# Growth Hormones

| Override(s) | Approval Duration |
|---|---|
| Prior Authorization<br>Quantity Limit | **Children with reconstructive indications:** 1 year for individuals 12 and younger; 6 months for individuals 13 and older<br><br>**Children with idiopathic growth hormone deficiency (GHD):** 1 year for all ages<br><br>**GH treatment in transitioning adolescents with childhood onset GH deficiency to adulthood:** 1 year<br><br>**GH deficiency in adults:** 1 year<br><br>**Other approvable conditions**: 1 Year |

| Medications | | |
|---|---|---|
| Omnitrope (somatropin) | Preferred Agent | May be subject to quantity limits |
| Genotropin (somatropin) | Non-Preferred Agents | |
| Humatrope (somatropin) | | |
| Ngenla (somatrogon-ghla) | | |
| Norditropin (somatropin) | | |
| Saizen (somatropin) | | |
| Saizenprep (somatropin) | | |
| Serostim (somatropin) | | |
| Skytrofa (lonapegsomatropin-tcgd) | | |
| Sogroya (somapacitan-beco) | | |
| Zomacton (somatropin) | | |
| Zorbtive (somatropin) | | |

| FDA Approved Indications | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Drug** | **Indication** | | | | | | | | | | |
| | **Growth Hormone Deficiency** | | **Growth Failure due to Chronic Renal Insufficiency** | **Growth Failure in Children Born Small for Gestational Age** | **Prader-Willi Syndrome in Children** | **Turner's Syndrome** | **Cachexia AIDs-related** | **Noonan syndrome** | **Idiopathic short Stature** | **Short stature homeobox containing gene deficiency** | **Short Bowel Syndrome** |
| | **Children** | **Adult** | | | | | | | | | |
| Genotropin | ✓ | ✓ | | ✓ | ✓ | ✓ | | | ✓ | | |
| Humatrope | ✓ | ✓ | | ✓ | | ✓ | | | ✓ | ✓ | |
| Ngenia | ✓ | | | | | | | | | | |
| Norditropin | ✓ | ✓ | | ✓ | | ✓ | | ✓ | | | |
| Nutropin AQ NuSpin (Preferred) | ✓ | ✓ | ✓ | | | ✓ | | | ✓ | | |
| Saizen Saizenprep | ✓ | ✓ | | | | | | | | | |
| Omnitrope | ✓ | ✓ | | ✓ | ✓ | ✓ | | | ✓ | | |
| Serostim | | | | | | | ✓ | | | | |
| Skytrofa | ✓ | | | | | | | | | | |
| Sogroya | ✓ | ✓ | | | | | | | | | |
| Zomacton | ✓ | ✓ | | ✓ | | ✓ | | | ✓ | ✓ | |
| Zorbtive | | | | | | | | | | | ✓ |

## APPROVAL CRITERIA

### Step Therapy

I. Requests (initial or continuation) for all Non-Preferred Growth Hormones require a trial and inadequate response or intolerance to Omnitrope and documentation is provided;

**OR**

II. Omnitrope is not FDA-approved and does not have an accepted off-label use per the off-label policy for the prescribed indication and the requested agent is. Refer to the above matrix by drug and indication.

**OR**

III. If request is for Ngenia, Sogroya or Skytrofa, individual or caregiver is unable to administer daily somatropin injections; **AND**

IV. Documentation is provided for why the long-acting formulation is clinically necessary and not for convenience.

***Reconstructive therapies** are intended to address a significant variation from normal, related to **accidental injury, disease, trauma, treatment of a disease or congenital defect**, but do not result in significant functional impairment to the individual. Growth hormone (GH) treatment is considered RECONSTRUCTIVE in nature for individuals who do not have growth

hormone deficiency. ***NOTE:*** **Not all benefit contracts include benefits for reconstructive services. Benefit language supersedes this document.**

**Prior Authorization**

Initial requests for growth hormone (GH) therapy (somatropin [Genotropin, Humatrope, Norditropin, Omnitrope, Saizen, Saizenprep, Zomacton], somatrogon-ghla [Ngenla], lonapegsomatropin-tcgd [Skytrofa], somapacitan-beco [Sogroya] **for growth hormone deficiency in children** may be approved if the following criteria are met: (GH Research Society 2000, Grimberg 2016):

I. Individual has a diagnosis of idiopathic growth hormone deficiency (GHD) as indicated by the following:
   A. Documentation is provided that individual has signs or symptoms of GHD such as growth velocity 2 Standard Deviations (SD) below age-appropriate mean or height 2.25 SD below the age-appropriate mean; **AND**
   B. Documentation is provided that individual has a subnormal response (less than10 ng/ml) to any **TWO** of the following standard growth hormone stimulation tests:
      1. Arginine;
      2. Clonidine;
      3. Glucagon;
      4. Insulin induced hypoglycemia;
      5. L-dopa - Propranolol);

**OR**

II. Documentation is provided that individual has presence of at least two other pituitary hormone deficiencies, in addition to Insulin-like growth factor 1 (IGF-1) measurement below age-appropriate level; **OR**

III. Individual is a neonates with hypoglycemia and clinical and hormone evidence of hypopituitarism (growth hormone level less than 10 ng/ml) **OR**

IV. Documentation is provided that individual has had cranial irradiation and have evidence of IGF-1 measurement below age-appropriate level with normal thyroid function tests results;

**AND**

V. If individual is requesting Skytrofa (lonapegsomatropin-tcgd), individual is 1 year of age or older; **AND**

VI. Individual weights at least 11.5kg; **OR**

VII. If individual is requesting Sogroya (somapacitan-beco), individual is 2.5 years of age or older; **OR**

VIII. If individual is requesting Ngenla (somatrogon-ghla), individual is 3 years of age or older.

Initial requests for growth hormone (GH) therapy (somatropin [Genotropin, Humatrope, Norditropin, Omnitrope, Saizen, Saizenprep, Zomacton]) **for reconstructive* (see above note for reconstructive diagnosis) therapy in children** may be approved if the following criteria are met:

I. Individual meets either of the following requirements (Grimberg 2016):

A. Documentation is provided that the child's height is at least 2.25 but less than 2.5 standard deviations below the mean for his or her age and gender *and* growth velocity is less than the 10th percentile over one year; **OR**
B. Documentation is provided that the child's height is at least 2.5 standard deviations below the mean for his or her age and gender, regardless of growth velocity;

**AND**

II. Individual has a condition known to be responsive to GH therapy, including but not limited to:
   A. Chronic renal insufficiency; **OR**
   B. Children with Prader-Willi syndrome who are not severely obese [body mass index (BMI) less than 35], do not have history of upper airway obstruction or sleep apnea, and do not have severe respiratory impairment, and who do not meet the criteria described above in RN I. – IV. In the section labeled *Initial requests for growth hormone (GH)* ***in children***; **OR**
   C. Noonan syndrome; **OR**
   D. Turner syndrome; **OR**
   E. Children with Short Stature Homeobox (SHOX) gene; **OR**
   F. Children who are born small for gestational age defined as **all** of the following:
      1. Child was born small for gestational age (SGA), defined as birth weight or length 2 or more standard deviations below the mean for gestational age (infants with intrauterine growth restriction or Russell-Silver Syndrome resulting in SGA are included in this category); **AND**
      2. Child fails to manifest catch up growth before 4 years of age, defined as height 2 or more standard deviations below the mean for age and sex (Clayton, 2007); **AND**
      3. Other causes for short stature such as growth inhibiting medication, chronic disease, endocrine disorders, and emotional deprivation or syndromes (except for Russell-Silver syndrome) have been ruled out.

Continuation of therapy with GH therapy (somatropin [Genotropin, Humatrope, Norditropin, Omnitrope, Saizen, Saizenprep, Zomacton, somatrogon-ghla [Ngenla], lonapegsomatropin-tcgd [Skytrofa], somapacitan-beco [Sogroya]) **in children** (**including** those who previously met criteria for GHD or reconstructive therapy) ] may be approved if the following criteria are met (if reconstructive, individual has not met the requirements for termination of GH therapy):

I. Individual is evaluated on an annual basis for all conditions; **AND**
II. Growth rate remains above 2.5 cm/year (does not apply to children with prior documented hypopituitarism) (Grimberg 2016); **AND**
III. For children over age 12, either of the following:
   A. Documentation is provided that an X-ray report with evidence that epiphyses have not yet closed (does not apply to children with prior documented hypopituitarism) **OR**
   B. A Sexual Maturity Rating (SMR, Tanner Stage) less than or equal to 3; **OR**
   C. If SMR, Tanner Stage is greater than or equal to 4, and request is for prior documented hypopituitarism, then follow the criteria titled, "Treatment with growth hormone (GH) (somatropin [Genotropin, Humatrope, Norditropin, Nutropin AQ,

Omnitrope, Saizen, Zomacton]) **in transitioning adolescents with childhood onset GH deficiency to adulthood**".

Treatment with growth hormone (GH) **for reconstructive therapy in children** should no longer continue if the following criteria are met:

I. Individual has bone age =16 years in males or = 14 years in females; **OR**
II. Individual has evidence of epiphyseal fusion; **OR**
III. Documentation is provided that "mid-parental height" is achieved [NOTE: Mid-parental height = (father's height + mother's height) divided by 2, plus 2.5 inches (male) or minus 2.5 inches (female)].

Treatment with growth hormone (GH) (somatropin [Genotropin, Humatrope, Norditropin, Omnitrope, Saizen, Saizenprep, Zomacton]) **in transitioning adolescents with childhood onset GH deficiency (GHD) to adulthood** may be approved if the following criteria are met:

I. SMR, Tanner Stage is greater than or equal to 4; **AND**
II. One of the following:
    A. GH treatment has been stopped for at least one (1) month; **and** the diagnosis of GHD is as follows:
        1. For individuals with idiopathic isolated GHD: A subnormal response *** to **two** (2) standard GH stimulation tests, **or** subnormal response to **one** (1) provocative test **and** low IGF-I/IGFBP-3, and documentation is provided; **OR**
        2. For individuals with multiple pituitary hormone deficiencies, a subnormal response*** to 1 provocative GH test and/or low IGF-1/IGFBP-3 and documentation is provided; **OR**
        3. For individuals who have had cranial irradiation, continued documentation is provided showing IGF-1 measurement below age-appropriate level with normal thyroid function test results;

        ***Subnormal response is defined as serum GH concentration of less than 10 ng/mL. Acceptable stimulation tests include: insulin induced hypoglycemia, arginine, glucagon, clonidine, L-dopa-propranolol.

    **OR**

    B. Documentation is provided showing presence of any of the following conditions (GH stimulation tests are not required):
        1. A known genetic mutation associated with deficient growth hormone production or secretion; **OR**
        2. Hypothalamic-pituitary tumor or structural defect; **OR**
        3. At least three (3) other pituitary hormone deficiencies.

Treatment with GH (somatropin [Genotropin, Humatrope, Norditropin, Omnitrope, Saizen, Saizenprep, Zomacton, somapacitan-beco [Sogroya]) **in adults** may be approved if the following criteria are met:

I. Documentation is provided that individual has GHD, also known as somatropin deficiency syndrome, in childhood; **OR**

II. Documentation is provided that individual has hypopituitarism as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, trauma or aneurismal subarachnoid hemorrhage (NOTE: Individuals being treated for GHD due to trauma or aneurysmal subarachnoid hemorrhage must have GHD reverified at 12 months after the event);

**AND**

III. GHD verified or reverified by any of the following:

A. Documentation is provided showing a subnormal response in adults to **two** standard growth hormone stimulation tests (possible stimulation tests include, but are not limited to: insulin-induced hypoglycemia and combined arginine-growth hormone releasing hormone); defined as:

1. Serum GH concentration of less than or equal to 5 ng/ml when using insulin induced hypoglycemia testing; **OR**
2. Serum GH concentration of less than or equal to4.1 ng/ml when using arginine; **OR**

B. Subnormal response to **one** (1) stimulation test for adults with hypothalamic or pituitary disease *and* one or more additional pituitary hormone deficits, and documentation is provided; **OR**

C. Documentation is provided showing presence of at least three other pituitary hormone deficiencies (that is, growth hormone stimulation tests are not required in this subgroup of individuals).

Initial requests for Serostim (somatropin) may be approved if the following criteria are met:

I. Documentation is provided that individual has HIV-associated wasting syndrome or cachexia, defined as one of the following (Schambelan 1996):

1. Unintentional weight loss that is greater than or equal to 10% of baseline weight: **OR**
2. Weight that is less than 90% of the lower limit of ideal body weight; **AND**

II. Weight loss cannot be explained by a concurrent illness other than HIV infection; **AND**

III. Individual is simultaneously being treated with antiretroviral therapy.

Continuation of therapy for Serostim (somatropin) may be approved if the following criteria are met:

I. Individual is simultaneously being treated with antiretroviral therapy; **AND**

II. Documentation is provided that weight is less than 90% of the lower limit of ideal body weight; **AND**

III. Documentation is provided that continued need is demonstrated by clinical effect (for example, patient has had a clinically significant improvement in body weight, lean body mass, or physical endurance from baseline with treatment).

Requests for Zorbtive (somatropin) may be approved if the following criteria are met:

I. Individual has been diagnosed with short bowel syndrome; **AND**
II. Individual is receiving specialized nutritional support (may consist of a high-carbohydrate, low-fat diet adjusted for individual requirements) in conjunction with optimal management of short bowel syndrome.

Treatment with GH may **not** be approved for the following criteria:

I. Individual has a diagnosis of idiopathic short stature (ISS); **OR**
II. Individual is a child who does not have signs or symptoms of idiopathic GHD (for example, reduced height or growth velocity), unless:
   A. Criteria for other pituitary hormone deficiencies are met; **OR**
   B. Criteria for neonate with hypoglycemia are met; **OR**
   C. Criteria for cranial irradiation are met. (Note: an individual who does not meet necessity criteria may meet reconstructive criteria); **OR**
III. Individual is an adult being treated for GHD due to trauma or aneurysmal subarachnoid hemorrhage and does not have re-testing confirmatory for growth hormone deficiency; **OR**
IV. Individual is using to treat conditions where applicable criteria have not been met, including, but not limited to, the following:
   A. After renal transplant; **OR**
   B. Anabolic therapy, except for AIDS, provided to counteract acute or chronic catabolic illness (e.g. surgery, trauma, cancer, chronic hemodialysis) producing catabolic (protein wasting) changes in both adults and children; **OR**
   C. Anabolic therapy to enhance body mass or strength for professional, recreational or social reasons; **OR**
   D. Constitutional delay of growth and development; **OR**
   E. Cystic Fibrosis; **OR**
   F. Growth hormone treatment in combination with GnRH agonist (Lupron) as a treatment of precocious puberty; **OR**
   G. Hypophosphatemic rickets; **OR**
   H. Osteogenesis imperfecta; **OR**
   I. Osteoporosis; **OR**
   J. Short stature associated with growth hormone insensitivity (Laron Syndrome) ; **OR**
   K. Therapy in older adults with normally occurring decrease in GH, who are not congenitally GH deficient and who have no evidence of organic pituitary disease (this is referred to as age-related GH deficiency) ; **OR**
   L. Treatment of congestive heart failure (CHF) ; **OR**
   M. Treatment of individuals with burns; **OR**
   N. Treatment of fibromyalgia; **OR**
   O. Treatment of glucocorticoid-induced growth failure; **OR**
   P. Treatment of HIV lipodystrophy (fat redistribution syndrome), also referred to as altered body habitus (e.g. buffalo hump), associated with antiviral therapy in individuals with HIV-infection; **OR**
   Q. Treatment of intrauterine growth restriction (IUGR) or Russell-Silver Syndrome that does not result in SGA; **OR**

R. Treatment of obesity; **OR**
S. Other etiologies of short stature where GH has not been shown to be associated with an increase in final height, including but not limited to achondrdoplasia and other skeletal dysplasias; **OR**

V. Individual is undergoing diagnostic testing requiring overnight hospitalization for spontaneous growth hormone secretion; **OR**

VI. When the above criteria are not met and for all other indications.

**Key References**:


1. Clayton PE, Cianfarani S, Czernichow P, Johannsson G, Rapaport R, Rogol A. Consensus statement: Management of the child born small for gestational age through to adulthood: A consensus statement of the international societies of pediatric endocrinology and the growth hormone research society. *J Clin Endocrinol Metab*. March 2007; 92(3):804-810. Accessed April 10, 2024.
2. Cook DM, Yuen KC, Biller BM, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in growth hormone-deficient adults and transition patients - 2009 update. Endocr Pract. 2009; 15(Suppl 2):1-29. Accessed April 10, 2024.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: April 10, 2024.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. GH Research Society. Consensus Guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: Summary statement of the GH Research Society. *J. Clin Endocrin Metab.* 2000 Nov; 85(11):3990-3993. Accessed April 10, 2024.
6. Grimberg A, DiVall SA, Polychronakos C, et.al. Guidelines for growth hormone and insulin-like growth factor-I treatment in children and adolescents: Growth hormone deficiency, idiopathic short stature, and primary insulin-like growth factor-I deficiency. *Horm Res Paediatr*. 2016;86:361-397. Accessed April 10, 2024.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; Updated periodically.
8. Molitch ME, Clemmons DR, Malozowski S, et al.; Endocrine Society. Evaluation and treatment of adult growth hormone deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011 Jun; 96(6):1587-1609. Accessed April 10, 2024.
9. Schambelan M, Mulligan K, Grunfeld C, et al. Recombinant human growth hormone in patients with HIV-associated wasting—A randomized, placebo controlled trial. Ann Intern Med 1996;125:873–882.
10. Tanner JM: Growth at Adolescence, 2nd ed. Oxford, England, Blackwell Scientific Publications, 1962. SMR, sexual maturity rating, and Marcell AV. Chapter 12- Adolescence. In: Kliegman RM, Behrman RE, Jenson HB, Stanson BF, Editors. Nelson Textbook of Pediatrics. 18th Ed. St. Louis, MO: WB. Saunders, Inc. 2007.
11. Yuen KCJ, Biller BMK, Radovick S, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Growth Hormone Deficiency in Adults and Patients Transitioning from Pediatric to Adult Care. *Endocr Pract*. 2019; 25: 1191-1232. Accessed April 10, 2024.


Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.