Pharmacy Policy Bulletin

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

INITIAL CRITERIA Somatropin (Omnitrope®, Humatrope®, Genotropin®, Nutropin®[AQ], Norditropin®, or Zomacton®) is approved when all of the following are met:

A. Prescribed by an endocrinologist; and
B. Height less than or equal to 2.25 standard deviations from the mean (1.2 percentile); and
C. Documentation of growth velocity; and
D. Epiphyses are not closed; and
E. For Humatrope®, Genotropin®, Zomacton® and Omnitrope® only, inadequate response or inability to tolerate Nutropin®/Nutropin AQ®, and Norditropin®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Humatrope®, Genotropin®, Nutropin®[AQ], Norditropin®, or Zomacton®) is re-approved when all of the following are met:

A. Growth velocity increased by at least 50 percent from baseline; and
B. For Humatrope®, Genotropin®, Zomacton® and Omnitrope® only, inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and

C. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

B. Turner Syndrome

INITIAL CRITERIA Somatropin (Humatrope®, Genotropin®, Norditropin®, Nutropin®[AQ], Omnitrope® or Zomacton®) is approved when all of the following are met:

A. Diagnosis of Turner syndrome; and
B. Prescribed by an endocrinologist; and
C. For Humatrope®, Genotropin®, Zomacton®, Omnitrope® only, inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin AQ®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Humatrope®, Genotropin®, Norditropin®, Nutropin®[AQ], Omnitrope® or Zomacton®) is re-approved when all of the following are met:

A. Growth velocity greater than or equal to 2.5 cm/year; and
B. For Humatrope®, Genotropin®, Zomacton® and Omnitrope® only, inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
C. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

C. Growth Hormone deficiency in children

INITIAL CRITERIA Somatropin (Omnitrope, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ], or Zomacton®) or lonapegsomatropin-tcgd (Skytrofa™) is approved when all of the following are met:

A. Prescribed by an endocrinologist; and
B. Growth velocity less than or equal to 5 cm/year after 2 years of age; and
C. Bone age determination documented; and
D. Either ONE of the following responses from provocative testing:
    1. Abnormal response on insulin-induced hypoglycemia test (less than 5 ng/ml); or
    2. 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; and
E. For Genotropin®, Humatrope®, Saizen®, Omnitrope®, Zomacton®, lonapegsomatropin-tcgd (Skytrofa™) only, inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin AQ®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin®[AQ], or Zomacton®) or lonapegsomatropin-tcgd (Skytrofa™) is re-approved when all of the following are met:

A. Growth velocity greater than or equal to 2.5cm/year; and
B. For Genotropin®, Humatrope®, Saizen®, Omnitrope®, Zomacton®, lonapegsomatropin-tcgd (Skytrofa™) only, inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
C. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

D. Growth hormone deficiency in adults with adult-onset hypothalamic or pituitary disease OR Replacement of endogenous growth hormone (GH) deficiency

INITIAL CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin®[AQ], or Zomacton®) is approved when all of the following are met:

A. Prescribed by an endocrinologist; and
B. 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
C. Deficiency in any two of the following:
    1. 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); or
    2. Thyroid-stimulating hormone (TSH) (demonstrated by a low serum T4 concentration and TSH concentration that is not elevated); or
    3. Adrenocorticotropic hormone (ACTH) (demonstrated by a low early morning serum cortisol and an ACTH that is not elevated); an
D. GH response of less than 5 ng/ml to insulin-induced hypoglycemia; and
E. For Genotropin®, Humatrope®, Saizen®, Zomacton®, Omnitrope® only, inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin AQ®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin®[AQ], or Zomacton®) is re-approved when all of the following are met:

A. For Genotropin®, Humatrope®, Saizen®, Zomacton®, Omnitrope® only, inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
B. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

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

INITIAL CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ] is approved when all of the following are met:

A. Prescribed by an endocrinologist; and
B. One of the following:
    1. Clinical history of organic or idiopathic panhypopituitarism as a child; and
    2. History of idiopathic, isolated GH deficiency in childhood requiring documentation of GH response of less than 5 ng/ml to Insulin-induced hypoglycemia
C. For Genotropin®, Humatrope®, Saizen®, Omnitrope® only, inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin® AQ

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ] is re-approved when all of the following are met:

A. For Genotropin®, Humatrope®, Saizen®, Omnitrope® only, inadequate response or inability to tolerate Nutropin®/Nutropin® AQ and Norditropin®; and
B. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

F. <u>Dwarfism-Noonan syndrome</u>

INITIAL CRITERIA Somatropin (Norditropin®) is approved when ALL of the following are met:

A. Diagnosis of Noonan syndrome; and

B. Prescribed by an endocrinologist

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Norditropin®) is re-approved when there is yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

G. Dwarfism short stature homeobox containing gene (SHOX) deficiency

INITIAL CRITERIA Somatropin (Humatrope® or Zomacton®) is approved when ALL of the following are met:

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

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Humatrope® or Zomacton®) is re-approved when there is yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

H. Small for gestational age

INITIAL CRITERIA Somatropin (Humatrope®, Genotropin®, Norditropin®, Omnitrope®, or Zomacton®) is approved when all of the following are met:

A. 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
B. Prescribed by an endocrinologist; and
C. One of the following:
    1. Birth length and/or weight less than the third percentile for gestational age
    2. Birth weight less than 2500 grams and gestational age greater than 37 weeks
D. For Humatrope®, Genotropin®, Zomacton® and Omnitrope® only, inadequate response or inability to tolerate Norditropin®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Humatrope®, Genotropin®, Norditropin®, Omnitrope®, or Zomacton®) is re-approved when all of the following are met:

A. Growth velocity greater than or equal to 2.5cm/year; and
B. For Humatrope®, Genotropin®, Zomacton® and Omnitrope® only, inadequate response or inability to tolerate Norditropin®; and
C. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

I. Hypopituitarism in childhood

INITIAL CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ] is approved when all of the following are met:

A. Clinical evidence of a pituitary lesion or midline central nervous system defect; and
B. Prescribed by an endocrinologist; and
C. Growth velocity less than or equal to 5 cm/year after 2 years of age; and
D. Documentation of one of the following:
    1. Provocative testing, such as but not limited to the following:
        a. Levadopa
        b. Clonidine
        c. Insulin-induced hypoglycemia
    2. Deficiencies in two or more other hypothalamic-pituitary axes; and
E. For Genotropin®, Humatrope®, Saizen®, Omnitrope® only, inadequate response or inability to tolerate Norditropin® and Nutropin®/Nutropin AQ®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ] is reapproved when all of the following are met:

A. For Genotropin®, Humatrope®, Saizen®, Omnitrope® only, inadequate response or inability to tolerate Nutropin®/Nutropin AQ® and Norditropin®; and
B. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

J. <u>Prader-Willi syndrome</u>

INITIAL CRITERIA Somatropin (Omnitrope®, Genotropin®, or Norditropin®) is approved when all of the following are met:

A. Diagnosis of Prader-Willi syndrome; and
B. Prescribed by an endocrinologist; and

For Genotropin® and Omnitrope® only, inadequate response or inability to tolerate Norditropin®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Genotropin®, or Norditropin®) is re-approved when BOTH of the following are met:

A. Yearly evaluation by an endocrinologist; and
B. For Genotropin® and Omnitrope® only, inadequate response or inability to tolerate Norditropin®

Continuation authorization duration: 1 year

K. <u>Chronic Kidney Disease (CKD)</u>

INITIAL CRITERIA Somatropin (Nutropin® [AQ]) is approved when all of the following are met:

A. Diagnosis of growth failure associated with CKD; and
B. Height below the third percentile on standardized growth charts; and
C. Member is not a renal transplant recipient; and
D. Prescribed by an endocrinologist or nephrologist

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Nutropin® [AQ]) is re-approved when all of the following are met:

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

Continuation authorization duration: 1 year

L. Short bowel syndrome

INITIAL CRITERIA Somatropin (Zorbtive®) is approved when there is a diagnosis of short bowel syndrome

Authorization duration: 6 weeks

M. AIDS wasting syndrome

INITIAL CRITERIA Somatropin (Serostim®) is approved when all of the following are met:

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

Initial authorization duration: 12 weeks

CONTINUATION CRITERIA Somatropin (Serostim®) is re-approved 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)

Continuation authorization duration: 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 October 05, 2022.

Humatrope® (somatoropin) [package insert]. Indianapolis, IN. Eli Lilly and Company. October 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=a774e1ae-3997-49ee-8b0e-99a2b315d409&type=display. Accessed October 05, 2022.

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 October 05, 2022.

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 October 05, 2022.

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 October 05, 2022.

Saizen® (somatoropin) [package insert]. Rockland, MA. EMD Serono, Inc. February 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=ab750de2-3eda-411a-924e-00c499eda39b&type=display. Accessed October 05, 2022.

Serostim® (somatoropin) [package insert]. Rockland, MA. EMD Serono, Inc. June 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=62b01d29-90f0-45b2-a0c4-3a750ba36c8a&type=display. Accessed October 05, 2022.

Skytrofa® (lonapegsomatropin-tcgd) [package insert]. Princeton, NJ. Ascendis Pharma Endocrinology, Inc.; August 2022. Available at: https://ascendispharma.us/products/pi/skytrofa/skytrofa_pi.pdf. Accessed October 05, 2022.

Zomacton® (somatoropin) [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 October 05, 2022.

Zorbtive® (somatoropin) [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 October 05, 2022.

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
Skytrofa®	Lonapegsomatropin-tcgd

Cross References:

Off Label Use Rx.01.33

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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.