

Title: Growth Hormones

Policy #: Rx.01.40

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for growth hormones as provided under the member's prescription drug benefit.

Description:

Growth hormones are indicated for several disorders including growth failure associated with chronic renal insufficiency, Noonan syndrome, Prader-Willi Syndrome, Turner Syndrome, growth failure in children due to inadequate secretion of endogenous growth hormone, growth hormone deficiency in adults, growth failure in children born small for gestational age, idiopathic short stature, short bowel syndrome, short stature homeobox containing gene deficiency, and HIV wasting.

Biosynthetic growth hormone is used to replace natural growth hormone and is produced by recombinant DNA technology using either E coli bacteria or mammalian cell lines. Biosynthetic growth hormone goes by the generic name somatropin and has an amino acid sequence identical to human growth hormone from the pituitary gland. Somatropin is available under several different brand names.

Policy:

**A. Children with idiopathic short stature
(Omnitrope®, Humatrope®, Genotropin®, Nutropin®[AQ], Norditropin®, Zomacton®)**

INITIAL CRITERIA

Growth hormones are approved when all of the following are met:

1. Prescribed by an endocrinologist; and
2. Height less than or equal to 2.25 standard deviations from the mean (1.2 percentile); and
3. Documentation of growth velocity; and
4. Epiphyses are not closed

5. Inadequate response or inability to tolerate Nutropin®/Nutropin AQ®, and Norditropin® (applies to Humatrope®, Genotropin®, Zomacton®, Omnitrope®)

CONTINUATION CRITERIA

Growth hormones are re-approved when all of the following are met:

1. Growth velocity increased by at least 50 percent from baseline; and
2. Inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
3. Yearly evaluation by an endocrinologist

Authorization length: 1 year

B. Turner Syndrome

(Humatrope®, Genotropin®, Norditropin®, Nutropin®[AQ], Omnitrope® and Zomacton®)

INITIAL CRITERIA

Growth hormones are approved when all of the following are met:

1. Diagnosis of Turner syndrome; and
2. Prescribed by an endocrinologist; and
3. Inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin AQ® (applies to Humatrope®, Genotropin®, Zomacton®, Omnitrope®)

CONTINUATION CRITERIA

Growth hormones are re-approved when all of the following are met:

1. Growth velocity greater than or equal to 2.5 cm/year; and
2. Inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
3. Yearly evaluation by an endocrinologist

Authorization length: 1 year

C. Growth Hormone deficiency in children

(Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin®[AQ], Zomacton®)

INITIAL CRITERIA

Growth hormones are approved when all of the following are met:

1. Subnormal serum insulin-like growth factor-1 (IGF-1); and
2. Prescribed by an endocrinologist; and
3. Growth velocity less than or equal to 5 cm/year after 2 years of age; and
4. Bone age determination documented; and
5. Either of the following responses from provocative testing:
 - a. Abnormal response on insulin-induced hypoglycemia test (less than 5 ng/ml)

- b. Abnormal response of less than 10 ng/ml to any other two provocative tests (performed sequentially, not simultaneously), such as but not limited to levodopa and clonidine
6. Inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin AQ® (applies to Genotropin®, Humatrope®, Saizen®, Omnitrope®)

CONTINUATION CRITERIA

Growth hormones are re-approved when all of the following are met:

1. Growth velocity greater than or equal to 2.5cm/year; and
2. Inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
3. Yearly evaluation by an endocrinologist

Authorization length: 1 year

D. Growth hormone deficiency in adults with adult onset hypothalamic pituitary disease

(Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin®[AQ]) OR Replacement of endogenous growth hormone (GH) deficiency (Zomacton®)

INITIAL CRITERIA

Growth hormones are approved when all of the following are met:

1. Prescribed by an endocrinologist; and
2. Clinical history of adult-onset hypothalamic or pituitary disease of organic origin or known causes (e.g., damage from surgery, cranial irradiation, head trauma, or subarachnoid hemorrhage); and
3. Deficiency in any two of the following:
 - a. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) (demonstrated by a low early morning serum testosterone concentration or a low serum estradiol concentration while FSH and LH concentrations are not elevated)
 - b. Thyroid-stimulating hormone (TSH) (demonstrated by a low serum T4 concentration and TSH concentration that is not elevated)
 - c. Adrenocorticotrophic hormone (ACTH) (demonstrated by a low early morning serum cortisol and an ACTH that is not elevated); and
4. One of the following:
 - a. Serum IGF-1 concentration that is subnormal for age and gender
 - b. GH response of less than 5 ng/ml to insulin-induced hypoglycemia; and
5. Inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin AQ® (applies to Genotropin®, Humatrope®, Saizen®, Zomacton®, Omnitrope®).

CONTINUATION CRITERIA

Growth hormones are reapproved when all of the following are met:

1. Normalization of serum IGF-1 concentration for age and gender; and
2. Inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
3. Yearly evaluation by an endocrinologist

Authorization length: 1 year

E. Growth Hormone deficiency in adults with childhood onset hypothalamic or pituitary disease

(Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin®[AQ])

INITIAL CRITERIA

Growth hormones are approved when all of the following are met:

1. Prescribed by an endocrinologist; and
2. One of the following:
 - a. Clinical history of organic or idiopathic panhypopituitarism as a child
 - b. History of idiopathic, isolated GH deficiency in childhood requiring documentation of one of the following:
 - i. Serum IGF-1 concentration that is subnormal for age and gender
 - ii. GH response of less than 5 ng/ml to Insulin-induced hypoglycemia
3. Inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin AQ® (applies to Genotropin®, Humatrope®, Saizen®, Omnitrope®)

CONTINUATION CRITERIA

Growth hormones are re-approved when all of the following are met:

1. Normalization of serum IGF-1 concentration for age and gender; and
2. Inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
3. Yearly evaluation by an endocrinologist

Authorization length: 1 year

F. Dwarfism-Noonan syndrome
(Norditropin® only)

INITIAL CRITERIA

Growth hormones are approved when ALL of the following are met:

1. Diagnosis of Noonan syndrome; and
2. Prescribed by an endocrinologist

CONTINUATION CRITERIA

Growth hormones are re-approved when there is yearly evaluation by an endocrinologist

Authorization length: 1 year

G. Dwarfism short stature homeobox containing gene (SHOX) deficiency (Humatrope® and Zomacton®)

INITIAL CRITERIA

Growth hormones are approved when ALL of the following are met:

1. Diagnosis of short stature or growth failure in children with short stature homeobox containing gene (SHOX) deficiency; and
2. Epiphyses are not closed; and
3. Prescribed by an endocrinologist

CONTINUATION CRITERIA

Growth hormones are re-approved when there is yearly evaluation by an endocrinologist

Authorization length: 1 year

H. Small for gestational age (Humatrope®, Genotropin®, Norditropin®, Omnitrope®, Zomacton®)

INITIAL CRITERIA

Growth hormones are approved when all of the following are met:

1. Failure to reach the third percentile for length/height by 2 years of age (Genotropin®, Omnitrope®) or 2 to 4 years of age (Norditropin®, Humatrope®); and
2. Prescriber is an endocrinologist; and
3. One of the following:
 - a. Birth length and/or weight less than the third percentile for gestational age
 - b. Birth weight less than 2500 grams and gestational age greater than 37 weeks
4. Documentation of inadequate response or inability to tolerate Norditropin® (applies to Humatrope®, Genotropin®, Zomacton®, Omnitrope®)

CONTINUATION CRITERIA

Growth hormones are re-approved when all of the following are met:

1. Growth velocity greater than or equal to 2.5cm/year; and
2. Inadequate response or inability to tolerate Norditropin®; and
3. Yearly evaluation by an endocrinologist

Authorization length: 1 year

I. Hypopituitarism in childhood

(Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ])

INITIAL CRITERIA

Growth hormones are approved when all of the following are met:

1. Clinical evidence of a pituitary lesion or midline central nervous system defect; and
2. Prescriber in an endocrinologist; and
3. Growth velocity less than or equal to 5 cm/year after 2 years of age; and
4. Documentation of one of the following:
 - a. A subnormal serum IGF-1
 - b. Provocative testing, such as but not limited to the following:
 - i. Levadopa
 - ii. Clonidine
 - iii. Insulin-induced hypoglycemia
 - c. Deficiencies in two or more other hypothalamic-pituitary axes
5. Inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin AQ® (applies to Genotropin®, Humatrope®, Saizen®, Omnitrope®)

CONTINUATION CRITERIA

Growth hormones are reapproved when all of the following are met:

1. Normalization of serum IGF-1 concentration for age and gender; and
2. Inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
3. Yearly evaluation by an endocrinologist

Authorization length: 1 year

**J. Prader-Willi syndrome
(Omnitrope®, Genotropin®, Norditropin®)**

INITIAL CRITERIA

Growth Hormones are approved when all of the following are met:

1. Diagnosis of Prader-Willi syndrome; and
2. Prescribed by an endocrinologist; and
3. Inadequate response or inability to tolerate Norditropin® (applies to Genotropin® and Omnitrope®)

CONTINUATION CRITERIA

Growth hormones are re-approved when BOTH of the following are met:

1. Yearly evaluation by an endocrinologist; and
2. Inadequate response or inability to tolerate Norditropin®

Authorization length: 1 year

**K. Chronic Kidney Disease (CKD)
(Nutropin® [AQ] only)**

INITIAL CRITERIA

Growth hormones are approved when all of the following are met:

1. Diagnosis of growth failure associated with CKD; and
2. Height below the third percentile on standardized growth charts; and
3. Member is not a renal transplant recipient; and
4. Prescribed by an endocrinologist or nephrologist

CONTINUATION CRITERIA

Growth hormones are re-approved when all of the following are met:

1. No documentation of a renal transplant; and
2. Yearly evaluation by an endocrinologist or nephrologist; and
3. Growth velocity greater than or equal to 2.5 cm/year

Authorization length: 1 year

**L. Short bowel syndrome
(Zorbtive® only)**

INITIAL CRITERIA

Growth hormones are approved when there is a diagnosis of short bowel syndrome

REAUTHORIZATION CRITERIA: N/A

Authorization length: 6 weeks

**M. AIDS wasting syndrome
(Serostim® only)**

INITIAL CRITERIA

Growth hormones are approved when all of the following are met:

1. Diagnosis of wasting (cachexia) associated with HIV; and
2. Concomitant antiretroviral therapy that has been optimized to decrease the viral load; and
3. Current weight less than 90 percent of ideal body weight; and
4. Nutritional evaluation since onset of wasting first occurred

Authorization length: Initial authorization - 12 weeks

Continuation criteria:

Growth hormones are reapproved when there is documentation of positive response to therapy (i.e. greater than or equal to 2% increase in body weight and/or body cell mass)

Authorization length-36 weeks (for 48 weeks of total treatment)

Black Box Warning as shown in the drug Prescribing Information:

None

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Genotropin® (somatoropin) [package insert]. New York, NY. Pharmacia and Upjohn Company. April 2019. Available from: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=ffebf88b-d257-4542-9808-74d9b7167765&type=display>. Accessed August 05, 2020.

Humatrope® (somatoropin) [package insert]. Indianapolis, IN. Eli Lilly and Company. November 2017. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=a774e1ae-3997-49ee-8b0e-99a2b315d409&type=display>. Accessed August 05, 2020.

Norditropin® (somatoropin) [package insert]. Plainsboro, NJ. Novo Nordisk. March 2020. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=1058e17c-9261-459c-a3e6-fae38d196c14&type=display>. Accessed August 05, 2020.

Nutropin® AQ (somatoropin) [package insert]. San Francisco, CA. Genentech, Inc. December 2016. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=139d2038-e6a9-4ab1-ab00-aa7d8aa8df5f&type=display>. Accessed August 05, 2020.

Omnitrope® (somatoropin) [package insert]. Princeton, NJ. Novartis. June 2019. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=58d84ffa-4056-4e36-ad67-7bd4aef444a5&type=display>. Accessed August 05, 2020.

Saizen® (somatoropin) [package insert]. Rockland, MA. EMD Serono, Inc. May 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=ab750de2-3eda-411a-924e-00c499eda39b&type=display>. Accessed August 05, 2020.

Serostim® (somatoropin) [package insert]. Rockland, MA. EMD Serono, Inc. May 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=62b01d29-90f0-45b2-a0c4-3a750ba36c8a&type=display>. Accessed August 05, 2020.

Zomacton® (somatotropin) [package insert]. Parsippany, NJ. Ferring Pharmaceuticals Inc. July 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=85ba081b-bee0-4a9a-aa0f-ae5b5e9a0886&type=display>. Accessed August 05, 2020.

Zorbtive® (somatotropin) [package insert]. Rockland, MA. EMD Serono, Inc. November 2019. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=c04b1b2c-5484-4a5d-887a-3f7ace8388a1&type=display>. Accessed August 05, 2020.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Genotropin®	Somatropin
Humatrope®	Somatropin
Norditropin®	Somatropin
Nutropin®/Nutropin® AQ	Somatropin
Omnitrope®	Somatropin
Saizen®	Somatropin
Serostim®	Somatropin
Zomacton®	Somatropin
Zorbtive®	Somatropin

Cross References:

Off Label Use Rx.01.33

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The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.

