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Growth Hormone (somatropin and analogs) Therapy

PRODUCTS AFFECTED

Genotropin (somatropin), Humatrope (somatropin), Ngenla (somatrogon-ghla), Norditropin (somatropin), Nutropin AQ (somatropin), Omnitrope (somatropin), Saizen (somatropin Non-Refrigerated), Serostim (somatropin Non-Refrigerated), Skytrofa (lonapegsomatropin-tcgd), Sogroya (somapacitan-beco), Zomacton (somatropin)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Growth Hormone Deficiency (GHD), Idiopathic Short Stature (ISS), Chronic Renal Insufficiency/Chronic Kidney Disease (CRI/CKD) up until the time of renal transplantation, Small for Gestational Age (SGA), Turner Syndrome (TS), Noonan Syndrome (NS), Prader-Willi syndrome (PWS), Short Stature Homeobox- Containing Gene (SHOX) Deficiency, Growth hormone deficiency due to hypothalamic or pituitary condition, Child onset growth hormone deficiency continuing into adulthood, Short-bowel syndrome (SBS), HIV-associated Wasting, and Neonatal Hypoglycemia related to GH Deficiency

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by- case basis

to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

Omnitrope brand of growth hormone is the preferred brand of growth hormone for Molina Healthcare. Other brands (e.g., Genotropin, Humatrope, Norditropin, Nutropin AQ, etc.) of growth hormone are highly expected to produce equivalent therapeutic results for the treatment of the member's disease. Other brands of growth hormone will be considered NON-PREFERRED and not authorized unless the member has a documented contraindication or serious side effect to the preferred brand of growth hormone (Omnitrope). If the preferred brand (Omnitrope) does not have the labeled indication for member's diagnosis, this is acknowledged.

ALL INDICATIONS (ADULT AND PEDIATRIC):

1. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to somatropin and analogs include: acute critical illness, active malignancy, hypersensitivity, active proliferative or severe non-proliferative diabetic retinopathy, pediatric members with closed epiphysis, and for pediatric members with Prader-Willi syndrome: severe obesity, history of severe upper airway obstruction, severe respiratory impairment.]
   AND
2. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT:
   a. Member meets all criteria specific for diagnosis/indication
      AND
   b. Documentation of failure or inadequate response, serious side effect, or contraindication to the preferred product(s) OR Member's diagnosis is not an FDA-labeled indication for the preferred product(s) [DOCUMENTATION REQUIRED]
      NOTE: Review for sensitivity to preservatives such as benzyl alcohol (a preservative in Omnitrope 5 Pen and Omnitrope 5.8mg/vial) and to phenol (a preservative in Omnitrope 10 Pen). Genotropin and Humatrope contain a different preservative.
      Children under the age of 3: Benzyl alcohol should not be used in children under the age of three. Omnitrope 5 & 5.8mg, which contain benzyl alcohol as a preservative, is contraindicated in children under the age of three. Omnitrope 10 can be used in children under the age of 3 as it does not contain benzyl alcohol.
      AND
   c. FOR NGENLA REQUESTS: i) Member is less than 18 years of age (Ngenla (somatrogon) is only FDA approved for pediatric growth hormone deficiency) AND ii) Documentation of a trial (6 months) and failure (lack of growth rate velocity increase over 6 months) of a non-long acting somatropin product *NOTE: Molina Healthcare, Inc. does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.*
      AND
   d. FOR SKYTROFA REQUESTS: Documentation of a trial (6 months) and failure (lack of growth rate velocity increase over 6 months, low IGF-1, glucose intolerance, etc.) of a non-long acting somatropin product *NOTE: Molina Healthcare, Inc. does not consider frequency of dosing and/or lack of compliance to dosing regimens an indication of medical necessity.*

PEDIATRIC INDICATIONS (MEMBERS LESS THAN 18 YEARS OF AGE):

A. PEDIATRIC GROWTH HORMONE DEFICIENCY (GHD):
   1. Documented diagnosis of growth hormone deficiency confirmed by ONE of the following [DOCUMENTATION REQUIRED]:
      a. 2 provocative stimulation tests producing peak growth hormone (GH) concentrations <10 ng/mL (e.g., L-dopa, clonidine, glucagon, propranolol, arginine, or insulin) AND IGF-1 and IGFBP- 3 below a clearly normal range
         OR

b. 1 abnormal GH stimulation test (serum peak level below 10 ng/mL) for members with a defined CNS pathology*, history of irradiation, multiple pituitary hormone deficiency** (MPHD), or a genetic defect affecting the GH axis
**CNS pathology:* e.g., empty sella syndrome, interruption of pituitary stalk, hypoplasia of the pituitary gland, craniofacial developmental defects, pituitary, or hypothalamic tumors, etc.
***MPHD:* 3 or more pituitary deficiencies (e.g., TSH, LH, FSH, ACTH, ADH) defined by at least 2 pituitary hormone deficiencies in addition to GHD
OR

c. Member has panhypopituitarism (defined as at least 3 pituitary hormone deficiencies) or has undergone pituitary surgery: No stimulation tests are required
OR

d. Radiographic documentation that bone age is > 2 standard deviations below the mean for chronological age AND IGF-1 and IGFBP-3 are below a clearly normal range
OR

e. Member produces two normal stimulation tests but has a height > 2.25 standard deviations below the age-related mean and a growth velocity below the 25th percentile for bone age AND IGF-1 and IGFBP-3 are below a clearly normal range
NOTE: When growth deficiency is significant (meeting the definition stated) results of stimulation tests may not be as clinically significant.

AND

2. Documentation of ONE of the following supporting member's growth failure:
   a. Severe growth retardation as evidenced by height standard deviation score (SDS) more than 3 SDS below the mean for chronological age and gender
   OR
   b. Moderate growth retardation with height SDS between 2 SD to 3 SD below the mean for chronological age/gender and decreased growth rate (growth velocity less than the 25th percentile for age/gender) tracked over at least 1 year documented by ONE of the following:
      i. 2 heights measured by an endocrinologist at least 6 months apart (> 1 year)
      OR
      ii. 4 heights measured by a primary physician at least 6 months apart (> 2 years)
      NOTE: Growth velocity (GV) should be tracked over at least 1 year
   OR
   c. Severe deceleration in growth rate as evidenced by growth velocity of 2 SDS (or 3rd percentile) below the mean for age and gender as measured over 1 year (or 3rd percentile for chronologic age and gender)
   OR
   d. Decreasing growth rate combined with a predisposing condition such as previous cranial irradiation or tumor
   OR
   e. Delayed skeletal maturation as evidenced by comparison of bone age to chronological age documented as abnormal by greater than or equal to 2 SDs below the mean for chronological age, which is generally greater than or equal to 2 years delayed growth.
   NOTE: Bone age estimation from x-ray of left wrist and hand

   AND

3. FOR MEMBERS 12 YEARS OF AGE AND OLDER ONLY: Documentation of open epiphyses confirmed by bone age X-ray (taken within 6 months of request) of the left hand and wrist showing one of the following:
   a. Males: Not to exceed 16 0/12 years of age
   b. Females: Not to exceed 14 0/12 years of age.

   AND

4. Documentation that thyroid function (TSH) tests are within normal range based on member's age. If TSH level is not within normal range, TSH deficiency should be corrected before performing GH stimulation tests since GH secretion may be subnormal as a result of the hypothyroidism. Documentation of normal TSH required. [DOCUMENTATION REQUIRED]
   AND

5. Other causes of GHD or secondary medical illnesses that affect GH

have been ruled out (e.g., liver/kidney disease, chronic systemic disease, intracranial malignancy or tumor, growth- inhibiting medication(s), endocrine disorders, cranial tumors, cranial irradiation, chronic systemic disease, infections of the central nervous system, genetic syndromes, skeletal disorders, or other organic causes)
AND

6. Other pituitary hormone deficiencies have been ruled out and/or corrected prior to time of testing (e.g., ACTH, TSH, gonadotropin deficiency [LH and/or FSH counted as 1 deficiency], prolactin, or AVP deficiency)
AND
7. Nutritional status has been optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum

B. **IDIOPATHIC SHORT STATURE (ISS)**: NON-COVERAGE (See Appendix)

Idiopathic short stature (ISS) is a clinical description rather than a disease. A practical definition of ISS is a height below 2 standard deviations (SD) of the mean for age (i.e., below the 2.3rd percentile), in the absence of any endocrine, metabolic, or other disease that explains the short stature. Assessment of the published clinical trials of growth hormone treatment in children and adolescents with ISS is complicated by the use of variable inclusion criteria, growth hormone doses, and outcomes, small sample sizes, high dropout rates (usually skewed to those with the smallest response), and lack of an adequate control group (in most studies). The studies generally support the view that growth hormone treatment results in modest increases in short- term growth rates and in adult height, although treated individuals remain relatively short compared with their peers.

Molina Healthcare does not consider ISS a disease as coverage of treatment extends to disease or injury. The basis of this policy is coverage of GH therapy as a replacement for endogenous GH in members with evidence of a deficiency. Therefore, GH treatment is not authorized when used for treatment of short stature in the absence of a GH deficiency or for the majority of other conditions in which GH has not been shown to provide clinical benefits or improvements in functional impairment or long-term health outcomes.(25-30)

C. **CHRONIC RENAL INSUFFICIENCY/CHRONIC KIDNEY DISEASE (CRI/CKD) [Nutropin AQ ONLY]:**
MOLINA REVIEWER NOTE: GH Provocative Stimulation Test: NOT required

1. Documented diagnosis of CRI/CKD as evidenced by ONE of the following:
    a. Creatinine clearance less than or equal to 75 mL/min per 1.73m^2 or serum creatinine greater than 3.0 mg/dl
    b. Member is dialysis dependent
    c. Member received a kidney transplant > 1 year ago and has failed to demonstrate catch up growth NOTE: GH is not approved post-transplant. Evaluation for GH therapy resumption should occur at least 1 year after the transplant to allow time to determine whether catch-up growth will occur.

    AND
2. Nutritional status has been optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum
    AND
3. Thyroid function (TSH) tests are within normal range for member's age
    AND
4. FOR MEMBERS 12 YEARS OF AGE AND OLDER ONLY: Documentation of open epiphyses confirmed by bone age X-ray (taken within 6 months of request) of the left hand and wrist showing one of the following:
    a. Males: Not to exceed 16 0/12 years of age
    b. Females: Not to exceed 14 0/12 years of age

D. **SMALL FOR GESTATIONAL AGE (SGA):**
MOLINA REVIEWER NOTE: GH Provocative Stimulation Test: NOT required for SGA

1. Member is currently between 2 years of age and 8 years [EXCEPTIONS for age > 8 years as determined by Molina Clinical Pharmacist or Medical Director on a case-by- case basis]
    a. Member is pre-pubertal [who meets ALL applicable criteria]: Authorization may be recommended for an initial 12-month trial basis. If growth increases by 2.5 cm/year with therapy, then authorization for continued therapy may be recommended. NOTE: Additional supporting documentation and peer- to-peer with Prescriber may be requested.
    OR
    b. Member is clearly pubertal: An exception is NOT recommended. Efficacy has not been established in pubertal adolescents born SGA.

AND

2. Documentation that member was born small for gestational age as evidenced by ONE of the following:
    a. Birth weight of less than 2,500 g at a gestational age of more than 37 weeks
    OR
    b. Birth weight or length below the 3rd percentile or > 2 standard deviations below the mean for gestational age

AND

3. Documentation of failure to manifest catch up growth by age 2 (defined as baseline pre-treatment height 2.5 SD below the mean for age and gender)
AND
4. Documentation of growth charts (plotting growth) from birth through age 2 required
AND
5. Thyroid function (TSH) tests are within normal range for member's age

E. **TURNER SYNDROME (TS):**
MOLINA REVIEWER NOTE: GH Provocative Stimulation Test: NOT required

1. Documented diagnosis of Turner syndrome
AND
2. Documentation diagnosis of Turner's Syndrome confirmed by karyotyping (Turner Syndrome Karyotypes include: 45,X (most common); 45,X/46,XX; 45,X/46,XY; 46,X,i(Xq); 46,X,idic(Xp); 45,X/47,XXX; 45,X/46,XX/47,XXX) [DOCUMENTATION REQUIRED]
AND
3. Thyroid function (TSH) tests are within normal range for member's age

F. **NOONAN SYNDROME (NS):**
MOLINA REVIEWER NOTE: GH Provocative Stimulation Test: NOT required

1. Documented diagnosis of Noonan Syndrome (NS)
AND
2. Documentation diagnosis of NS confirmed by molecular or genetic testing OR documentation of member's physical features which define the clinical diagnosis of NS. (Clinical diagnosis may include the following: Facial features such as philtrum, wide spaced eyes, low-set ears, high arched palate, micrognathia, or short neck; pectus excavatum or pectus carinatum; presence of a critical congenital heart disease) [DOCUMENTATION REQUIRED]
AND
3. Thyroid function (TSH) tests are within normal range for member's age

G. **PRADER-WILLI SYNDROME (PWS):**
MOLINA REVIEWER NOTE: GH Provocative Stimulation Test: NOT required

1. Documented diagnosis of Prader-Willi Syndrome (PWS)
AND
2. Documentation diagnosis of PWS confirmed by genetic testing. [DOCUMENTATION REQUIRED]
AND
3. Documentation supporting that member does NOT have the following conditions (contraindications): Severely obese (defined as a body mass index (BMI) ≥97th percentile for age and gender OR a BMI ≥35), OR Upper airway obstruction or severe respiratory impairment

AND

4. Documentation supporting an absence of obstructive sleep apnea by sleep study or treated obstructive sleep apnea. NOTE: Any sleep disorders or upper airway obstruction must be effectively treated prior to starting GH therapy
   AND
5. Thyroid function (TSH) tests are within normal range for member's age

H. **SHORT STATURE HOMEOBOX-CONTAINING GENE (SHOX) DEFICIENCY [Humatrope, Zomacton only]:**
MOLINA REVIEWER NOTE: GH Provocative Stimulation Test: NOT required for SHOX deficiency

1. Documented diagnosis of short stature homeobox-containing gene (SHOX) deficiency
   AND
2. Documentation diagnosis of pediatric growth failure with SHOX gene deficiency confirmed by molecular or genetic testing [DOCUMENTATION REQUIRED]
   AND
3. Thyroid function (TSH) tests are within normal range for member's age

I. **NEONATAL HYPOGLYCEMIA RELATED TO GH DEFICIENCY:**

1. Requested medication is prescribed and managed by a board-certified neonatologist (in the neonatal period)
   AND
2. Member is 30 days old or less at time of diagnosis
   AND
3. All of the following documentation requested for the criteria below must be submitted for review [DOCUMENTATION REQUIRED]:
   a. Presence of neonatal hypoglycemia in the absence of a metabolic disorder
      AND
   b. Other metabolic disorders have been ruled out as a cause of hypoglycemia (e.g., prematurity, delayed feedings, hyperinsulinism, birth asphyxia, insulin- dependent) NOTE: Chart documentation indicating that other metabolic disorders have been ruled out as a cause of hypoglycemia through clinical work-up must be submitted
      AND
   c. Randomly assessed GH levels less than 20mcg/L as confirmed by polyclonal radioimmunoassay (RIA) **No stimulation test required for neonates**
      NOTE: A GH level should be measured in the presence of neonatal hypoglycemia in the absence of a metabolic disorder. A random GH measurement in a polyclonal RIA of less than 20mcg/L would suggest GHD in the newborn. An IGFBP-3 measurement is of value for the diagnosis of GHD in infancy.
      AND
   c. Thyroid function tests are within normal range based on laboratory normal values for members age NOTE: Documentation of normal thyroid function (TSH) required. If TSH level is not within normal range, TSH deficiency should be corrected. TSH levels decrease sharply during the first week of life.
      AND
   d. Other pituitary hormone deficiencies (e.g., ACTH, TSH, FSH, LH, prolactin) have been evaluated, ruled out, and/or corrected prior to time of testing
      AND
   e. Appropriate imaging (magnetic resonance imaging [MRI] or computed tomography [CT]) of the brain with particular attention to the hypothalamic pituitary region to exclude the possibility of pituitary or hypothalamic neoplasms or to identify contributing pituitary malformations has been performed

FOR ALL ADULT INDICATIONS (MEMBERS 18 YEARS OF AGE AND OLDER):

A. HIV/AIDS-ASSOCIATED WASTING AND CACHEXIA [Serostim only]:
MOLINA REVIEWER NOTE: Stimulation testing requirements not applicable for diagnosis of

HIV/AIDS- associated wasting and cachexia

1. Diagnosis of HIV/AIDs-associated wasting syndrome/cachexia, defined by ONE of the following, not attributable to other concurrent illness(es) or medical condition(s) [DOCUMENTATION REQUIRED]:
   a. Unintentional weight loss of at least 10% of baseline weight within the past 12 months
      OR
   b. BMI < 20 kg/m^2
      OR
   c. Weight less than 90% Ideal Body Weight
      OR
   d. Baseline bioelectrical impedance analysis (BIA) or total body DEXA showing body cell mass (BCM) below 40% in males and 35% in females

   AND
2. The member is currently receiving optimal antiretroviral therapy for > 30 days prior to beginning somatropin therapy and will continue antiretroviral therapy throughout the course of somatropin treatment
   AND
3. Documentation of a trial and failure, serious side effects, or contraindication to an appetite stimulant (Marinol or Megace). Failure is defined as continued weight loss despite the agent used in addition to adequate nutrition.
   AND
4. Documentation of a nutritional evaluation by a registered dietician (RD) including RD has assessed, intervened, and monitored the Member according to the American Dietetic Association (ADA) Nutrition Therapy Protocol for HIV/AIDS. [DOCUMENTATION REQUIRED]
   AND
5. Other underlying treatable conditions that may potentially cause weight loss have been ruled out, including ALL of the following:
   a. Presence of significant anxiety and/or depression affecting food intake
      AND
   b. Growth inhibiting medication, chronic disease or chronic infectious diarrhea or endocrine disorders
      AND
   c. Opportunistic infections (i.e., Mycobacterium avium, Pneumocystis carinii, esophageal candidiasis, cryptosporidiosis, microsporidiosis, Salmonella, Shigella, cytomegalovirus, tuberculosis)
      AND
   d. Other causes of wasting and cachexia, such as: hypothyroidism, chronic systemic disease, nutritional/emotional deprivation, intracranial malignancy or tumor

   AND
6. Male members only: Documentation of a normal testosterone blood levels (lab result within the past 2 months). If serum testosterone level is low, a documented trial of testosterone replacement therapy is required.
   AND
7. Documentation of the following baseline measurements:
   a. Height, weight, ideal body weight, body mass index (BMI)
      AND
   b. Body cell mass (BCM) by bioelectrical impedance analysis (BIA)
      AND
   c. Weekly weight measurements

B. TRANSITION FROM CHILDHOOD TO ADULT GROWTH HORMONE THERAPY (Continuation of Growth Hormone Therapy After Completion of Linear Growth)

1. Documentation of a diagnosis of childhood-onset GHD supported by member's clinical documentation (as a result of congenital, genetic, acquired, or idiopathic causes)
   AND
2. Documentation that member has completed linear growth as defined by growth rate less than 2.5 cm per year
   AND

3. Other pituitary hormone deficiencies have been ruled out and/or corrected prior to time of testing (e.g., ACTH, TSH, gonadotropin deficiency [LH and/or FSH counted as 1 deficiency], prolactin, or AVP deficiency)
   AND
4. Documentation that thyroid function (TSH) tests are within normal range (TSH 0.4 - 4.0 mIU/L). If TSH level is not within normal range, TSH deficiency should be corrected before performing GH stimulation tests since GH secretion may be subnormal as a result of the hypothyroidism. Documentation of normal TSH required. [DOCUMENTATION REQUIRED]
   AND
5. Member meets criteria for persistent growth hormone deficiency by meeting ONE of the following (a or b) [DOCUMENTATION REQUIRED]:
   a. GH treatment has been stopped for at least 3 months AND diagnosis of GHD has been reconfirmed as follows:
      i. Subnormal response to TWO (2) provocative GH stimulation tests (ng/mL = mcg/L):
         - ITT ≤ 5.0 mcg/L
         - Glucagon: ≤ 3 mcg/L for normal weight, ≤ 1 mcg/L for obese BMI > 30 kg/m^2
         - Macimorelin: ≤ 2.8 mcg/L
         - Arginine: ≤ 0.4 mcg/L
         - Arginine/GHRH: ≤ 4.1mcg/L OR cutoff value varies by waist circumference, BMI, and age: peak GH values ≤ 11 ng/mL if BMI <25 kg/m2; ≤ 8 ng/mL if BMI ≥ 25 and < 30 kg/m2; ≤ 4 ng/L if BMI ≥ 30 kg/m2);
         - Arginine/L- Dopa: peak GH ≤ 1.7 mcg/L
           NOTE: Clonidine is not an adequate agent for adult testing. Arginine and levodopa (L- Dopa) testing is no longer recommended. GHRH-arginine testing agent Geref has been discontinued and is no longer available for stimulation testing.

      OR

      ii. Subnormal response to 1 provocative test (similar to the stimulation tests and values above criterion) AND low IGF-1/IGFBP-3 level based on specific laboratory reference range

   OR

   b. GH treatment has been stopped for at least 1 month AND the diagnosis of GHD has been reconfirmed with the documented presence of ANY of the following conditions:
      i. Multiple Pituitary Hormone Deficiencies with a subnormal response (similar to the stimulation tests and values above criterion) to 1 provocative GH test AND/OR low IGF-1/IGFBP-3 level based on specific laboratory reference range
         OR
      ii. Panhypopituitarism: defined by at least 3 pituitary hormone deficiencies (ACTH, TSH, FSH, LH, prolactin) AND IGF-1 level below the normal range for age and gender, based on specific lab reference values (IGF-1 while not receiving GH therapy)
         OR
      iii. Member has a diagnosis of Severe GHD in childhood due to a genetic cause or structural lesion: Genetic mutations associated with deficient GH production or secretion (e.g.GH- 1 or GHRH-R); Structural hypothalamic- pituitary disease; CNS tumors; Severe GHD and the receipt of high-dose cranial radiation therapy AND IGF-1 level below the normal range for age and gender, based on specific lab reference values (IGF-1 while not receiving GH therapy)
         NOTE: Peak GH level must be adjusted if monoclonal-based assay or recombinant human GH reference preparations are used, based upon specific lab reference values.

FOR ALL OTHER ADULT INDICATIONS (MEMBERS 18 YEARS OF AGE AND OLDER):

1. Documentation that member has significant clinical symptoms related to GHD [e.g. increased body fat, increased abdominal fat mass, insulin resistance (although hyperglycemia does not usually develop), decreased lean body mass, decreased muscle mass and strength, decreased exercise capacity, impaired sense of well- being, excessive fatigue, poor sense of well-being

persist despite maximizing treatment of other hormonal disorders, mood disorders, and medical illness), decreased bone density, and cardiovascular risk factors (such as increased clotting factors, decreased cardiac function, increase LDL, decrease HDL)]
AND

2. Documentation that Thyroid function (TSH) tests are within normal range (TSH 0.4 - 4.0 mIU/L). If TSH level is not within normal range, TSH deficiency should be corrected before performing GH stimulation tests since GH secretion may be subnormal as a result of the hypothyroidism. Documentation of normal TSH required. [DOCUMENTATION REQUIRED]
AND
3. Other causes of GHD or secondary medical illnesses that affect GH have been ruled out (e.g., liver/kidney disease, chronic systemic disease, intracranial malignancy or tumor, growth- inhibiting medication(s), endocrine disorders, cranial tumors, chronic systemic disease, infections of the central nervous system, genetic syndromes, skeletal disorders, or other organic causes)
AND
4. Other pituitary hormone deficiencies have been ruled out and/or corrected prior to time of testing (e.g., ACTH, TSH, gonadotropin deficiency [LH and/or FSH counted as 1 deficiency], prolactin, or AVP deficiency)
AND
5. Member's nutritional status has been optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum
AND
6. Imaging Studies [RECOMMENDED but not required; submit if available]: MRI of the hypothalamic-pituitary area to rule out tumors, investigate for structural causes of GHD, and to evaluate the severity and prognosis of the deficiency
AND
7. ANY DIAGNOSIS/INDICATION SPECIFIC CRITERIA BELOW (C-E)

ANY DIAGNOSIS/INDICATION SPECIFIC CRITERIA BELOW (C-E):

C. PITUITARY OR HYPOTHALAMIC DISEASE [Except Panhypopituitarism, see Section E]:

1. Adult GHD is due to or the result of ONE of the following:
    i. Pituitary-hypothalamic disease (e.g., Sheehan's syndrome, autoimmune hypophysitis, or hypophysitis associated with other inflammatory conditions, such as sarcoidosis), OR
    ii. Cranial surgery, OR
    iii. Cranial radiation therapy, OR
    iv. Head trauma

    AND
2. (a) An abnormal response to 1 provocative stimulation test (ng/mL = mcg/L)
    - ITT ≤ 5.0 mcg/L
    - Glucagon: ≤ 3 mcg/L for normal weight, ≤ 1 mcg/L for obese BMI > 30 kg/m^2
    - Macimorelin: ≤ 2.8 mcg/L
    - Arginine: ≤ 0.4 mcg/L
    - Arginine/GHRH: ≤ 4.1mcg/L OR cutoff value varies by waist circumference, BMI, and age: peak GH values ≤ 11 ng/mL if BMI <25 kg/m2; ≤ 8 ng/mL if BMI ≥ 25 and < 30 kg/m2; ≤ 4 ng/L if BMI ≥ 30 kg/m2);
    - Arginine/L- Dopa: peak GH ≤ 1.7 mcg/L

      NOTE: Clonidine is not an adequate agent for adult testing. Arginine and levodopa (L-Dopa) testing is no longer recommended. GHRH-arginine testing agent Geref has been discontinued and is no longer available for stimulation testing.

    OR

    (b) EXCEPTION to GH provocation tests: NOT required for members where it would not be expected to produce a clinical response (in absence of all pituitary hormones): Surgical removal of the pituitary, OR Panhypopituitarism (criteria below)

D. PANHYPOPITUITARISM:
MOLINA REVIEWER NOTE: Growth hormone stimulation testing is not required for panhypopituitarism.

1. Documented diagnosis of panhypopituitarism defined by at least 3 pituitary hormone deficiencies (ACTH, TSH, FSH, LH, prolactin)
   AND
2. IGF-1 level below the normal range for age and gender, based on specific lab reference values (IGF-1 while not receiving growth hormone therapy) NOTE: Peak GH level must be adjusted if monoclonal-based assay or recombinant human GH reference preparations are used, based upon specific lab reference values.

E. IDIOPATHIC GHD:

1. Documentation of an abnormal response to 2 provocative stimulation tests (ng/mL = mcg/L) [DOCUMENTATION REQUIRED]:
   NOTE: EXCEPTION to GH provocation tests: NOT required for members where it would not be expected to produce a clinical response (in absence of all pituitary hormones): Surgical removal of the pituitary, OR Panhypopituitarism [See section E above]
   - ITT ≤ 5.0 mcg/L
   - Glucagon: ≤ 3 mcg/L for normal weight, ≤ 1 mcg/L for obese BMI > 30 kg/m^2
   - Macimorelin: ≤ 2.8 mcg/L
   - Arginine: ≤ 0.4 mcg/L
   - Arginine/GHRH: ≤ 4.1mcg/L OR cutoff value varies by waist circumference, BMI, and age: peak GH values ≤ 11 ng/mL if BMI <25 kg/m2; ≤ 8 ng/mL if BMI ≥ 25 and < 30 kg/m2; ≤ 4 ng/L if BMI ≥ 30 kg/m2);
   - Arginine/L- Dopa: peak GH ≤ 1.7 mcg/L
     NOTE: Clonidine is not an adequate agent for adult testing. Arginine and levodopa (L-Dopa) testing is no longer recommended. GHRH-arginine testing agent Geref has been discontinued and is no longer available for stimulation testing.

   OR
2. For members with a low IGF-1 (a marker of GH response) concentrations (SDS less than -2): Documentation of a failure to respond to only 1 standard GH stimulation test [DOCUMENTATION REQUIRED].

CONTINUATION OF THERAPY:

A. PEDIATRIC INDICATIONS: Pediatric GHD (including previous diagnosis of neonatal hypoglycemia due to GHD), Chronic Renal Insufficiency/Chronic Kidney Disease, Small for Gestational Age, Turner syndrome, Prader-Willi syndrome, Short Stature Homeobox-Containing Gene deficiency

1. Member is 18 years of age or younger
   AND
2. Compliance with GH therapy as verified by Prescriber and member's medication fill history
   AND
3. FOR MEMBERS 12 YEARS AND AGE AND OLDER ONLY: Documentation of open epiphyses confirmed by bone age X-ray (taken within 6 months of request and obtained at least annually) of the left hand and wrist showing one of the following:
   a. Males: not to exceed 16 0/12 years of age
   b. Females: not to exceed 14 0/12 years of age

   NOTE: For CLOSED EPIPHYSES review per initial criteria section TRANSITION FROM CHILDHOOD TO ADULT GROWTH HORMONE THERAPY (Continuation of Growth Hormone Therapy After Completion of Linear Growth)
   AND
4. Documentation expected adult height has NOT been reached defined as 5th percentile for adults (65 inches for men and 60 inches for women) or 50th percentile for height based on age calculated using mid-parental height
   NOTE: If expected adult height has been reached, review per initial criteria section TRANSITION FROM CHILDHOOD TO ADULT GROWTH HORMONE THERAPY (Continuation of Growth Hormone Therapy After Completion of Linear Growth)
   AND
5. Documented positive response to therapy as evidenced by ONE of the following:
   a. First year of therapy: A doubling of pre-treatment growth, OR Growth velocity while on

therapy is ≥ 2.5cm/year
   b. After the first year of therapy: Growth velocity remains above 2.5 cm/year (Not applicable to children with prior documented hypopituitarism)
   c. For PWS only: Body composition: Increase in lean body mass and decreases in fat mass. Documentation required.
   d. For previous diagnosis of Neonatal Hypoglycemia due to GH deficiency only: Member has had resolution of persistent hypoglycemia and provider attestation that member is attaining expected growth (no evidence of failure to thrive).

AND

6. Thyroid function (TSH) tests are within normal range for member's age
   AND
7. Member's nutritional status has been re-evaluated and optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum, if applicable
   AND
8. Provider attests to (or the clinical reviewer has found that) the member has no contraindication to continued growth hormone therapy: Hypersensitivity to somatropin or any component of the formulation; Progression or recurrence of any underlying intracranial lesion or actively growing intracranial tumor; Acute critical illness caused by complications following open-heart or abdominal surgery, multiple accidental trauma, or acute respiratory failure; Active malignancy; Active proliferative or severe non- proliferative diabetic retinopathy

B. ADULT HIV-ASSOCIATED WASTING AND CACHEXIA:

1. Documentation members who received a 3-month (12-week) course for HIV/AIDs-associated wasting syndrome/cachexia must have been off somatropin for at least ONE month
   AND
2. Diagnosis of HIV/AIDs-associated wasting syndrome/cachexia continues to be met [defined as: a) Unintentional weight loss of at least 10% of baseline weight within the past 12 months; b) BMI < 20 kg/m2, not attributable to other concurrent illness(es) or medical condition(s); c) Weighs less than 90% Ideal Body Weight, OR d) Baseline bioelectrical impedance analysis (BIA) or total body DEXA showing body cell mass (BCM) below 40% in males and 35% in females]
   AND
3. Documentation of positive clinical response to therapy in ONE of the following baseline measures:
   a. Body mass index (BMI)
      OR
   b. Body cell mass (BCM) by bioelectrical impedance analysis (BIA)
      OR
   c. For members who experienced weight loss after the initial four weeks of therapy ONLY: Continuation of treatment will be considered after re-evaluation and documentation of ALL of the following: a) Intervention of a clinical event (e.g., opportunistic infection) and resolution/treatment of this clinical event, AND b) Current clinical status, AND c) Measured BMI and BCM

C. NOONAN SYNDROME (NS):

1. Compliance with GH therapy is verified by Prescriber and member's medication fill history
   AND
2. Documentation expected adult height has not been reached based on NS growth chart
   AND
3. Documentation of open epiphyses confirmed by bone age X-ray of the left hand within 6 months of request and at least once annually.
   NOTE: Some Noonan Syndrome patients will continue to grow into their late teens/twenties because of late puberty. As bone maturity is usually delayed, prolonged growth into the 20s is possible (DYSCERNE— Noonan Syndrome Guideline Development Group, 2011; NIH, 2022)
   AND
4. Documentation of continued positive response to therapy as evidenced by growth velocity ≥ 2.5 cm/year

AND

5. Thyroid function tests are within normal range for member's age
AND
6. Provider attests to (or the clinical reviewer has found that) the member has no contraindication to continued growth hormone therapy: Hypersensitivity to somatropin or any component of the formulation; Progression or recurrence of any underlying intracranial lesion or actively growing intracranial tumor; Acute critical illness caused by complications following open-heart or abdominal surgery, multiple accidental trauma or acute respiratory failure; Active malignancy; Active proliferative or severe non- proliferative diabetic retinopathy

D. ADULT GROWTH HORMONE DEFICIENCY INDICATIONS:

NOTE: For initial transition from childhood to adult growth hormone therapy following completion of linear growth, see adult initial criteria.

1. Member is 18 years years of age or older OR is an adolescent whose epiphyses have closed
AND
2. Compliance with GH therapy as verified by Prescriber and member's medication fill history
AND
3. Thyroid function tests are within normal range (TSH 0.4 - 4.0 mIU/L)
AND
4. Nutritional status has been optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum
AND
5. Documentation of IGF-1 within the normal range for age and gender based on specific lab reference values. (If above normal, dose reduction required)
NOTE: For continuation, yearly reassessment of serum levels of IGF-I is required with appropriate dosage adjustments as GH requirements in adults will decrease with age
AND
6. Documentation of continual clinical benefit from growth hormone therapy (e.g., improvements in cardiovascular risk markers, improvement in body composition; weight loss; body mineral density; increase bone mass; Improvement on lipid profile; serum cholesterol; Increase in physical or muscle strength; Improvement in 'Quality of Life Assessment of Growth Hormone Deficiency in Adults' (QoL-AGHDA) score)
AND
7. Provider attests to (or the clinical reviewer has found that) the member has no contraindication to continued growth hormone therapy: Hypersensitivity to somatropin or any component of the formulation; Progression or recurrence of any underlying intracranial lesion or actively growing intracranial tumor; Acute critical illness caused by complications following open-heart or abdominal surgery, multiple accidental trauma or acute respiratory failure; Active malignancy; Active proliferative or severe non-proliferative diabetic retinopathy

DURATION OF APPROVAL:

HIV/AIDS-ASSOCIATED WASTING AND CACHEXIA: Initial authorization 12 weeks
Continuation of Therapy or Repeat Courses: May be authorized for an additional 12 weeks
Duration of therapy: 48 weeks of active treatment [Four 12-week authorizations] (No additional authorizations after 48 weeks of therapy. Therapy duration is for active treatment and not inclusive of one month break from therapy.)

ALL OTHER INDICATIONS: Initial authorization: 6 months, Continuation of therapy: 12 months, OR for pediatric indications: until maximum bone age is met, whichever is shorter (In males up to 16 0/12 years of age; In females, up to 14 0/12 years of age)

PRESCRIBER REQUIREMENTS:

Prescribed by a specialist based on the condition treated: pediatric endocrinologist or pediatric nephrologist (for pediatric diagnoses), endocrinologist (for adult diagnoses) or infectious disease specialist (for AIDs only) or neonatologist (for neonatal hypoglycemia only)

AGE RESTRICTIONS:
Under 18 years of age: 'Pediatric' criteria
18 years of age and older or closed epiphysis: 'Adult' criteria

QUANTITY:
30-day supply per fill based on FDA-approved dosage for indication

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Growth Hormones

FDA-APPROVED USES:
PEDIATRIC
Treatment of children with growth failure due to: Growth Hormone Deficiency (GHD), Idiopathic Short Stature (ISS), Chronic Renal Insufficiency/Chronic Kidney Disease (CRI/CKD) up until the time of renal transplantation, Small for Gestational Age (SGA), Turner Syndrome (TS), Noonan Syndrome (NS), Prader-Willi syndrome (PWS), Short Stature Homeobox-Containing Gene (SHOX) Deficiency

Ngenla (somatrogon-ghla) is a human growth hormone analog indicated for treatment of pediatric patients aged 3 years and older who have growth failure due to inadequate secretion of endogenous growth hormone.

Skytrofa (lonapegsomatropin-tcgd) is indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).

ADULTS
Treatment of adults with either adult-onset or childhood-onset GHD, Growth hormone deficiency due to hypothalamic or pituitary condition, Child onset growth hormone deficiency continuing into adulthood, HIV Wasting

Sogroya (somapacitan-beco) is a human growth hormone analog indicated for treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH) and replacement of endogenous growth hormone in adults with growth hormone deficiency.

Skytrofa (lonapegsomatropin-tcgd) is indicated for replacement of endogenous growth hormone in adults with growth hormone deficiency (GHD).

COMPENDIAL APPROVED OFF-LABELED USES:
Neonatal Hypoglycemia related to GH Deficiency

APPENDIX

APPENDIX:

DEFINITIONS:

Mid-parental height = (father's height + mother's height) divided by 2, plus 2.5 inches (male) or minus 2.5 inches (female)

Growth Hormone (GH) Provocative Stimulation Test: A provocative agent is used to stimulate the pituitary gland to secrete GH. The intent is to determine the maximum peak GH response from the provocative agent. This peak is the value used to determine whether the response is considered normal or abnormal for the purpose of supporting the diagnosis of GHD. Serum levels may be measured by radioimmunoassay (RIA) or immunoradiometric assay (IRMA). Baseline testing is performed prior to administration of the provocative agent and frequent blood sampling is done thereafter. Sampling occurs approximately 30, 60, 90, 120 and 180 minutes after provocative agent administration. Sampling defines the “curve” of the response (going from a lower GH value prior to provocation to the highest, or peak, GH value after provocation and then a drop from peak) and must provide sufficient information to determine a peak value. Normal Results of a GH Stimulation Test: Normal peak value: at least 10 ng/ml; Indeterminate: 5 to 10 ng/ml; Subnormal: 5 ng/ml

Insulin-Like Growth Factor 1 (IGF-1): A hormone created mainly by the liver that mediates most of the effects of growth hormone. IGF-1 blood tests may be used in the diagnosis of growth hormone deficiency.

HIV/AIDS-associated wasting and cachexia: Unintentional and progressive weight loss (cachexia) often accompanied by weakness, fever, nutritional deficiencies and diarrhea. The wasting can be caused by opportunistic infections that interfere with the gut’s ability to absorb nutrients, altered metabolism of nutrients or by inadequate food intake due to nausea and vomiting. The syndrome reduces the quality of life, exacerbates the illness and increases the risk of death for people with HIV. The goal of therapy is to increase the person’s body weight and promote an increase in lean body mass(muscle). Short Bowel Syndrome (SBS) is a result of extensive surgical resection of the bowel resulting in various degrees of malabsorption depending on the area and site of resection and persistence of damage to the remaining bowel.

GF-1 Ranges (ng/mL)

Reference Interval (ng/mL)

AGE	MALE	FEMALE	AGE	MALE	FEMALE
0.25	12 -94.1	13.8-86.4	40	98.5-229	91.4-227
0.5	11.8-94.6	15.4-92	41	96.4-226	89.8-225
1	11.8-96.4	18.7-104	42	94.4-223	88.1-224
2	13.9-104	26.1-128	43	92.4-221	86.5-222
3	18.9-116	34.2-155	44	90.5-218	84.9-221
4	26.8-134	43.2-185	45	88.5-216	83.3-220
5	36.6-156	53-216	46	86.5-214	81.8-219
6	47.1-184	63.6-250	47	84.6-211	80.2-218
7	57.5-216	75-286	48	82.6-209	78.7-218
8	67.5-254	87.3-324	49	80.6-207	77.2-217
9	76.9-296	99.9-363	50	78.7-205	75.7-215
10	85.9-343	112-398	51	76.7-203	74.3-214
11	93.9-392	123-427	52	74.8-201	72.8-212
12	101-434	132-451	53	72.8-200	71.4-210
13	108-467	140-468	54	70.9-198	70-207
14	115-489	146-480	55	68.9-196	68.6-204
15	120-501	151-485	56	67-195	67.3-201
16	125-503	154-485	57	65.3-194	65.9-198
17	129-495	156-479	58	63.7-193	64.6-194
18	132-476	156-466	59	62.3-192	63.3-190
19	134-450	155-449	60	61.1-191	62-186
20	136-421	152-429	61	60-190	60.7-182
21	137-394	148-410	62	59.2-189	59.5-179
22	137-370	143-392	63	58.5-188	58.3-176
23	136-348	138-375	64	57.9-188	57.3-173
24	135-328	134-359	65	57.4-187	56.3-170
25	132-310	130-343	66	56.8-186	55.5-168
26	130-295	126-329	67	56.3-186	54.8-166
27	128-282	122-315	68	55.8-185	54.2-164
28	125-271	118-303	69	55.2-185	53.8-163
29	123-263	115-292	70	54.7-185	53.5-162
30	120-257	112-280	71	54.1-184	53.3-161
31	118-253	109-271	72	53.6-184	53.2-160
32	116-250	107-263	73	53-184	53.2-160
33	114-247	104-255	74	52.4-184	53.3-160
34	111-244	102-248	75	51.9-184	53.5-160
35	109-242	100-242	76	51.3-184	53.7-161
36	107-239	98.3-238	77	50.7-184	54-162
37	105-236	96.5-234	78	50.2-184	54.3-163
38	103-234	94.8-231	79	49.6-184	54.7-164
39	101-231	93.1-228	80		55.1-166

Insulin-like growth factor I (IGF-1) serum/plasma concentrations are age- and sex-dependent and should be interpreted in conjunction with the appropriate reference range. In addition to the IGF-1 concentration and corresponding reference range, Z scores are provided for all results for patients younger than 80 years old. A Z score is the number of standard deviations a given result is above (positive score) or below (negative score) the age- and sex-adjusted population mean. Results that are within the IGF-1 reference interval will have a Z score between -2.0 and +2.0. Z scores are calculated using the IGF-1 concentration and parameters provided by the assay manufacturer.

IGF-1 concentrations can be used to assess growth hormone (GH) deficiency or excess. Serum IGF- 1 concentrations below the 2.5th percentile (Z-score < -2) are consistent with GH deficiency or severe GH resistance. Definitive diagnosis of GH deficiency or resistance may require additional diagnostic testing such as GH stimulation tests. The aim of GH replacement therapy in children and adults with GH deficiency is to achieve IGF-1 concentrations within the age- and sex-appropriate reference range, ideally the middle-to-upper third of that range.
Elevated IGF-1 concentrations help support diagnosis of acromegaly in conjunction with compatible clinical signs and symptoms. Additional diagnostic tests and imaging studies may aid in diagnosis.

Persons with anorexia or malnutrition often have low IGF-1 concentrations.

Reference ranges in pregnancy have not been formally established. IGF-1 concentrations increase approximately 2-fold during normal uterine pregnancy compared to pre-pregnancy baseline.

Note: Both patient age and sex are required for Z score calculation

Insulin Like Growth Factor Binding Protein III (IGFBP-3)

Age	Male	Female
0-12 months	1039-3169 ng/mL	1039-3169 ng/mL
1-3 years	972-4123 ng/mL	1590-4225 ng/mL
4-5 years	1843-4968 ng/mL	2169-4790 ng/mL
6-7 years	1838-4968 ng/mL	2188-4996 ng/mL
8-9 years	1932-5858 ng/mL	2072-5504 ng/mL
10-11 years	1828-6592 ng/mL	2456-6992 ng/mL
12-13 years	2134-6598 ng/mL	2838-6846 ng/mL
14-15 years	2330-6550 ng/mL	2654-6680 ng/mL
16-17 years	2380-6400 ng/mL	2756-6908 ng/mL
18-19 years	2340-6632 ng/mL	2700-6492 ng/mL
20-24 years	2404-5948 ng/mL	3032-5992 ng/mL
25-29 years	2614-5792 ng/mL	2926-5858 ng/mL
30-34 years	2500-5806 ng/mL	2878-6650 ng/mL
35-39 years	2474-5208 ng/mL	2786-6084 ng/mL
40-44 years	2360-5560 ng/mL	2514-6014 ng/mL
45-49 years	2314-5700 ng/mL	2838-4954 ng/mL
50-54 years	2528-5050 ng/mL	2562-5596 ng/mL
55-59 years	2482-5460 ng/mL	2574-5914 ng/mL
60-64 years	2592-4770 ng/mL	2684-5130 ng/mL
65 years and older	2698-5688 ng/mL	2462-5274 ng/mL
Tanner Stage I	1878-6190 ng/mL	2314-6086 ng/mL
Tanner Stage II	2112-6208 ng/mL	2732-6738 ng/mL
Tanner Stage III	2372-6602 ng/mL	2870-7068 ng/mL
Tanner Stage IV & V	2336-6414 ng/mL	2756-7232 ng/mL

ABBREVIATIONS:
Adrenocorticotropin hormone (ACTH)
Thyroid stimulating hormone (TSH)
Luteinizing hormone (LH)
Follicle stimulating hormone (FSH)

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Molina Healthcare authorize GH therapy if there is a significant physical functional impairment and treatment with GH treatment can be reasonably expected to improve the physical functional impairment of the member as a result of an illness, disease or injury.
Growth hormone treatment is not authorized for treatment of short stature in the absence of a growth hormone deficiency or for the majority of other conditions in which growth hormone has not been shown to provide clinical benefits or improvements in functional impairment or long-term health outcomes.

Patients with childhood-onset growth hormone deficiency (GHD) who are appropriate candidates for GH therapy should be re-tested for GHD as adults unless they have known mutations, embryopathic lesions, or irreversible structural lesions/damage (level of evidence, high).
Growth Hormone Deficiency (GHD) is the inadequate secretion of endogenous growth hormone. GHD may be idiopathic or organic and may occur in childhood or adulthood. Pathophysiology differs between childhood or adulthood onsets. GHD is diagnosed through a combination of clinical and biochemical examination, testing and analysis.
Generally, results from conditions affecting the hypothalamus or pituitary gland including surgery and radiation therapy. Adults frequently report symptoms such as unintentional weight gain or difficult losing weight, low energy, reduced physical performance, decreased libido, impaired psychological well-being and a feeling that things are not right. Physical findings may include increased fat mass, decreased lean body and muscle mass, decreased bone density as well as reduced muscle strength and exercise capacity. There is however no single symptom or sign that is pathognomonic for GHD in adults. In addition, some adults with GHD may be entirely asymptomatic.
Recombinant human growth hormone (rhGH, somatotropin) is used as replacement therapy in adults with endogenous growth hormone deficiency (GHD), such as those with idiopathic or acquired GHD. Human growth hormone (hGH, somatotropin) is secreted by the anterior pituitary. Most of its anabolic effects are mediated by insulin-like growth factor-I (IGF-I, somatomedin C), which is synthesized in the liver and other tissues in response to growth hormone stimulation. Growth hormone stimulates linear growth in children and influences metabolism of carbohydrates, fats, minerals, and proteins. Somatropin is produced by recombinant DNA technology and has the same amino acid sequence as naturally occurring hGH (a single polypeptide chain of 191 amino acids). The goal of GH replacement in adults is to minimize the symptoms of GHD (e.g., fatigue, poor endurance, and poor sense of well-being), improve the quality of life, and achieve serum insulin–like growth factor (IGF-1) concentration in the normal range for age and sex. The major endpoints of treatment are to improve blood lipid levels, improve the patient's waist-to-hip ratio, improve body composition, improve quality of life, and reduce cardiovascular risk factors.

A stimulation test is needed to confirm the diagnosis of GHD in adults. Numerous tests are available. (AACE 2009) There is a lack of universal agreement on cutoff points for GH levels. Most experts suggest a peak value of less than 5 nanograms per milliliter (ng/ml) after stimulation as an indication of GHD. Regardless of the stimulation test and GH assay used, 5 ng/ml is the suggested cutoff point for all provocative tests.
Stimulation tests used to diagnose growth hormone deficiency in adults include insulin tolerance (ITT), arginine, growth hormone releasing hormone (GHRH), and glucagon.
The ITT is currently considered the gold standard of the tests available and is the preferred stimulation test agent. ITT is contraindicated in patients with cardiovascular disease, cerebrovascular disease, or seizure disorders, or in patients older than 65 years.
A provocation test using arginine and GHRH (ARG + GHRH) is also acceptable and is considered more stringent than tests using arginine alone or levodopa alone. In patients where the ITT is not desirable and when recombinant GHRH is not available, the glucagon test is a reliable alternative, but not the levodopa and clonidine tests.
Twenty-four-hour continuous measurements of GH, serum levels of IGF-I, or serum of levels IGFBP [insulin-like growth factor-binding protein] are considered inadequate to document GHD. AACE (2009) does not

recommend GH stimulation testing in patients with three or more pituitary hormone deficiencies and low IGF1.
Transition from Childhood to Adult Growth Hormone Therapy (Continuation of Therapy after Completion of Linear Growth):
The transition period is the period from late puberty to establishment of adult muscle and bone composition and encompasses attainment of adult height. As attainment of adult or near-adult height is an easily measurable variable, re-evaluation of the somatotropic axis is most conveniently performed when growth has slowed to the point when pediatric GH dosing will be discontinued.

Since all children with GHD will not require continued treatment into adulthood, the transition period is significant. The transition period can be defined as beginning in late puberty the time when near adult height has been attained and ending with full adult maturation (6-7 years after achievement of adult height).
During this period ongoing growth hormone therapy may be necessary to attain somatic maturation, normal intermediary metabolism, and appropriate quality of life. Once adult height has
been achieved, subjects should be retested for GH deficiency to determine if continuing replacement therapy is necessary. The level of GH considered normal for an adult is m Much lower than that for a child, especially one undergoing the pubertal growth spurt.
The American Association of Clinical Endocrinologists published guidelines in 2009 that stressed the need for and use of GH for continued treatment of persistently GH-deficient transition and adult patients. The metabolic improvements and long-term benefit with continuation of GH treatment in GH- deficient adolescents transitioning to adulthood remains uncertain.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of human growth hormone analog are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications include: acute critical illness, active malignancy, hypersensitivity, active proliferative or severe non- proliferative diabetic retinopathy, pediatric members with closed epiphysis, and for pediatric members with Prader-Willi syndrome: severe obesity, history of severe upper airway obstruction, severe respiratory impairment.

Exclusions/Discontinuation:

For pediatric indications associated with growth failure:

1. Epiphyseal closure (Bone age≥ 16 years (male), or ≥ 14 years (female) is reached); or
2. Attained any of the following height goals (at any age):
    a) 5th percentile for adults (65 inches for men and 60 inches for women)
    b) 50th percentile for height based on age
    c) Expected adult height has not been reached [Mid-parental height = (father's height + mother's height) divided by 2, plus 2.5 inches (male) or minus 2.5 inches (female)]
3. Poor response to treatment, generally defined as an increase in growth velocity of less than 50% from baseline, in the 1st year of therapy; or
4. Prader-Willi syndrome: Evaluation of response to therapy should also take into account whether body composition (i.e., ratio of lean-to fat mass) has significantly improved; or
5. Increase in height velocity is less than 2.5 cm total growth in 1 year of therapy; or
6. Persistent and uncorrectable problems with adherence to treatment; or
7. Adverse reactions or side effects

For CRI/CKD: Renal transplantation. GH therapy must be discontinued at the time of renal transplantation.
Short stature in the absence of a GH deficiency or for the majority of other conditions in which GH has not been shown to provide clinical benefits or improvements in functional impairment or long- term health outcomes.
For patients with a history of malignancy, anti-malignancy treatment should be completed and the patient in complete remission for at least 12 months free of recurrence. Active malignancy is a contraindication.
Do not use concurrently with Increlex (mecasermin).

OTHER SPECIAL CONSIDERATIONS:

Equivalence of Products

GH products are equally safe and effective, although they differ in how the medication is prepared and injected. No clinical trials have been conducted to evaluate the comparative efficacy or safety of available synthetic growth hormone products.

There is a lack of reliable evidence that any one brand of GH is superior to other brands for medically necessary indications.

Omnitrope brand of growth hormone is the preferred brand of growth hormone for Molina Healthcare. Other brands (e.g., Genotropin, Humatrope, Norditropin, Nutropin AQ, etc.) of growth hormone are highly expected to produce equivalent therapeutic results for the treatment of the member's disease. Other brands of growth hormone will be considered NON-PREFERRED and not authorized unless the member has a documented contraindication or serious side effect to the preferred brand of growth hormone (Omnitrope). If the preferred brand (Omnitrope) does not have the labeled indication for member's diagnosis, this is acknowledged.

PREFERRED AGENT: Omnitrope vial: Medicaid and Marketplace; Omnitrope pen: Marketplace

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:

Genotropin CART 12MG
Genotropin CART 5MG
Genotropin MiniQuick PRSY 0.2MG
Genotropin MiniQuick PRSY 0.4MG
Genotropin MiniQuick PRSY 0.6MG
Genotropin MiniQuick PRSY 0.8MG
Genotropin MiniQuick PRSY 1.2MG
Genotropin MiniQuick PRSY 1.4MG
Genotropin MiniQuick PRSY 1.6MG
Genotropin MiniQuick PRSY 1.8MG
Genotropin MiniQuick PRSY 1MG
Genotropin MiniQuick PRSY 2MG
Humatrope CART 12MG
Humatrope CART 24MG
Humatrope CART 6MG
Ngenla SOPN 24MG/1.2ML
Ngenla SOPN 60MG/1.2ML
Norditropin FlexPro SOPN 10MG/1.5ML
Norditropin FlexPro SOPN 15MG/1.5ML
Norditropin FlexPro SOPN 30MG/3ML
Norditropin FlexPro SOPN 5MG/1.5ML
Nutropin AQ NuSpin 10 SOPN 10MG/2ML

Nutropin AQ NuSpin 20 SOPN 20MG/2ML
Nutropin AQ NuSpin 5 SOPN 5MG/2ML
Omnitrope SOCT 10MG/1.5ML
Omnitrope SOCT 5MG/1.5ML
Omnitrope SOLR 5.8MG
Saizen SOLR 5MG
Saizen SOLR 8.8MG
Saizenprep SOLR 8.8MG
Serostim SOLR 4MG
Serostim SOLR 5MG
Serostim SOLR 6MG
Skytrofa CART 0.7MG
Skytrofa CART 1.4MG
Skytrofa CART 1.8MG
Skytrofa CART 2.1MG
Skytrofa CART 2.5MG
Skytrofa CART 3.6MG
Skytrofa CART 3MG
Skytrofa CART 4.3MG
Skytrofa CART 5.2MG
Skytrofa CART 6.3MG
Skytrofa CART 7.6MG
Skytrofa CART 9.1MG
Skytrofa CART 11MG
Skytrofa CART 13.3MG
Sogroya SOPN 5MG/1.5ML
Sogroya SOPN 10MG/1.5ML
Sogroya SOPN 15MG/1.5ML
Zomacton (for Zoma-Jet 10) SOLR 10MG
Zomacton SOLR 10MG
Zomacton SOLR 5MG

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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information FDA-Approved Uses	Q4 2025

REVISION- Notable revisions: Diagnosis Required Medical Information Other Special Considerations Available Dosage Forms References	Q3 2025
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements FDA-Approved Uses Contraindications/Exclusions/Discontinuation References	Q3 2024
REVISION- Notable revisions: Required Medical Information	Q4 2023
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy FDA-Approved Uses Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file