Mass General Brigham
Health Plan

Growth Hormone:
Genotropin (somatropin)
Humatrope (somatropin)
Norditropin (somatropin)
Nutropin AQ (somatropin)
Omnitrope (somatropin)
Saizen (somatropin)
Zomacton (somatropin)
Skytrofa (lonapegsomatropin-tcgd)
Sogroya (somapacitan-beco)
Ngenla (somatrogon-ghla)
Effective 03/01/2025

<table>
<tr><td>Plan</td><td>☐ MassHealth UPPL
☒Commercial/Exchange</td><td rowspan="2">Program Type</td><td rowspan="2">☒ Prior Authorization
☐ Quantity Limit
☐ Step Therapy</td></tr>
<tr><td>Benefit</td><td>☒ Pharmacy Benefit
☐ Medical Benefit</td></tr>
<tr><td>Specialty Limitations</td><td colspan="3">This medication has been designated specialty and must be filled at a contracted specialty pharmacy.</td></tr>
<tr><td rowspan="2">Contact Information</td><td colspan="3">Medical and Specialty Medications
All Plans | Phone: 877-519-1908 | Fax: 855-540-3693</td></tr>
<tr><td colspan="3">Non-Specialty Medications
All Plans | Phone: 800-711-4555 | Fax: 844-403-1029</td></tr>
<tr><td>Exceptions</td><td colspan="3">N/A</td></tr>
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Overview

FDA-Approved Indications

1. Pediatric patients with growth failure due to any of the following:
    a. Growth hormone (GH) deficiency
    b. Turner syndrome
    c. Noonan syndrome
    d. Small for gestational age (SGA)
    e. Prader-Willi syndrome
    f. Chronic kidney disease (CKD)
    g. Short stature homeobox-containing gene (SHOX) deficiency
2. Adults with childhood-onset or adult-onset GH deficiency

Compendial Uses

1. Human immunodeficiency virus (HIV)-associated wasting/cachexia
2. Short bowel syndrome (SBS)
3. Growth failure associated with any of the following:
    a. Cerebral palsy
    b. Congenital adrenal hyperplasia

c. Cystic fibrosis
d. Russell-Silver syndrome

Note: Skytrofa and Ngenla are only FDA approved for pediatric growth hormone deficiency. Sogroya is only FDA approved for adult growth hormone deficiency and pediatric growth hormone deficiency.

Coverage Guidelines
Authorization may be reviewed for members new to the plan within the past 90 days who are currently receiving treatment with the requested medication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
OR
Authorization may be granted for members when ALL the following criteria are met:

Pediatric Growth Hormone (GH) Deficiency
1. Member meets ONE of the following:
    a. Both of the following
        i. Infant is less than 4 months of age
        ii. Infant is suspected of GH deficiency based on clinical presentation (e.g., persistent neonatal hypoglycemia, persistent or prolonged neonatal jaundice/elevated bilirubin, male infant with microgenitalia, midline anatomical defects, failure to thrive, etc)
    b. History of neonatal hypoglycemia associated with pituitary disease
    c. Diagnosis of panhypopituitarism
    d. Member meets ALL of the following:
        i. Member meets ONE of the following:
            1. Two pretreatment pharmacologic provocative GH tests with both GH response values < 10 ng/mL
            2. A documented pituitary or CNS disorder (refer to Appendix for examples) and a pretreatment IGF-1 level > 2 standard deviations (SD) below the mean
            3. Member is < 1 year of age AND one of the following labs is below the age and gender adjusted normal range: insulin-like growth factor 1 (IGF-1/Somatomedin-C), insulin growth factor binding protein-3 (IGFBP-3)
        ii. Member meets ONE of the following:
            1. Pretreatment height is > 2 SD below the population mean or midparental height
            2. Pretreatment height velocity is > 2 SD below the mean for age and gender
            3. Delayed skeletal maturation is > 2 SD below mean for age and gender
2. For Humatrope, Ngenla, Nutropin, Omnitrope, Saizen, Skytrofa, Sogroya, and Zomacton: Provider documents intolerance, adverse effect or contraindication to Genotropin and Norditropin

Small for Gestational Age
Member meets ALL of the following:
1. Member meets at least one of the following:
    a. Birth weight < 2500 g at gestational age > 37 weeks
    b. Birth weight or length less than 3rd percentile for gestational age
    c. Birth weight or length ≥ 2 SD below the mean for gestational age
2. Pretreatment age is ≥ 2 years
3. Member failed to manifest catch-up growth by age 2 (i.e., pretreatment height > 2 SD below the mean)
4. For Humatrope, Nutropin, Omnitrope, Saizen, and Zomacton: Provider documents intolerance, adverse effect or contraindication to Genotropin and Norditropin

Growth Failure Associated with Chronic Kidney Disease, Noonan Syndrome, Prader-Willi Syndrome, Turner Syndrome, SHOX deficiency, Russell-Silver Syndrome, Cystic Fibrosis, Cerebral Palsy, Congenital Adrenal Hyperplasia

Member meets all of the following:

1. Documentation of growth failure or short stature due to one of the following diagnoses:
    a. Pediatric growth failure associated with chronic renal insufficiency
    b. Noonan Syndrome
    c. Prader-Willi Syndrome
    d. Turner Syndrome
    e. Short Stature Homeobox (SHOX) gene deficiency, as confirmed by genetic testing
    f. Russell-Silver Syndrome
    g. Cystic fibrosis
    h. Cerebral palsy
    i. Congenital adrenal hyperplasia
2. For Humatrope, Nutropin, Omnitrope, Saizen, and Zomacton: Provider documents intolerance, adverse effect or contraindication to Genotropin and Norditropin

Adult GH Deficiency

Member meets ALL of the following:

1. Member meets ONE of the following:
    a. Member has childhood-onset growth hormone deficiency
    b. Member meets ALL of the following:
        i. Member has adult-onset growth hormone deficiency resulting from hypothalamic pituitary disease from organic or known causes (e.g., damage from surgery, cranial irridiation, head trauma, or subarachnoid hemorrhage)
        ii. Member meets ONE of the following:
            1. Member has undergone a GH stimulation test and has ONE of the following peak values:
                a. Insulin tolerance test (ITT): ≤5 mcg/L
                b. Glucagon: ≤3 mcg/L
                c. Macrelin: ≤ 2.8 ng/mL
            2. Member has a deficiency of THREE of the following anterior pituitary hormones:
                a. Prolactin
                b. Adrenocorticotropic hormone (ACTH)
                c. Thyroid stimulating hormone (TSH)
                d. Follicle-stimulating hormone/luteinizing hormone (FSH/LH)
2. For Humatrope, Nutropin, Omnitrope, Saizen, Sogroya, and Zomacton: Provider documents intolerance, adverse effect or contraindication to Genotropin and Norditropin

HIV-Associated Wasting/Cachexia

Member meets ALL of the following:

1. Member has trialed and experienced a suboptimal response to alternative therapies (e.g., cyproheptadine, dronabinol, megestrol acetate or testosterone if hypogonadal) or contraindication or intolerance to alternative therapies
2. Member is currently on antiretroviral therapy
3. Member meets ONE of the following:
    a. Unintentional weight loss of greater than 10% over the past 12 months

b. Unintentional weight loss of greater than 7.5% over the past 6 months
c. Loss of 5% body cell mass (BCM) within 6 months
d. BMI is less than 20 kg/m^2

4. For Humatrope, Nutropin, Omnitrope, Saizen, and Zomacton: Provider documents intolerance, adverse effect or contraindication to Genotropin and Norditropin

Short Bowel Syndrome (SBS)

Member meets ALL of the following:

1. Member depends on intravenous (IV) parenteral nutrition
2. GH will be used in conjunction with optimal management of SBS
3. For Humatrope, Nutropin, Omnitrope, Saizen, and Zomacton: Provider documents intolerance, adverse effect or contraindication to Genotropin and Norditropin

Continuation of Therapy

Requests for reauthorization will be approved when the following criteria are met:

1. **Pediatric GHD, Turner Syndrome, Noonan Syndrome, CKD, SGA, SHOX deficiency, Congenital Adrenal Hyperplasia, Cerebral Palsy, Cystic Fibrosis and Russel-Silver Syndrome:**
    a. Documentation is submitted demonstrating the Member's growth rate is > 2 cm/year, unless there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty)
2. **Prader-Willi Syndrome (PWS):**
    a. Documentation member meets ONE of the following:
        i. Member's body composition and psychomotor function have improved or stabilized in response to GH therapy
        ii. Member's growth rate is > 2 cm/year
3. **Adult GHD:**
    a. Documentation is submitted demonstrating ongoing monitoring within the past 12 months
4. **HIV-Associated Wasting/Cachexia:**
    a. Member is diagnosed with HIV-associated wasting/cachexia
    b. Member is currently on antiretroviral therapy.
    c. Member is currently receiving treatment with growth hormone excluding obtainment as samples or via manufacturer's patient assistance programs
    d. Current BMI is less than 27 kg/m^2
5. All requests for Humatrope, Ngenla, Nutropin, Omnitrope, Saizen, Skytrofa, Sogroya, and Zomacton: Provider documents intolerance, adverse effect or contraindication to Genotropin and Norditropin

Limitations

1. Ngenla and Skytrofa will only be approved for the treatment for pediatric growth hormone deficiency. Sogroya will only be approved for the treatment of pediatric growth hormone deficiency or adult growth hormone deficiency.
2. Initial approvals will be varied based on the treatment:
    a. **For Short Bowel Syndrome,** approvals will be for up to 8 weeks
    b. **For HIV-Associated Wasting/Cachexia,** approvals will be for up to 12 weeks.
    c. **For ALL other indications,** approvals will be for up to 12 months.
3. Reauthorizations will be varied based on the treatment:
    a. **For HIV-Associated Wasting/Cachexia,** approvals will be for up to 12 weeks.
    b. **For ALL other indications,** approvals will be for up to 12 months.

c. Treatment for Short Bowel Syndrome past 8 weeks has not been studied and will be reviewed on a case by case basis.

Appendix

Examples of Hypothalamic/Pituitary/CNS Disorders

1. Congenital genetic abnormalities
    a. Known mutations in growth-hormone-releasing hormone (GHRH) receptor, GH gene, GH receptor, or pituitary transcription factors
2. Congenital structural abnormalities
    a. Optic nerve hypoplasia/septo-optic dysplasia
    b. Agenesis of corpus callosum
    c. Empty sella syndrome
    d. Ectopic posterior pituitary
    e. Pituitary aplasia/hypoplasia
    f. Pituitary stalk defect
    g. Anencephaly or prosencephaly
    h. Other mid-line defects
    i. Vascular malformations
3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
    a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma, pituitary adenoma)
    b. Cysts (Rathke cleft cyst or arachnoid cleft cyst)
    c. Surgery
    d. Radiation
    e. Chemotherapy
    f. CNS infections
    g. CNS infarction (e.g., Sheehan's syndrome)
    h. Inflammatory lesions (e.g., autoimmune hypophysitis)
    i. Infiltrative lesions (e.g., sarcoidosis, histiocytosis)
    j. Head trauma/traumatic brain injury
    k. Aneurysmal subarachnoid hemorrhage

References

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3. Humatrope (somatropin) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; December 2023.
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5. Lin-Siu K, Harbison MD, Lekarev O, et al. Final adult height in children with congenital adrenal hyperplasia treated with growth hormone. *J Clin Endocrinol Metab*. 2011;96:1710.
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8. Ngenla (somatrogon-ghla) [prescribing information]. New York, NY: Pfizer Labs; June 2023.
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10. Nutropin AQ (somatropin) [prescribing information]. South San Francisco, CA: Genentech, Inc.; December 2016.
11. Omnitrope (somatropin) [prescribing information]. Princeton, NJ: Sandoz Inc.; December 2016.
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13. Saizen (somatropin) [prescribing information]. Rockland, MA: EMD Serono Inc.; December 2020.
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17. Wakeling EL, Brioude F, Lokulo-Sodipe O, et al. Diagnosis and management of Silver-Russell syndrome: first international consensus statement. *Nature Reviews Endocrinology*. 2017;13:105-124.
18. Zomacton (somatropin) [prescribing information]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; January 2018.

Review History

05/18/2022 – Created and Reviewed for May P&T; switched from CVS SGM to custom. Effective 07/01/2022
09/21/2022 – Reviewed and Updated for Sept P&T; Updated verbiage for growth failure associated with chronic kidney disease. Updated preferred products to Genotropin and Norditropin. Humatrope, Omnitrope, Saizen, and Zomacton require failure of Genotropin and Norditropin.
09/13/2023 – Reviewed and Updated for Sept P&T; Added new drug Sogroya to criteria. Effective 11/1/2023
11/15/2023 – Reviewed and Updated for Nov P&T; Added new drug Ngenla to criteria. Effective 1/1/2024
12/11/2024 – Reviewed and updated for December P&T. Updated pediatric GH criteria to allow for approval if member is less than 4 months of age with suspected GH deficiency, history of neonatal hypoglycemia associated with pituitary disease, or diagnosis of panhypopituitarism. For lab values for pediatric GH, added ranges for insulin growth factor 1 and insulin growth factor binding protein-3 for members under the age of 1. Streamlined pretreatment height and height velocity requirements to be > 2 SD below the population mean or midparental height, height velocity > 2 SD below the mean for age and gender, or delayed skeletal maturation > 2 SD below the mean for age and gender. Removed requirements that epiphyses are open. Updated criteria for Turner Syndrome, growth failure associated with CKD, Noonan Syndrome, Prader-Willi, SHOX deficiency, Russell-Silver Syndrome, cerebral palsy, congenital adrenal hyperplasia, and cystic fibrosis to require documentation for growth failure or short stature associated with the diagnosis. Updated adult growth hormone deficiency criteria to require that either the member had adult-onset growth hormone deficiency or that they have adult-onset growth hormone deficiency resulting from hypothalamic pituitary disease and either have a GH stimulation test below a specified peak value or are deficient in three anterior pituitary hormones. Updated HIV-associated Wasting/Cachexia criteria to allow for approval if the member had unintentional weight loss greater than 10 % in 12 months, greater than 7.5% in 6 months, loss of 5% body cell mass within 6 months, or BMI less than 20 kg/m^2. Throughout policy added Ngenla, Skytrofa and Sogroya to list of nonpreferred growth hormone products and completed administrative updates to clarify that trial and failure with preferred agents is in addition to the diagnosis-specific criteria. Effective 3/1/2025.
01/08/2025 – Reviewed and updated for January P&T. Clarified that Ngenla and Skytrofa will only be approved for pediatric growth hormone deficiency and Sogroya will only be approved for pediatric growth hormone deficiency and adult growth hormone deficiency. Effective 3/1/2025.