases the number of skeletal muscle cells, influences organ size and increases red cell mass.
- GH is used in children who have growth failure due to a lack of adequate endogenous growth hormone and in the treatment of children who have growth failure associated with chronic renal insufficiency. It also is used to accelerate growth in patients with Turner syndrome (gonadal dysgenesis), a chromosomal abnormality seen in females. GH is also used in children with Prader-Willi syndrome, a rare genetic disorder that is characterized by short stature, an involuntary continuous urge to eat, low muscle tone, obesity and cognitive disabilities. GH treatment of children with Prader-Willi syndrome improves growth, increases muscle mass and reduces body fat.
- Children born small for gestational age (SGA) have a higher risk of short stature in adulthood in comparison with non-SGA children. SGA is defined as birth weight and/or birth length below standard limits (below the 10th percentile for gestational age), usually 2 standard deviations below the normal means following adjustment for age and sex. Almost 90% of SGA newborns will catch up to growth by age 2. Ten percent will fail to manifest catch-up growth and thus would be candidates for GH therapy.
- Short stature is one of many symptoms that affect children with the rare genetic disorder called Noonan syndrome. These children grow to the lower limits of normal adult height even though they do not have low growth hormone levels. Daily GH injections can increase height by an average of 9-11 cm within 2 years.
- GH therapy is used for adults with childhood-onset growth hormone deficiency, pituitary or hypothalamic disease, or GH deficiency due to surgery, radiation therapy, or previous trauma. Adult GH deficiency is characterized by increased weight and body fat mass, decreased lean body mass, decreased exercise capacity, decreased muscle mass and strength, reduced cardiac performance, reduced bone density and impaired sense of well-being. In adults, the goals of GH therapy are to restore normal body composition, improve muscle and cardiac function, normalize serum lipid concentrations and improve the quality of life.
- Short bowel syndrome is a rare condition affecting approximately 10,000 to 20,000 patients. These patients are most often dependent on supplemental intravenous feedings for nutritional support. Short-bowel syndrome results from having a significant amount of small intestine removed during surgery. Conditions such as insufficient blood flow to the GI tract, intestinal obstruction, or Crohn's disease may warrant the removal of intestines. GH therapy is used in the management of short bowel syndrome patients to decrease the need for intravenous nutritional support by increasing the bowel's ability to absorb nutrients from oral intake. Patients with short bowel syndrome are assessed for treatment benefit after 4 weeks of GH therapy.
- *Serostim*® is used for the treatment of AIDS-related cachexia or wasting. GH has been shown to increase lean body mass and decrease fat mass in patients with AIDS.
- Other conditions for which there is insufficient information to support the use of GH include:
 - Constitutional delay of growth, which is characterized by normal prenatal growth followed by growth deceleration during infancy and childhood. In general, these patients can achieve normal adult height if no treatment is given.
 - Delaying or reversing the aging process in older adults
 - Adjunct to infertility treatment
 - Treatment of burn injuries
 - Treatment of obesity
- GH is administered subcutaneously or intramuscularly one to six times weekly for all indications other than short bowel syndrome, in which it is administered daily.
- In healthy children, GH is secreted into the bloodstream and acts to stimulate production of IGF-1. IGF-1 is the main hormone responsible for carrying out the effects of GH, and it must be present in order for children's bones, cartilage and organs to grow normally. In primary IGF-1 deficiency, GH levels are not low, but rather, cells are unable to produce adequate IGF-1 in response to GH stimulation. Primary IGF-1 deficiency is caused by any defect in the process of IGF-1 production.
- *Increlex*® (recombinant human IGF-1) is used in children who have growth failure due to severe primary IGF-1 deficiency. Primary IGF-1 deficiency affects approximately 30,000 children with short stature in the

United States, and 6,000 of these children have *severe* primary IGF-1 deficiency. Severe primary IGF-1 deficiency is characterized in children with height and serum IGF-1 levels ≥ 3 standard deviations below normal in the presence of normal or elevated GH levels.

- IGF-1 is being investigated for use in the treatment of less severe forms of primary IGF-1 deficiency and in the treatment of severe insulin-resistant diabetes.
- *Increlex* is administered subcutaneously twice daily for severe primary IGF-1 deficiency.

Rationale for Prior Authorization

- To reduce exposure to costs associated with use of growth hormone or IGF-1 for conditions for which its effectiveness is not known (e.g., treatment of constitutional delayed growth, infertility, severe insulin-resistant diabetes or less severe forms of primary IGF-1 deficiency). Growth hormone therapy is not covered for use in reversing or delaying the aging process.

Benefit Design

- Coverage is determined through a prior authorization process for every claim.

Prior Authorization Criteria

This prescription benefit provides coverage for growth hormone therapy in accord with the following criteria:

1. Coverage is provided for pediatric growth hormone deficiency in the presence of the following:
 - Patient's height must be below the third percentile for their age- and gender-related height OR
 - growth velocity subnormal ≥ 2 standard deviations from the age-related mean OR
 - delayed skeletal maturation ≥ 2 standard deviations below the age- and gender-related mean AND
 - epiphyses confirmed as open in patients ≥ 10 years of age AND
 - growth hormone deficiency confirmed by any two provocative tests OR by insulin growth factor-1 (IGF-1), a.k.a. somatomedin C, or IGF binding protein-3 (IGFBP-3) levels.

 - For continuation of coverage, a growth response of ≥ 4.5 cm/yr (prepubertal growth phase) or ≥ 2.5 cm/yr (postpubertal) must occur.
2. Coverage is provided for:
 - 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 syndrome (provocative tests not required)
 - treatment of Prader-Willi syndrome (provocative tests not required)
 - treatment of short stature associated with Noonan syndrome (provocative tests not required)
3. Coverage is not provided for idiopathic short stature (non-growth hormone-deficient short stature).
4. Coverage is not provided for constitutional delayed growth.
5. Coverage is provided for adult growth hormone deficiency (in the presence of a growth hormone stimulation test) due to:
 - childhood onset growth hormone deficiency
 - pituitary or hypothalamic disease
 - surgery or radiation therapy
 - trauma
6. Coverage is provided for the treatment of short bowel syndrome in patients receiving supplemental nutritional support.
7. Coverage for *Serostim*[®] for the treatment of AIDS-related cachexia is provided in the presence of ALL of the following:
 - patient ≥ 18 years of age
 - wasting syndrome 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)

- confirmation of wasting syndrome (e.g., unintentional weight loss of $\geq 10\%$ of body weight)
- in situations where optimal antiretroviral therapy has been attempted

8. Coverage for *Increlex* is provided in accord with the following:

1. For the long-term 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:
 - patient's height standard deviation score must be ≤ -3.0 AND
 - the basal IGF-1 score must be below the lower limits of normal for the reporting lab AND
 - the patient must have normal or elevated growth hormone (except for patients with growth hormone gene deletion) AND
 - epiphyses must be confirmed as open in patients ≥ 10 years of age
2. Coverage is provided in situations where the diagnosis of primary IGF-1 deficiency has been made by an endocrinologist.
3. Coverage is not provided in the presence of:
 - Concurrent treatment with growth hormone
 - Pharmacologic doses of corticosteroids

Coverage Duration

Pediatric human growth hormone deficiency, growth failure in SGA children, growth failure due to Turner 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 (postpubertal growth rate).

Adult growth hormone deficient syndrome; benefit approved for 6 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 and is renewable in the presence of clinical benefit (e.g., a decrease in the patient's intravenous nutritional requirements).

AIDS-related cachexia (*Serostim*[®] only); benefit approved for 3 months and is renewable in the presence of weight stabilization or increase.

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).

Increlex[™]:

Growth failure for children with severe primary IGF-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone; initial coverage duration: 12 months. Coverage may be renewed for 12 months in the presence of open epiphyses and a growth response of ≥ 4.5 cm/yr (prepubertal growth) or ≥ 2.5 cm/yr (postpubertal growth).

References

Product Information:	mecasermin (<i>Increlex</i> [®] — Tercica) 2005.
Product Information:	sermorelin (<i>Geref</i> [®] — Serono) 2003.
Product Information:	somatrem (<i>Protropin</i> [®] — Genentech) 2001.
Product Information:	somatropin (<i>Genotropin</i> [®] , <i>Genotropin MiniQuick</i> [®] — Pharmacia) 2003.
Product Information:	somatropin (<i>Humatrope</i> [®] — Lilly) 2004.
Product Information:	somatropin (<i>Norditropin</i> [®] — Novo Nordisk) 2002.
Product Information:	somatropin (<i>Nutropin</i> [®] , <i>Nutropin Depot</i> [®] , <i>Nutropin AQ</i> [®] , <i>Nutropin AQ Pen</i> [®] — Genentech) 2004.
Product Information:	somatropin (<i>Saizen</i> [®] — Serono) 2004.

Product Information: somatropin (*Serostim*[®] — Serono) 2003.

Product Information: somatropin (*Zorbitive*[®] — Serono) 2004.

Product Information: somatropin (*Tev-Tropin*[®] — Teva Pharmaceuticals USA) 2005.

Product Information: Somatropin (*Omnitrope*[™] — Sandoz) 2006.

Product Information: Somatropin (*Valtropin*[®] — LG Life Sciences) 2007.

<http://www.aace.com/clin/guidelines/hgh.pdf>

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