Growth Hormone - Children

Generic Name: Somatropin, somapacitan-beco, somatropin-ghla, lonapegsomatropin-tcgd (children)

Therapeutic Class or Brand Name: Growth Hormone (children)

Applicable Drugs (if Therapeutic Class): Genotropin, Humatrope, Ngenla, Norditropin, Nutropin AQ, Omnitrope, Saizen, Skytrofa, Sogroya, Zomacton.

Preferred: Genotropin, Ngenla, Norditropin, Sogroya

Non-preferred: Humatrope, Nutropin AQ, Omnitrope, Saizen, Skytrofa, Zomacton.

Date of Origin: 2/1/2013

Date Last Reviewed / Revised: 1/1/2025

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through III are met)

I. Documented diagnosis of one of the following conditions A through H AND must meet criteria listed under applicable diagnosis:

A. Growth hormone deficiency (GHD) and criteria 1 through 3 are met:

1. Documented biochemical growth hormone deficiency by meeting ONE of the criteria a through d:

a) Two growth hormone (GH) stimulation tests below 10 ng/ml (microgram/L).

(1) Documentation of sex steroid priming before GH stimulation test in prepubertal boys older than 11 years and prepubertal girls older than 10 years with adult height prognosis within 2 standard deviation (SDS) below the reference mean for age and gender.

b) Hypothalmic-pituitary axis (HPA) defect (e.g., major congenital malformation such as ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk), tumor, or irradiation and deficiency of at least one additional pituitary hormone deficiency.

c) Multiple pituitary hormone deficiencies (MPHDs) exist (at least two others in addition to GHD).

d) Congenital GHD (GH levels < 5ng/ml detected during an acute episode of hypoglycemia).

2. Documented initial bone age confirming open growth plates.

3. Documented short stature/growth failure (subnormal growth rate) by meeting ONE of the criteria a, b, OR c:

a) Height is below the 3rd percentile for the patient's age and gender.

b) Height is below the 5th percentile for the patient's age and gender, and untreated growth velocity with a minimum of 1 year of growth data is below the 25th percentile for the patient's age and gender.

c) If GHD criteria under 1d are met, short stature/growth failure is not needed.

4. Documentation that other causes for short stature such as growth-inhibiting medication, endocrine disorders, and psychosocial short stature have been ruled out.

B. GHD in adolescents during the transition period and criteria 1 through 4 are met:

1. Documentation that the patient has persistent biochemical GHD by meeting ONE of the criteria a, b, or c:

a) Documented congenital defects of HPA, genetic defects of HPA, or organic hypothalamic-pituitary disease (e.g., craniopharyngioma, pituitary hypoplasia, ectopic posterior pituitary, or previous cranial irradiation) with ≥ 3 MPHDs (at least two others in addition to GHD) and one serum IGF-1 level (> 2.0 SDS below the mean for the patient's age and gender).

b) Documented organic GHD (e.g., craniopharyngioma, pituitary hypoplasia, ectopic posterior pituitary, or previous cranial irradiation) with 0 to 2 pituitary hormone deficiencies, one serum IGF-1 (> 0 SDS below the mean for the patient's age and gender), and one GH provocative stimulation test (with insulin, macimorelin, or glucagon) with a measured peak level as indicated for the respective provocation agent (Table 1) at least 1 month following the discontinuation of GH therapy.

c) Documented idiopathic childhood GHD with one serum IGF-1 level (> 0 SDS below the age and gender-adjusted normal range) and one GH provocative stimulation test (with insulin, macimorelin, or glucagon) with a measured peak level as indicated for respective provocation agent (Table 1) at least 1 month following the discontinuation of GH therapy.

2. The patient does not have disorders other than GHD for which GH treatment is indicated, including Prader-Willi syndrome (PWS), children born small for gestational age (SGA), Turner syndrome, Noonan syndrome, chronic kidney disease (CKD), and idiopathic short stature.

3. Documentation of closed epiphyses on the bone radiograph.

4. Documentation that the patient has attained the expected adult height.

C. Growth failure in children born SGA who fail to demonstrate catch-up growth by age 2 to 4 years and criteria 1 through 5 are met:

1. Minimum age requirement: 2 years old.

2. Documentation that the patient was born SGA, defined as a birth weight and/or length ≥ 2 SDS below the mean for gestational age and gender (including infants born with intrauterine growth restriction or Russell-Silver Syndrome resulting in SGA).

3. Documented short stature/growth failure (subnormal growth rate) by 2 years of age when height is ≥ 2 SDS below the mean for the patient's age and gender.
4. Documentation that other causes for short stature such as growth-inhibiting medication, endocrine disorders, and psychosocial short stature have been ruled out.
5. Documented initial bone age confirming open growth plates

D. Growth failure due to PWS and criteria 1 through 3 are met:
   1. Documentation that the diagnosis of PWS has been confirmed by genetic testing.
   2. Documented short stature/growth failure (subnormal growth rate) when height is ≥ 2 SDS below the normal mean for the patient's age and gender.
   3. Documented initial bone age confirming open growth plates.

E. Growth failure associated with Turner's Syndrome and criteria 1 through 3 are met:
   1. Documentation that the diagnosis of Turner's syndrome has been confirmed by karyotype analysis.
   2. Documented short stature/growth failure (subnormal growth rate) when height is ≥ 2 SDS below the normal mean for the patient's age and gender.
   3. Documented initial bone age confirming open growth plates.

F. Growth failure associated with Noonan's Syndrome and criteria 1 through 3 are met:
   1. Documentation that the diagnosis of Noonan's syndrome has been confirmed by genetic testing and/or by characteristic clinical features.
   2. Documented short stature/growth failure (subnormal growth rate) when height is ≥ 2 SDS below the normal mean for the patient's age and gender.
   3. Documented initial bone age confirming open growth plates.

G. Short stature or growth failure in children with short stature homeobox-containing gene (SHOX) deficiency and criteria 1 through 3 are met:
   1. Documentation that the diagnosis of SHOX deficiency has been confirmed by genetic testing.
   2. Documented short stature/growth failure (subnormal growth rate) when height is ≥ 2 SDS below the normal mean for the patient's age and gender.
   3. Documented initial bone age confirming open growth plates.

H. Growth failure associated with chronic kidney disease (CKD) and criteria 1 through 3 are met:
   1. Documented diagnosis of CKD with estimated glomerular filtration rate (eGFR) ≤60 mL/min/1.73/m^2.
   2. Documented short stature/growth failure (subnormal growth rate) when height is < the 5th percentile for the patient's age and gender, and untreated growth velocity with a

minimum of 1 year of growth data is < the 25th percentile for the patient's age and gender.

3. Documented initial bone age confirming open growth plates.

II. Treatment must be prescribed by or in consultation with a pediatric endocrinologist or pediatric nephrologist.

III. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to a preferred product(s).

EXCLUSION CRITERIA

- Acute critical illness due to complications following open heart surgery, abdominal surgery, or multiple accidental trauma, or those with acute respiratory failure.
- Children with PWS who are severely obese, have a history of upper airway obstruction or sleep apnea, or have severe respiratory impairment.
- Active malignancy.
- Active proliferative or severe non-proliferative diabetic retinopathy.
- Children with closed epiphyses (except for GHD in adolescents during the transition period).

OTHER CRITERIA

- N/A

QUANTITY / DAYS SUPPLY RESTRICTIONS

- The quantity is limited to a maximum of a 30-day supply per fill.

APPROVAL LENGTH

- **Authorization:**
  - All diagnoses except GHD during the transition period: Up to 12 months or until maximum bone age is met (up to 16 years of age for males or 14 years of age for females), whichever is shorter.
  - GHD in adolescents during the transition period: 12 months
- **Re-Authorization:**
  - All other diagnoses: An updated letter of medical necessity or progress notes showing current medical necessity criteria are met and that the patient's growth velocity is > 2.5 cm/year. Must also include documentation of a through b below, if applicable:

a. Bone age must be obtained annually when chronological age reaches 15 years for males or 13 years for females. Therapy must not exceed a bone age of 16 years for males or 14 years for females.

b. If the diagnosis is chronic kidney disease (CKD), the patient must still have an eGFR < 60 ml/min/1.73 m^2.

APPENDIX

Table 1. GH Stimulation Test Peak Cutoffs by Provocation Test Type.

GH provocation test	Peak GH Cut-Off Range for GHD in the Transition Period
ITT	≤ 5 ng/ml
Macimorelin	≤ 2.8 ng/ml
GST	BMI < 25 kg/m2: ≤ 3.0 ng/ml. BMI 25 to 30 kg/m2: ≤ 3.0 ng/ml with a high pre-test probability. BMI 25 to 30 kg/m2: ≤ 1.0 ng/ml with a low pre-test probability. BMI > 30 kg/m2: ≤ 1.0 ng/ml.

Abbreviations: BMI, body mass index; GH, growth hormone, GHD, growth hormone deficiency, GST, glucagon stimulation test; ITT, insulin tolerance test.

Table 2. GH products by FDA-approved pediatric indications

GH product (brand)	GHD	PWS	SGA	Turner Syndrome	SHOX deficiency	Noonan Syndrome	CKD
Genotropin	X	X	X	X			
Humatrope	X		X	X	X		
Ngenla	X						
Norditropin	X	X	X	X		X	
Nutropin AQ	X			X			X
Omnitrope	X	X	X	X			
Saizen	X						
Sogroya	X						
Skytrofa	X						
Zomacton	X		X	X	X		

Abbreviations: CKD, chronic kidney disease stages 3-5; GHD, growth hormone deficiency, GHD; PWS, Prader-Willi Syndrome; SGA, small for gestational age with no catch-up growth by 2 to 4 years; SHOX, short stature homeobox-containing gene.

REFERENCES

1. Grimberg A., 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(6):361-397. doi: 10.1159/000452150
2. Richmond EJ, Rogol AD. Diagnostic approach to children and adolescents with short stature. In: UpToDate, Geffner ME, Kremen J (Eds), Wolters Kluwer. Accessed on November 19, 2024.

3. Nwosu BU, Lee MM. Evaluation of short and tall stature in children. *Am Fam Physician.* 2008;78(5):597-604.
4. Yuen, K.C.J., 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(11), 1191-1232. doi: 10.4158/GL-2019-0405
5. Clayton PE, Cianfarani S, Czernichow P, et al. 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.* 2007;92(3):804-10. doi: 10.1210/jc.2006-2017
6. Deal CL, Tony M, Höybye C, et al; 2011 Growth Hormone in Prader-Willi Syndrome Clinical Care Guidelines Workshop Participants. GrowthHormone Research Society workshop summary: consensus guidelines for recombinant human growth hormone therapy in Prader-Willi syndrome. *J Clin Endocrinol Metab*. 2013;98(6):E1072-87. doi: 10.1210/jc.2012-3888
7. Collett-Solberg PF, Ambler G, Backeljauw PF, et al. Diagnosis, Genetics, and Therapy of Short Stature in Children: A Growth Hormone Research Society International Perspective. *Horm Res Paediatr*. 2019;92(1):1-14. doi: 10.1159/000502231
8. Drube J, Wan M, Bonthuis M, et al; European Society for Paediatric Nephrology Chronic Kidney Disease Mineral and Bone Disorders, Dialysis, and Transplantation Working Groups. Clinical practice recommendations for growth hormone treatment in children with chronic kidney disease. *Nat Rev Nephrol.* 2019;15(9):577-589. doi: 10.1038/s41581-019-0161-4
9. Genotropin. Prescribing Information. Pfizer; 2019. Accessed November 19, 2024. http://labeling.pfizer.com/ShowLabeling.aspx?id=577
10. Humatrope. Prescribing Information. Eli Lilly; 2023. Accessed November 19, 2024. http://uspl.lilly.com/humatrope/humatrope.html#pi
11. Ngenla. Prescribing Information. Pfizer; 2023. Accessed November 19, 2024. https://labeling.pfizer.com/ShowLabeling.aspx?id=19642
12. Norditropin. Prescribing Information. Novo Nordisk; 2020. Accessed November 19, 2024. http://www.novo-pi.com/norditropin.pdf
13. Nutropin AQ. Prescribing Information. Genentech; 2016. Accessed November 19, 2024. http://www.gene.com/download/pdf/nutropin_aq_PI.pdf
14. Omnitrope. Prescribing Information. Sandoz; 2019. Accessed November 19, 2024. https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=58d84ffa-4056-4e36-ad67-7bd4aef444a5&type=display
15. Saizen. Prescribing Information. EMD Serono; 2020. Accessed November 19, 2024. https://www.emdserono.com/us-en/pi/saizen-ce-pi.pdf
16. Skytrofa. Prescribing Information. Asendis Pharma, Inc;2022. Accessed November 19, 2024. https://ascendispharma.us/products/pi/skytrofa/skytrofa_pi.pdf

17. Sogroya. Prescribing Information. Novo Nordisk Inc; 2023. Accessed November 19, 2024. https://www.novo-pi.com/sogroya.pdf
18. Zomacton. Prescribing Information. Ferring Pharmaceuticals Inc; 2024. Accessed November 19, 2024. https://ferringusa.com/wp-content/uploads/sites/12/2024/04/Zomacton-USPI-CLEAN-4.2024.pdf