CareSource Rxinnovations

PHARMACY POLICY STATEMENT
Marketplace

DRUG NAME	Short-Acting Somatropin Injections for Growth Hormone Deficiency - Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Saizen, Zomacton
BILLING CODE	Must use valid NDC code
BENEFIT TYPE	Pharmacy
SITE OF SERVICE ALLOWED	Home
STATUS	Prior Authorization Required

Somatropin is a recombinant human growth hormone with initial FDA approval in 1987. There are currently seven brands of short-acting Somatropin used daily as replacement therapy for growth failure and growth hormone deficiency. Somatropin binds to a dimeric GH receptor in the cell membrane of target cells resulting in intracellular signal transduction and a host of pharmacodynamic effects. They are: Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Saizen and Zomacton.

Short-Acting Somatropin Injections will be considered for coverage when the following criteria are met:

Adult Growth Hormone Deficiency (GHD) – Adult or Childhood Onset

For **initial** authorization:

1. Member is at least eighteen years of age or older;
2. Medication must be prescribed by an endocrinologist; AND
3. Member must have a diagnosis of GHD confirmed by **one** of the following:
   a) Two pre-treatment stimulation tests with a peak serum growth hormone concentration < 5 µg/mL (must include lab results with reference ranges), unless Macrilen (prior authorization required) was used, in which case a GH level must be < 2.8 ng/ml; OR
   b) One pre-treatment stimulation test with a peak serum growth hormone concentration < 5 µg/mL (must include lab results with reference ranges) AND one of the following:
      i) Documentation of structural abnormalities of the growth hormone axis (see appendix)
      ii) Documentation of childhood-onset GHD due to congenital abnormalities of the growth hormone axis (see appendix)
      iii) Documentation of at least two other pituitary growth hormone deficiencies (see appendix)
4. Member must have a 90-day trial of Omnitrope 5.8 mg vial which was documented as ineffective, or contraindicated.
5. **Dosage allowed/Quantity limit:**

Drug	Dosage/Quantity Limit
Genotropin/Omnitrope	Weight based dosing: 0.04-0.08 mg/kg/week. Non-weight based dosing: starting dose 0.2 mg/day (0.15-0.30 mg/day) and increased every 1-2 months in increments of 0.1-0.2 mg/day, doses vary considerably.
Humatrope	Weight based dosing: 0.006 mg/kg/day - 0.0125 mg/kg/day. Non-weight based dosing: starting dose 0.2 mg/day (0.15-0.30 mg/day) and increased every 1-2 months in increments of 0.1-0.2 mg/day, doses vary considerably.
Norditropin	Weight based dosing: 0.004-0.016 mg/kg/day. Non-weight based dosing: starting dose 0.2 mg/day (0.15-0.30 mg/day) and increased every 1-2 months in increments of 0.1-0.2 mg/day, doses vary considerably

Nutropin/Nutropin AQ	Weight based dosing: 0.006-0.025 mg/kg/day if ≤ 35 years or 0.0125 mg/kg/day > 35 years. Non-weight based dosing: starting dose 0.2 mg/day (0.15-0.30 mg/day) and increased every 1-2 months in increments of 0.1-0.2 mg/day, doses vary considerably.
Saizen	Weight based dosing: 0.005 mg/kg/day initially; can be increased as tolerated to not more than 0.01 mg/kg/day after 4 weeks. Non-weight based dosing: starting dose 0.2 mg/day (0.15- 0.30 mg/day) and increased every 1-2 months in increments of 0.1-0.2 mg/day, doses vary considerably.
Zomacton	Weight based dosing: 0.006 mg/kg/day - 0.0125 mg/kg/day. Non-weight based dosing: starting dose 0.2 mg/day (0.15-0.30 mg/day) and increased every 1-2 months in increments of 0.1-0.2 mg/day, doses vary considerably.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
Short-acting Somatropin Injections will be reauthorized when chart notes show all of the following:
1. Member must be in compliance with all of the initial criteria; AND
2. Member's current IGF-1 level not elevated for age/gender (does not apply to members w/ structural abnormality of hypothalamus/pituitary and at least pituitary hormone deficiencies or childhood onset GHD and congenital abnormality of hypothalamus/pituitary).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Noonan Syndrome – Norditropin Only

For **initial** authorization:
1. Member must have a diagnosis of Noonan Syndrome confirmed by genetic analyses (must include documentation); AND
2. Member is 17 years of age or younger; AND
3. Medication must be prescribed by an endocrinologist; AND
4. Member's pre-treatment height is > 2 SD below the mean and 1 year height velocity is > 1 SD below the mean for age (must include growth charts and documentation); AND
5. If member is age 12 or older, the member's epiphyses are open, confirmed by radiograph of the wrist and hand (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age.
6. **Dosage allowed/Quantity limit:** 0.46 mg/kg/week.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
Norditropin will be reauthorized when chart notes show all of the following:
1. Member must be in compliance with all of the initial criteria; AND
2. If member is age 12 or older, the member's epiphyses are open, confirmed by radiograph of the wrist and hand (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age; AND
3. Member has a growth rate > 2.5 cm/year unless there is a documented reason for lack of efficacy (on treatment < 1 year, off treatment for a reason for a period of time, nearing final adult height, late stages of puberty).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Pediatric Growth Failure due to Chronic Kidney Disease – Nutropin Only

For **initial** authorization:
1. Member is age 17 years or younger; AND
2. Member must have a diagnosis of growth failure due to chronic kidney disease (i.e., irreversible renal insufficiency with CrCl < 75 mL/min per 1.73 m2 or dialysis dependent awaiting renal transplant (must include documentation)); AND

3. Medication must be prescribed by an endocrinologist or nephrologist; AND
4. Member's pre-treatment height is > 2 SD below the mean and 1 year height velocity is > 1 SD below the mean for age (must include growth charts and documentation); AND
5. If member is age 12 or older, the member's epiphyses are open, confirmed by radiograph of the wrist and hand (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age.
6. **Dosage allowed/Quantity limit:** 0.35 mg/kg/week.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
Nutropin will be reauthorized when chart notes show at least one of the following:
1. Member must be in compliance with all of the initial criteria; AND
2. If member is age 12 or older, the member's epiphyses are open, confirmed by radiograph of the wrist and hand (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age; AND
3. Member has a growth rate > 2.5 cm/year unless there is a documented reason for lack of efficacy (on treatment < 1 year, off treatment for a reason for a period of time, nearing final adult height, late stages of puberty).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Pediatric Growth Hormone Deficiency

For **initial** authorization:
7. Member is one year of age or older and weighs at least 11.5kg;
8. Medication must be prescribed by an endocrinologist; AND
9. Member must have a diagnosis of GHD confirmed by **one** of the following:
   a) Two pre-treatment stimulation tests with a peak serum growth hormone concentration < 10 ng/mL (must include lab results with reference ranges); OR
   b) One pre-treatment treatment stimulation test with a peak serum growth hormone concentration < 10 ng/mL (must include lab results with reference ranges) AND one of the following:
      i) Documentation of structural abnormalities of the growth hormone axis (see appendix)
      ii) Documentation of congenital abnormalities of the growth hormone axis (see appendix)
      iii) Documentation of at least two other pituitary growth hormone deficiencies (see appendix)
10. Member must have a pretreatment height (must include growth charts) of > 2 SD below the mean for age and gender; AND
11. Member must have a documented 90-day trial and failure of Omnitrope 5.8 mg vial; AND
12. If member is age 12 or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
13. **Dosage allowed/Quantity limit:**

Drug	Dosage/Quantity Limit
Genotropin/Omnitrope	0.16-0.24 mg/kg/week
Humatrope	0.18-0.30 mg/kg/week
Norditropin	0.17-0.24 mg/kg/week
Nutropin/Nutropin AQ	Pediatric: up to 0.3 mg/kg/week Pubertal patient: up to 0.7 mg/kg/week
Saizen	0.18 mg/kg/week
Zomacton	0.18-0.30 mg/kg/week

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
Short-acting Somatropin Injections will be reauthorized when chart notes show at least one of the following:

4. Member has a growth rate of at least 2 cm/year;
5. If member is age 12 or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Prader-Willi Syndrome

For **initial** authorization:

1. Member is 17 years of age or younger; AND
2. Medication must be prescribed by an endocrinologist; AND
3. Member must have a diagnosis of Prader-Willi Syndrome confirmed by genetic analyses (must include documentation); AND
4. Member's pre-treatment height is > 2 SD below the mean and 1 year height velocity is > 1 SD below the mean for age (must include growth charts and documentation); AND
5. Member must have a documented 90-day trial and failure of Omnitrope 5.8 mg vial;
6. If member is age 12 or older, radiographic evidence the member's epiphyses are open (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age
7. **Dosage allowed/Quantity limit:**

Drug	Dosage/Quantity Limit
Genotropin/Omnitrope	0.24 mg/kg/week
Norditropin	0.24 mg/kg/week

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
Short-acting Somatropin Injections will be reauthorized when chart notes show at least one of the following:

1. Member must be in compliance with all of the initial criteria; AND
2. If member is age 12 or older, radiographic evidence the member's epiphyses are open (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age; AND
3. Member has a growth rate > 2.5 cm/year unless there is a documented reason for lack of efficacy (on treatment < 1 year, off treatment for a reason for a period of time, nearing final adult height, late stages of puberty).

If all the above requirements are met, the medication will be approved for an additional 12 months.

SHOX Deficiency

For **initial** authorization:

1. Member must have a diagnosis of SHOX gene deficiency confirmed by genetic analyses (must include documentation); AND
2. Medication must be prescribed by an endocrinologist; AND
3. Member's pre-treatment height is > 2 SD below the mean and 1 year height velocity is > 1 SD below the mean for age (must include growth charts and documentation); AND
4. If member is age 12 or older, the member's epiphyses are open, confirmed by radiograph of the wrist and hand (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age.
5. **Dosage allowed/Quantity limit:** 0.35 mg/kg/week.

Drug	Dosage/Quantity Limit
Humatrope	0.35 mg/kg/week

Zomacton	0.35 mg/kg/week

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
Humatrope and Zomacton will be reauthorized when chart notes show at least one of the following:
1. Member must be in compliance with all of the initial criteria; AND
2. If member is age 12 or older, the member's epiphyses are open, confirmed by radiograph of the wrist and hand (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age; AND
3. Member has a growth rate > 2.5 cm/year unless there is a documented reason for lack of efficacy (on treatment < 1 year, off treatment for a reason for a period of time, nearing final adult height, late stages of puberty).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Small for Gestational Age

For **initial** authorization:
1. Member is 2 years of age or older prior to initiating treatment; AND
2. Medication must be prescribed by an endocrinologist; AND
3. Member must have a diagnosis of small for gestational age (SGA) and failed to catch up growth by 2 years of age; AND
4. Member's birth weight and/or length are > 2 SD below the mean for gestational age (must include growth charts and documentation); AND
5. Member's height remains > 2 SD below population for age and gender (must include growth charts and documentation); AND
6. Member must have a documented 90-day trial and failure of Omnitrope 5.8 mg vial;
7. If member is age 12 or older, radiographic evidence the member's epiphyses are open (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age.
8. **Dosage allowed/Quantity limit:**

Drug	Dosage/Quantity Limit
Genotropin/Omnitrope	Up to 0.48 mg/kg/week
Humatrope	Up to 0.47 mg/kg/week
Norditropin	Up to 0.47 mg/kg/week
Zomacton	Up to 0.47 mg/kg/week

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
Short-acting Somatropin Injections will be reauthorized when chart notes show at least one of the following:
1. Member must be in compliance with all of the initial criteria; AND
2. If member is age 12 or older, radiographic evidence the member's epiphyses are open (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age; AND
3. Member has a growth rate > 2.5 cm/year unless there is a documented reason for lack of efficacy (on treatment < 1 year, off treatment for a reason for a period of time, nearing final adult height, late stages of puberty).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Turner Syndrome

For **initial** authorization:

1. Member is female age 2 to 17 years; AND
2. Medication must be prescribed by an endocrinologist; AND
3. Member must have a diagnosis of Turner Syndrome confirmed by genetic analyses (must include documentation); AND
4. Member's pre-treatment height is > 2 SD below the mean and 1 year height velocity is > 1 SD below the mean for age (must include growth charts and documentation); AND
5. Member must have a documented 90-day trial and failure of Omnitrope 5.8 mg vial
6. If member is age 12 or older, radiographic evidence the member's epiphyses are open (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age.
7. **Dosage allowed/Quantity limit:**

Drug	Dosage/Quantity Limit
Genotropin/Omnitrope	0.33 mg/kg/week
Humatrope	Up to 0.375 mg/kg/week
Norditropin	Up to 0.47 mg/kg/week
Nutropin/Nutropin AQ	Up to 0.375 mg/kg/week
Zomacton	Up to 0.375 mg/kg/week

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:

Short-acting Somatropin Injections will be reauthorized when chart notes show at least one of the following:

1. Member must be in compliance with all of the initial criteria; AND
2. If member is age 12 or older, radiographic evidence the member's epiphyses are open (x-ray results must be included). Comparison of bone age to chronological age should be documented as abnormal by > 2 SD below the mean for chronological age; AND
3. Member has a growth rate > 2.5 cm/year unless there is a documented reason for lack of efficacy (on treatment < 1 year, off treatment for a reason for a period of time, nearing final adult height, late stages of puberty).

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Short-acting Somatropin Injections not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
11/17/2021	New policy for Short-Acting Somatropin Injections created; combined short-acting somatropin into a single policy and updated the adult and pediatric GHD sections per current literature

Appendix:

1) Acquired structural abnormalities
    - CNS tumor or neoplasm (craniopharyngioma, glioma, pituitary adenoma, etc.)
    - Cysts (Rathke cleft cyst or arachnoid cleft cyst)
    - Surgery
    - Radiation
    - Chemotherapy
    - CNS infection
    - CNS infarction (e.g., Sheehan's syndrome)
    - Inflammatory lesions (e.g., autoimmune hypohysitis)
    - Infiltrative lesions (e.g., sarcoidosis, histiocytosis)
    - Head trauma or traumatic brain injury
    - Aneurysmal subarachnoid hemorrhage
    - Panhypopituitarism or multiple pituitary hormone deficiency

2) Congenital abnormalities
    - Known genetic mutations in growth-hormone releasing hormone (GHRH) receptor, GH gene, GH receptor or pituitary transcription factors
    - Optic nerve hypoplasia/septo-optic dysplasia
    - Empty sella syndrome
    - Ectopic posterior pituitary
    - Pituitary aplasia/hypoplasia
    - Pituitary stalk defect
    - Anencephaly or prosencephaly
    - Vascular malformations

3) Pituitary hormones, other than growth hormone (GH)
    - Adrenocorticotropic hormone (ACTH)
    - Antidiuretic hormone (ADH)
    - Follicle stimulating hormone (FSH)
    - Luteinizing hormone (LH)
    - Oxytocin
    - Prolactin
    - Thyroid stimulating hormone (TSH)

References:

1. Genotropin [prescribing information]. New York, NY: Pfizer, Inc.; April 2019.
2. Omnitrope (somatropin) package insert. Princeton, NY: Sandoz, Inc.; June 2019.
3. Humatrope [prescribing information]. Indianapolis, IN: Eli Lilly; December 2016.
4. Nutropin AQ [prescribing information]. South San Fransico, CA: Genetech, Inc.; December 2016.
5. Saizen [prescribing information]. Rockland, MD: EMD Serono, Inc.; May 2018.
6. Zomacton [prescribing information]. Parsippany, NJ: Ferring Pharmaceuticals; July 2018.
7. Norditropin [prescribing information]. Plainsboro, NJ: Novo Nordisk; February 2018.
8. Cook DM, Yuen KCJ, Biller BMK, 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(2): 1-29.
9. Gharib H, Cook DM, Saenger PH, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use Adults and Children – 2003 update. Endocr Pract. 2003; 9(1): 64-76.
10. American Association of Clinical Endocrinologists. American Association of Clinical Endocrinologists Position Statement Growth Hormone Usage in Short Children. December 2003.
11. Molitch ME, Clemmons Dr, Malozowski S, et al. Evaluation and treatment of adult growth hormone deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011; 96: 1587-1609.
12. National Institute for Clinical Excellence: Guidance on the use of human growth hormone (somatropin) for the treatment of growth failure in children. May 2010.
13. National Institute for Clinical Excellence: Human growth hormone (somatropin) in adults with growth hormone deficiency. August 2003.
14. Wilson TA, Rose SR, Cohen P, et al. Update of guidelines for the use of growth hormone in children: The Lawson Wilkins Endocrinology Society Drug and Therapeutics Committee. J Pediatr. 2003; 143: 415-421.
15. Deal CL, Tony M, Hoybye C, et al. Growth Hormone Research Society workshop summary: consensus guidelines for recombinant human growth hormone therapy in Prader-Willi syndrome. J Clin Endocrinol Metab. 2013; 98: 1072-1087.
16. Blum WF, Crowe BJ, Quigley CA, et al. Growth hormone in effective in treatment of short stature associated with short stature homeobox-containing gene deficiency: two-year results of a randomized, controlled, multicenter trial. J Clin Endocinol Metab. 2007; 92: 219-228.
17. Blum WF, Ross JL, Zimmermann Ag, et al. Growth hormone treatment to final height produces similar height gains in patients with SHOX deficiency and Tuner syndrome: results of a multicenter trial. J Clin Endocrinol Metab. 2013; 98 (8): 1383-1392.
18. Kirk J, Betts P, Butler G, et al. Short stature in Noonan syndrome: response to growth hormone therapy. Arch Dis Child. 2001; 84(5): 440-443.
19. Raynal P. Growth hormone and noonan syndrome: update in dysfunctional signaling aspects and in therapy for short stature.
20. Mahan JD, Warady BA. Assessment and treatment of short stature in pediatric patients with chronic kidney disease: a consensus statement. Pediatr Nephrol. 2006; 21(7): 917-930.
21. Romano AA, Allanson JE, Dahlgren J, et al. Noonan syndrome: clinical features, diagnosis, and management guidelines. Pediatrics 2010;126(4): 746-759
22. 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 Endrocrinol Metab. 2007; 92(3): 804-810.
23. Baxter L, Bryant J, Cave CB, Milne R. Recombinant growth hormone for children and adolescents with Turner syndrome.
24. Nemecheck PM, Polsky B, Gottlieb MS. Treatment Guidelines for HIV-associated wasting. May Clinc Proc. 2000; 27: 386-394.
25. Goldstone AP, Holland AJ, Hauffa BP, et al. Recommendations for the diagnosis and management of Prader-Willi Syndrome. J Clin Endocrinol Metab. 2008; 93: 4183-4197.
26. Blum WF, Crowe BJ, Quigley CA, et al. Growth hormone in effective in treatment of short stature associated with short stature homeobox-containing gene deficiency: two-year results of a randomized, controlled, multicenter trial. J Clin Endocinol Metab. 2007; 92: 219-228.
27. Blum WF, Ross JL, Zimmermann Ag, et al. Growth hormone treatment to final height produces similar height gains in patients with SHOX deficiency and Tuner syndrome: results of a multicenter trial. J Clin Endocrinol Metab. 2013; 98 (8): 1383-1392.
28. Kirk J, Betts P, Butler G, et al. Short stature in Noonan syndrome: response to growth hormone therapy. Arch Dis Child. 2001; 84(5): 440-443.

29. Raynal P. Growth hormone and noonan syndrome: update in dysfunctional signaling aspects and in therapy for short stature.
30. Mahan JD, Warady BA. Assessment and treatment of short stature in pediatric patients with chronic kidney disease: a consensus statement. Pediatr Nephrol. 2006; 21(7): 917-930.
31. Romano AA, Allanson JE, Dahlgren J, et al. Noonan syndrome: clinical features, diagnosis, and management guidelines. Pediatrics 2010;126(4): 746-759.
32. 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 Endrocrinol Metab. 2007; 92(3): 804-810.
33. Baxter L, Bryant J, Cave CB, Milne R. Recombinant growth hormone for children and adolescents with Turner syndrome.

Effective date: 04/01/2022
Revised date: 11/17/2021