

Growth Hormones (GH) UTILIZATION MANAGEMENT CRITERIA

DRUG CLASS: Synthetic recombinant Growth Hormone (Somatropin)

BRAND NAMES:

- Genotropin
- Humatrope, HumatroPen
- Norditropin Nordiflex, Norditropin Flexpro
- Nutropin, Nutropin AQ, Nutropin AQ Nuspin
- Omnitrope
- Saizen
- Serostim
- Tev-Tropin
- Zorbitive

FDA-APPROVED INDICATIONS

- Growth failure associated with chronic renal insufficiency
- Growth failure associated with Noonan syndrome
- Growth failure associated with Prader-Willi syndrome
- Growth failure associated with Turner syndrome
- Growth failure in children
 - For children born small for gestational age (SGA) who fail to manifest catch-up growth by 2 years of age
 - For the treatment of children with short stature born SGA with no catch-up growth by 2 to 4 years of age
- Growth hormone deficiency in adults
 - For the replacement of endogenous growth hormone in adults with growth hormone deficiency (GHD) who meet either of the following 2 criteria:
 - Adult-onset: Patients who have GHD, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation, or trauma.
 - Childhood-onset: Patients who were GHD during childhood as a result of congenital, genetic, acquired, or idiopathic causes.

In general, confirmation of the diagnosis of adult GHD in both groups usually requires an appropriate growth hormone stimulation test. However, confirmatory testing may not be required in patients with congenital/genetic GHD or multiple pituitary hormone deficiencies caused by organic disease.

- Idiopathic short stature
- Short bowel syndrome
- Short stature homeobox-containing gene deficiency
- Wasting or cachexia associated with HIV (Serostim): For the treatment of patients with HIV with wasting or cachexia to increase lean body mass (LBM) and body weight, and improve physical endurance. Concomitant antiretroviral therapy is necessary.

COVERAGE AUTHORIZATION CRITERIA:

Requests for products other than Omnitrope will be approved if the patient has tried Omnitrope and had an inadequate response to this product or could not tolerate it as long as the below criteria are met. (effective 3/1/2012)

A. In children (under age 18) with open epiphyses, Growth Hormone (GH) therapy may be considered medically necessary and is eligible for coverage for the following conditions:

1. Children who have growth failure due to inadequate secretion of GH, as documented by failure of at least one GH stimulation test (e.g., L-dopa, clonidine, glucagon, propranolol, arginine, or insulin challenge test), and as documented by serial height/length and weight records showing linear growth failure, and who are persistently under the 3rd percentile (i.e., > 1.88 SD below mean for age and sex) in height.
 - a. Documentation of significant growth deceleration is sufficient for children with history of relevant CNS pathology or history of brain irradiation.
 - b. Neonates with hypoglycemia and growth hormone deficiency (one abnormal GH test is sufficient for hypoglycemic neonates in whom growth hormone deficiency is suspected)
2. Female children with Turner Syndrome who are under the 5th percentile in height.
3. Children with SHOX (short stature homeobox-containing gene) deficiency who are persistently under the 3rd percentile (i.e., > 1.88 SD below mean for age and sex) in height.
4. Children with growth failure due to Prader-Willi Syndrome (PWS) or Noonan Syndrome.
5. Children with severe burns (3rd degree) have been successfully treated with GH during their hospitalization and for up to 1 year after burn to prevent observed growth delays. Treatment can be covered for no more than one year after discharge from hospital. There is no evidence of benefit for treatment beyond one year. (See also C.3 below.)
6. Children who were born small for gestational age (SGA) or with intrauterine growth retardation (IUGR) in whom the birth weight and/or length were more than 2 standard deviations (SD) below the mean for the gestational age, and fail to show catch-up growth by age 2 (defined as a height velocity below 1 standard deviation score, adjusted for age). For children with intrauterine growth retardation (IUGR) or who are small for gestational age (SGA) who have been previously treated with Growth Hormone, coverage may be continued if the criteria under 9.a-d below are met and the medical records indicate that the child met the criteria above at the time of initiation of Growth Hormone therapy.
7. Children with chronic renal failure or insufficiency (defined as GFR [glomerular filtration rate] of < 75 ml/min/1.73m²) resulting in short stature (i.e., persistently under 3rd percentile in height). GH therapy should be discontinued at the time of kidney transplant. GH therapy may be resumed one year following kidney transplant if catch up growth has not occurred.
8. A 6 month trial of growth hormone may be considered medically necessary in children who do not fail a growth hormone (GH) stimulation test but are identified to have biochemical abnormalities in the growth hormone metabolic pathway and meet the following criteria:
(***NOTE***These cases should be reviewed by the Medical Director for individual consideration.***)
 - a. Persistently below the 1.2 percentile in height, (2.25 standard deviation below the mean for age & sex or >2 standard deviations below the mid parental height percentile); AND
 - b. Growth velocity <25 th percentile for bone age; AND

c. Bone age > 2 standard deviations below the mean for age; AND

d. Low serum insulin-like growth factor 1 (IGF-1, also called Somatomedin C) AND/OR insulin-like growth factor binding protein 3 (IGFBP3). ***Children whose height is >3.0 SD below age-matched mean and whose IGF-1 levels are also >3 SD below mean may be diagnosed with primary IGF-1 deficiency. See policy, [Treatment for Severe Primary IGF-1 Deficiency](#). (link)

9. Continued pediatric GH therapy is considered medically necessary, and will be covered, if, after a suitable course of initial therapy (6 - 12 months) **ALL** of the following apply:

a. Increase in growth velocity over pre-treatment level is >50 percent; AND

b. Annual growth velocity in response to therapy is calculated to be > 4.5 cm/year in a pre-pubertal child or > 2.5 cm/yr in a post-pubertal child; AND

c. Expected final adult (estimated mid-parental) height has not been achieved; AND

d. Epiphyses have not closed. Epiphyseal closure is defined as a bone age of 16 years in a male or 14 years in a female on wrist films. Note: Wrist films for bone age must be obtained annually for renewal submission for girls > 10 years old and boys > 12 years old.

B. Adults with inadequate GH production may experience any of the following symptoms: abnormal weight gain with increased body fat content, decreased lean body mass (muscle and bone), decreased exercise capacity and endurance, decreased muscle mass and strength, decreased bone density, reduced cardiac performance, impaired sense of well-being and depression. In adults, GH therapy may be considered medically necessary and is eligible for coverage for the following conditions:

1. Adult onset symptomatic GH deficiency associated with low GH levels (documented by failure of at least two GH stimulation tests). 24-hour continuous measurements of GH, serum levels of IGF-1, or serum levels of IGFBP-3 are considered inadequate to document GH deficiency.

2. Childhood onset symptomatic GH deficiency, where persistent GH deficiency is documented by at least one failed GH stimulation test performed at least 3 months after the cessation of prior GH therapy.

3. Adult onset symptomatic GH deficiency associated with multiple hormone deficiencies (i.e., panhypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery radiation therapy, or trauma. The diagnosis of panhypopituitarism is established when either one of the two following criteria (a or b) are met:

a. At least 2 additional hormone deficiencies (other than GH) requiring hormone replacement therapy are documented (e.g., TSH, ACTH, ADH or gonadotropin hormones) as well as failure of at least 1 GH stimulation test, OR

b. Three pituitary hormone deficiencies (other than GH) requiring hormone replacement therapy (where clinically appropriate) are documented AND a low IGF-1 level (below 80 ng/ml) is documented in lieu of GH stimulation testing.

4. Renewal of coverage for adult GH therapy may be granted on an annual basis without additional testing if the original documentation of failed GH stimulation testing is made available with the request for renewal of coverage, and there is continued clinical benefit in symptoms or signs.

C. Other conditions in which GH therapy may be considered medically necessary and are eligible for coverage include the following:

1. HIV cachexia or "wasting syndrome," defined by unintentional weight loss of at least 10% of baseline weight, or BMI < 20 kg/m², not attributable to other causes (such as AIDS-associated diarrhea, infection, malignancy or depression), when optimal anti-viral therapy has been instituted. Therapy is continued until this definition is no longer met.

2. Short Bowel Syndrome (SBS), defined as the inability to maintain adequate nutritional status without parenteral (intravenous) supplementation required at least 5 days/week for a total of at least 3,000 calories/week, due to surgical or functional loss of small bowel.

a. Continued coverage for Short Bowel Syndrome will be approved on a quarterly basis (every 3 months) when continued benefit is documented by a sustained decrease in IV nutritional requirements and sustained weight.

3. Promotion of wound healing in children or adults with 3rd degree burns.

Criteria for GH NOT being covered:

A. When Omnitrope has **NOT** been tried to treat the patient's condition.
(updated as of 12/1/2011, effective 3/1/2012)

B. When none of the conditions under "Coverage Authorization Criteria" are present, OR when any of the conditions for continued therapy ("renewal criteria") are not met, the use of GH therapy will be considered not medically necessary.

C. The use of Growth Hormone for short stature in patients with no proven Growth Hormone deficiency (e.g., idiopathic short stature without evidence of biologic impairment of the growth hormone pituitary axis) is not covered. It is considered cosmetic.

D. Investigational conditions. The use of GH therapy is considered investigational and is not covered for certain conditions, including but not limited to:

1. Constitutional delay (defined as lower than expected height percentiles compared with their target height percentiles and delayed skeletal maturation when growth velocities and rates of bone age advancement are normal.)

2. Therapy for geriatric patients, defined as age > 65.

3. Anabolic therapy provided to counteract acute or chronic catabolic illness due to surgery outcomes, trauma (except for children with severe burns or for promotion of wound healing in children or adults with third degree burns), cancer, chronic hemodialysis (except as specified above for chronic renal insufficiency) or chronic infectious disease producing catabolic (protein wasting) changes in both adult and pediatric patients (except for the specific covered indication of AIDS wasting noted above, under "Coverage Authorization Criteria").

4. Anabolic therapy provided to enhance body mass or strength for professional, recreational or social reasons.

5. Glucocorticoid-induced growth failure.

6. Short stature after renal transplantation.

7. Short stature due to Bloom or Down Syndrome.

8. Treatment of altered body habitus (e.g., buffalo hump) associated with antiviral therapy in HIV infected patients.

9. Precocious puberty.

10. Obesity.
11. Cystic fibrosis.
12. Idiopathic dilated cardiomyopathy.
13. Infertility.
14. Juvenile rheumatoid (or idiopathic chronic) arthritis.
15. Chronic hepatitis.
16. Diabetes.

E. Contraindications. The use of synthetic GH is contraindicated and should not be used in the following individuals:

1. Children or adults with active malignancies or other tumors.
2. Patients with a known sensitivity to any ingredients in the synthetic GH product.
3. Patients with proliferative or preproliferative diabetic retinopathy.
4. Patients with benign intracranial hypertension (BIH), also called pseudotumor cerebri.
5. Critically ill patients (e.g., post-surgical, ICU, respiratory failure or multiple trauma patients).
6. Pregnant or lactating females

CONTRAINDICATIONS:

- Acute Critical Illness
- Children with Prader-Willi Syndrome who are severely obese or have severe respiratory impairment—reports of sudden death
- Active Malignancy
- Active Proliferative or Severe Non-Proliferative Diabetic Retinopathy
- Children with closed epiphyses
- Known hypersensitivity to somatotropin or excipients

WARNINGS AND PRECAUTIONS:

- Acute Critical Illness: Potential benefit of treatment continuation should be weighed against the potential risk
- Prader-Willi Syndrome in children: Evaluate for signs of upper airway obstruction and sleep apnea before initiation of treatment.
- Neoplasm: Monitor patients with preexisting tumors for progression or recurrence. Increased risk of a second neoplasm in childhood cancer survivors treated with somatotropin—in particular meningiomas in patients treated with radiation to the head for their first neoplasm
- Impaired Glucose Tolerance and Diabetes Mellitus: May be unmasked. Periodically monitor glucose levels in all patients. Doses of concurrent antihyperglycemic drugs in diabetics may require adjustment
- Intracranial Hypertension: Exclude preexisting papilledema. May develop and is usually reversible after discontinuation or dose reduction
- Fluid Retention (i.e., edema, arthralgia, carpal tunnel syndrome, especially in adults): May occur frequently. Reduce dose as necessary

- Hypopituitarism: Closely monitor other hormone replacement therapies
- Hypothyroidism: May first become evident or worsen
- Slipped Capital Femoral Epiphysis: May develop. Evaluate children with the onset of a limp or hip/knee pain
- Progression of Preexisting Scoliosis: May develop
- Otitis Media and Cardiovascular Disorders in Turner syndrome: Patients with Turner syndrome should be evaluated for otitis media and other ear disorders and monitored for cardiovascular disorders
- Pancreatitis: Consider pancreatitis in patients with persistent severe abdominal pain, especially children
- Adverse events and death associated with benzyl alcohol: Formulations containing benzyl alcohol should not be used in premature babies or neonates. Consider the combined daily metabolic load of benzyl alcohol from all sources

REFERENCES:

Growth Hormone Medical Policy.

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http://www.omnitrope.com/omnitrope/PDFs/Prescribing_Information.pdf

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