CareSource Rxinnovations

PHARMACY POLICY STATEMENT
Marketplace

DRUG NAME	Short-Acting Somatropin Injections for Growth Hormone Deficiency (Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Saizen, Zomacton)
BENEFIT TYPE	Pharmacy
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 as follows: 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)

For **initial** authorization:

1. Member is at least 18 years of age or older; AND
2. Medication must be prescribed by or in consultation with an endocrinologist; AND
3. Member has genetic or structural brain hypothalamic-pituitary defect that does not require testing (see appendix B); OR
4. Member must have documentation of **ALL** of the following:
   a) Hypothalamic-pituitary defect (see appendix A);
   b) IGF-1 <-2 standard deviations for age and gender;
   c) Deficiencies in at least **THREE** pituitary axes (see appendix C); OR
5. Member must have documentation of **ALL** of the following:
   a) Hypothalamic-pituitary defect (see appendix A);
   b) IGF-1 <-2 standard deviations for age and gender;
   c) Suboptimal response to **ONE** pre-treatment stimulation test defined as:
      i) Insulin tolerance test (ITT) with a peak serum growth hormone concentration < 5 µg/L (must include lab results with reference ranges);
      ii) Macrilen (prior authorization required) with a peak serum growth hormone concentration < 2.8 µg/L;
      iii) Glucagon stimulation test (GST) with a peak serum growth hormone concentration meeting **ONE** of the following:
         (1) <3 µg/L for members with a BMI <25 kg/m2;
         (2) <3 µg/L for members with a BMI 25 to 30 kg/m2 with a high pretest probability;
         (3) <1 µg/L for members with a BMI >30 kg/m2;
         (4) <1 µg/Lfor members with a BMI 25 to 30 kg/m2 with a low pretest probability; OR
6. Member must have documentation of **ALL** of the following:
   a) Diagnosis of idiopathic isolated GHD;
   b) IGF-1 between 0 to –2 or <-2 standard deviations for age and gender;
   c) Human growth hormone therapy has been discontinued for at least one month;
   d) Suboptimal response to **TWO** pre-treatment stimulation tests defined as:

i) Insulin tolerance test (ITT) with a peak serum growth hormone concentration < 5 µg/L (must include lab results with reference ranges);
ii) Macrilen (prior authorization required) with a peak serum growth hormone concentration < 2.8 µg/L;
iii) Glucagon stimulation test (GST) with a peak serum growth hormone concentration meeting **ONE** of the following:
(1) <3 µg/L in members with a BMI <25 kg/m2;
(2) <3 µg/L for members with a BMI 25 to 30 kg/m2 with a high pretest probability;
(3) <1 µg/L for members with a BMI >30 kg/m2;
(4) <1 µg/Lfor members with a BMI 25 to 30 kg/m2 with a low pretest probability; AND

7. Member must have a documented 6-month trial and failure of Omnitrope 5.8 mg vial; AND
8. Member does **NOT** have a history of active malignancy.
9. **Dosage allowed/Quantity limit:**

Drug	Dosage
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 6 months.

For **reauthorization**:

1. Member's current IGF-1 level is within -2 and +2 standard deviations for age and gender (must include lab results with reference range).

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 is 17 years of age or younger; AND
2. Medication must be prescribed by or in consultation with an endocrinologist; AND
3. Member must have a diagnosis of Noonan Syndrome confirmed by genetic testing (must include documentation); AND
4. Member's pre-treatment height is > 2 SD below the mean for age and gender (must include growth charts); AND
5. Member's pre-treatment height velocity is > 1 SD below the mean for age and gender (must include growth charts); AND
6. Member does **NOT** have a history of active malignancy; AND

7. Member's weight is provided for dose calculation; AND
8. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
9. **Dosage allowed/Quantity limit:** Up to 0.46 mg/kg/week divided in 6 or 7 doses.

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

For **reauthorization**:
1. Member has a growth rate of at least 2 cm/year; AND
2. If member is 12 years 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.

Pediatric Growth Failure due to Chronic Kidney Disease – Nutropin Only

For **initial** authorization:
1. Member is 6 months to 17 years of age; AND
2. Medication must be prescribed by or in consultation with an endocrinologist or nephrologist; AND
3. Member must have a diagnosis of growth failure due to chronic kidney disease (i.e., stage 3-5 (GFR <60) chronic kidney disease or dialysis dependent); AND
4. Member's pre-treatment height is below the 3rd percentile for age and gender (must include growth charts); AND
5. Member's pre-treatment height velocity is below the 25th percentile for age and gender (must include growth charts); AND
6. Medication is used in combination with optimal management of CKD (i.e., blood pressure management, use of statins, ACE inhibitors or ARBs); AND
7. Member has **NOT** received a renal transplant; AND
8. Member does **NOT** have a history of active malignancy; AND
9. Member's weight is provided for dose calculation; AND
10. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
11. **Dosage allowed/Quantity limit:** Up to 0.35 mg/kg/week divided into daily doses.

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

For **reauthorization**:
1. Member has a growth rate of at least 2 cm/year; AND
2. Member has **NOT** received a renal transplant; AND
3. If member is 12 years 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.

Pediatric Growth Hormone Deficiency

For **initial** authorization:
1. Member is 17 years of age or younger; AND
2. Medication must be prescribed by or in consultation with an endocrinologist; AND
3. Member was diagnosed with congenital hypopituitarism as a newborn and had **BOTH** of the following:
   a. Hypoglycemia with a serum GH concentration ≤ 5 µg/L;
   b. At least **one** additional pituitary hormone deficiency (see appendix C) or classical imaging triad (ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk); OR
4. Member has documentation of **BOTH** of the following:

a. Hypothalamic-pituitary defect (see appendix A);
b. At least **one** additional pituitary hormone deficiency (see appendix C); OR

5. Member must have documentation of **TWO** pre-treatment stimulation tests with a peak serum growth hormone concentration < 10 ng/mL (must include lab results with reference ranges); AND
6. Member must have a pre-treatment height (must include growth charts) of > 2 SD below the mean for age and gender; AND
7. Member must have a pre-treatment height velocity (must include growth charts) below the 25th percentile for age and gender; AND
8. Member must have a documented 6-month trial and failure of Omnitrope 5.8 mg vial; AND
9. Member does **NOT** have a history of active malignancy; AND
10. Member's weight is provided for dose calculation; AND
11. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
12. **Dosage allowed/Quantity limit:**

Drug	Dosage
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**:

1. Member has a growth rate of at least 2 cm/year; AND
2. If member is 12 years 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 – Genotropin, Omnitrope, Norditropin Only

For **initial** authorization:

1. Member is 17 years of age or younger; AND
2. Medication must be prescribed by or in consultation with an endocrinologist; AND
3. Member must have a diagnosis of Prader-Willi Syndrome confirmed by genetic testing (must include documentation); AND
4. Member must have a documented 6-month trial and failure of Omnitrope 5.8 mg vial; AND
5. Member's weight is provided for dose calculation; AND
6. Member's baseline height is provided; AND
7. Member does **NOT** have ANY of the following:
   a) History of active malignancy;
   b) Severe obesity;
   c) Severe respiratory impairment; AND
8. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
9. **Dosage allowed/Quantity limit:** 0.24 mg/kg/week divided into 6 or 7 daily doses.

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

For **reauthorization**:

1. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
2. Chart notes have been provided showing improvement of signs and symptoms of disease (ex. increased height velocity, decreased fat mass, increased lean body mass, etc)

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

SHOX Deficiency – Humatrope and Zomacton Only

For **initial** authorization:

1. Member is 17 years of age or younger; AND
2. Medication must be prescribed by or in consultation with an endocrinologist; AND
3. Member must have a diagnosis of SHOX gene deficiency confirmed by genetic testing (must include documentation); AND
4. Member meets **ONE** of the following:
   a) Member's pre-treatment height is below the 10th percentile and growth velocity is below the 25th percentile for age and gender (must include growth charts); OR
   b) Member's pre-treatment height is below the 3rd percentile for age and gender (must include growth charts); AND
5. Member's weight is provided for dose calculation; AND
6. Member does **NOT** have a history of active malignancy; AND
7. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
8. **Dosage allowed/Quantity limit:** Administer 0.35 mg/kg/week divided into daily doses.

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

For **reauthorization**:

1. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).; AND
2. Chart notes have been provided showing improvement of height, height velocity or height standard deviation.

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 between 2 years of age and 17 years of age; AND
2. Medication must be prescribed by or in consultation with an endocrinologist; AND
3. Member must have a diagnosis of small for gestational age defined as birth weight and/or length > 2 SD below the mean for gestational age (must include growth charts); AND
4. Member's height remains > 2.5 SD below the mean for age and gender by age two years (must include growth charts); OR
5. Member's height remains > 2 SD below the mean for age and gender by age four years (must include growth charts); AND
6. Member must have a documented 6-month trial and failure of Omnitrope 5.8 mg vial; AND
7. Member's weight is provided for dose calculation; AND
8. Member does **NOT** have a history of active malignancy; AND
9. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
10. **Dosage allowed/Quantity limit:**

Drug	Dosage
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**:
1. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included); AND
2. Chart notes have been provided showing improvement of height and/or height standard deviation.

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 a female under 17 years of age; AND
2. Medication must be prescribed by or in consultation with an endocrinologist; AND
3. Member must have a diagnosis of Turner Syndrome confirmed by karyotype analysis (must include documentation); AND
4. Member's pre-treatment height is below the 5th percentile for age and gender (must include growth charts); AND
5. Member must have a documented 6-month trial and failure of Omnitrope 5.8 mg vial; AND
6. Member's weight is provided for dose calculation; AND
7. Member does **NOT** have a history of active malignancy; AND
8. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
9. **Dosage allowed/Quantity limit:**

Drug	Dosage
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**:
1. If member is 12 years or older, radiographic evidence the member's epiphyses are open (x-ray results must be included).
2. Chart notes that been provided showing improvement of height, height velocity and/or height standard deviation.

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
08/29/2023	Adult GHD: Updated requirements for diagnosis of GHD including when testing is not required and the addition of IGF-1 levels; updated and added to appendix; removed

	diagnoses that were excluded from reauthorization criteria; added/updated references; added glucagon stimulation test option, added exclusion of active malignancy; added in consultation with for prescribe specialty; increased Omnitrope trial from 90 days to 6 months; reduced initial authorization length from 12 months to 6 months. Pediatric GHD: Increased Omnitrope trial from 90 days to 6 months; updated requirements for diagnosis of GHD including when testing is not required; updated appendix, added/updated references; added exclusion of active malignancy; added in consultation with for prescriber specialty; added documentation of height velocity below the 25th percentile; added documentation of weight for dose calculation; age limit changed from at least 1 year and 11.5 kg to less than 17 years.
10/02/2023	Updated references. Noonan Syndrome: added in consultation with for prescriber specialty; removed compliance of initial criteria from reauthorization criteria; added member does not have a history of active malignancy; added confirmation member's weight; simplified open epiphyses x-ray requirement; reduced reauthorization requirement from 2.5 cm/year to 2 cm/year and removed exclusions; added that pre-treatment height and HV is based on age and gender; removed requirement that HV was taken in the past year; added dosing clarification. CKD: added in consultation with for prescriber specialty; removed compliance of initial criteria from reauthorization criteria; added member does not have a history of active malignancy; added confirmation member's weight; simplified open epiphyses x-ray requirement; reduced reauthorization requirement from 2.5 cm/year to 2 cm/year and removed exclusions; replaced height is > 2 SD below the mean and height velocity is > 1 with cut offs specific to height and height velocity percentiles; added medication is used in combination with optimal management of CKD and member has NOT received a renal transplant; replaced examples of dx with stage 3-5 CKD or dialysis dependent; changed age limit from less than 17 years to 6 months to 17 years of age; clarified dosing Prader Willi Syndrome: added in consultation with for prescriber specialty; removed compliance of initial criteria from reauthorization criteria; added member does not have a history of active malignancy; added confirmation member's weight; simplified open epiphyses x-ray requirement; replaced growth rate of 2.5 cm/year in reauthorization criteria with improvement of signs and symptoms of height or weight; added exclusion of severe obesity or respiratory impairment; clarified dosing; added baseline height requirement.
01/24/2024	Updated, added, removed references. <u>Prader Willi Syndrome:</u> Increased Omnitrope trial from 90 days to 6 months <u>SHOX:</u> added weight requirement; removed member must be in compliance with initial criteria from reauthorization criteria; added member does not have a history of active malignancy; added in consultation with for prescriber specialty; added age limit of 17 years or younger; modified pretreatment height and height velocity measurement in SD to height and growth velocity measurement in percentile; simplified open epiphyses x-ray requirement; replaced growth rate of 2.5 cm/year in reauthorization criteria with improvement in height, height velocity or height SD. <u>Small Gestational Age:</u> added member does not have a history of active malignancy; added confirmation member's weight; simplified open epiphyses x-ray requirement; added in consultation with for prescriber specialty; removed compliance of initial criteria from reauthorization criteria; increased Omnitrope trial from 90 days to 6 months; added requirement member is 17 years of age or less; replaced that member's height remains >2 SD with 2.5 SD. <u>Turner Syndrome:</u> added member does not have a history of active malignancy; added confirmation member's weight; simplified open epiphyses x-ray requirement; added in consultation with for prescriber specialty; removed compliance of initial criteria from reauthorization criteria; increased Omnitrope trial from 90 days to 6 months; replaced > 2 SD below the mean and height velocity > 1 SD with below 5th

	percentile on growth charts; replaced growth rate of 2.5 cm/year in reauthorization criteria with improvement in height, height velocity or height SD; removed age requirement of at least 2 years of age.
08/20/2025	Adult GHD: added GST test cut off for BMI 25 to 30 kg/m2 with a high pretest probability and corrected ITT and Macrilen test from ng/mL to µg/L per AACE 2019

Appendix A:

A) 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

B) 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
- Other mid-line defects
- Vascular malformations

Appendix B:

A) Congenital and acquired abnormalities that do not require adult testing

- Genetic
- Transcription factor defects (PIT-1, PROP-1, LHX3/4, HESX-1, PITX-2)
- GHRH receptor-gene defects
- GH-gene defects
- GH-receptor/post-receptor defects
- Associated with brain structural defects
- Single central incisor
- Cleft lip/palate
- Perinatal insults

Appendix C:

A) Pituitary hormones (other than growth hormone)

- Adrenocorticotropic hormone (ACTH)
- Antidiuretic hormone (ADH)
- Follicle stimulating hormone (FSH)
- Luteinizing hormone (LH)
- Oxytocin
- Prolactin
- Thyroid stimulating hormone (TSH)

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