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 Policy Number: C22969-A

Growth Hormone (hGH, somatropin) Therapy - IL Medicaid Only

PRODUCTS AFFECTED

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

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

Genotropin brand of growth hormone (GH) is the PREFERRED brand of GH for Illinois Medicaid. Other brands of GH are NON-PREFERRED and not authorized unless the member has a documented contraindication or intolerance to PREFERRED brand of GH, Genotropin.

Drug and Biologic Coverage Criteria

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.

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 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-PREFERRED PRODUCT:
 - a) Member meets all criteria specific for diagnosis/indication
AND
 - b) Documentation of a failure or inadequate response to the PREFERRED product(s) either through previous claims history or by member's medical records OR Member's diagnosis is not an FDA-labeled indication for the PREFERRED product(s) OR previous hypersensitivity/allergy, clinical intolerance or labeled contraindication to the PREFERRED product(s). [DOCUMENTATION REQUIRED]
NOTE: Documented sensitivity to benzyl alcohol (a preservative in Omnitrope 5 Pen and Omnitrope 5.8mg/vial) and to phenol (a preservative in Omnitrope 10 Pen). Genotropin or Humatrope contains 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 contains benzyl alcohol as a preservative is contraindicated in children under the age of three. Omnitrope 10 should be used in children under the age of 3 as it does not contain benzyl alcohol.
AND
 - c) FOR SKYTROFA OR NGENLA REQUESTS: i) Member is less than or equal to 18 years of age [Skytrofa (lonapegsomatropin-tcgd) and Ngenla (somatrogon) are 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.

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

A. PEDIATRIC GROWTH HORMONE DEFICIENCY (GHD) (18 years of age or younger)

1. Documentation of diagnosis confirmed by [Documentation required]:
 - a. 2 provocative stimulation tests producing peak growth hormone concentrations <10 ng/mL (e.g., L-dopa, clonidine, glucagon, propranolol, arginine, or insulin) AND IGF-1 andIGFBP-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,

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etc., history of irradiation or genetic conditions associated with GHD

**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 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 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 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: 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 1 of the following: 2 heights measured by an endocrinologist at least 6 months apart (> 1 year), OR 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: growth velocity of 2 SDS (or 3rd percentile) below the mean for age and gender as measured over 1 year (or 3rd percentile for chronological 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: Comparison of bone age to chronological age should be 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. Documentation of an open epiphyses confirmed by bone age X-ray of the left hand and wrist (12 years of age and older only). Males: not to exceed 16 0/12 years of age; Females: not to exceed 14 0/12 years of age. X- ray must be taken within 6 months of request.

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.

AND

- 5. Prescriber attestation that 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, infections of the central nervous system, geneticsyndromes, skeletal disorders, or other organic causes]

AND

- 6. Prescriber attestation that 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

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7. Prescriber attestation that nutritional status has been optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum
AND
8. For members with a history of malignancy: Documentation that anti-malignancy treatment has been completed AND evidence of complete remission for at least 12 months free of recurrence
AND
9. Prescriber attests (or medical records support) that requested agent is not prescribed concurrently with Increlex (mecasermin)

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]: NOTE TO REVIEWER: GH Provocative Stimulation Test: NOT required**

1. Diagnosis of CRI/CKD with creatinine clearance less than or equal to 75 mL/min per 1.73m² or serum creatinine greater than 3.0 mg/dl, or dialysis dependent
AND
2. Documentation that member has not received a renal transplantation (GH is not approved post-transplant; and 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
3. Prescriber attestation that nutritional status has been optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum
AND
4. Prescriber attestation that thyroid function (TSH) tests are within normal range for member's age.
AND
5. Documentation of an open epiphyses confirmed by bone age X-ray of the left hand and wrist (12 years of age and older only). Males: not to exceed 16 0/12 years of age; Females: not to exceed 14 0/12years of age. X- ray must be taken within 6 months of request.
AND
6. For members with a history of malignancy: Documentation that anti-malignancy treatment has been completed AND evidence of complete remission for at least 12 months free of recurrence
AND
7. Prescriber attests (or medical records support) that requested agent is not prescribed concurrently with Increlex (mecasermin)

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

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Drug and Biologic Coverage Criteria

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. Pre-pubertal [who meets ALL applicable criteria]: Authorization may be recommended for an initial 12-month trial basis. If growth increases by 3 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. 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, defined as 1 of the following: Birth weight of less than 2,500 g at a gestational age of more than 37 weeks, OR 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

E. TURNER SYNDROME (TS):

NOTE TO REVIEWER: GH Provocative Stimulation Test: NOT required

1. 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,XX, del(p22.3); 46,X,r(X)/46,XX] [DOCUMENTATION REQUIRED]
AND
2. Prescriber attestation that thyroid function (TSH) tests are within normal range for member's age.

F. NOONAN SYNDROME (NS) (18 years of age or younger)

NOTE TO REVIEWER: GH Provocative Stimulation Test: NOT required

1. 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; pectum excavatum or pectus carinatum; presence of a critical congenital heart disease] [DOCUMENTATION REQUIRED]
AND
2. Prescriber attests that the member does not have a significant cardiac disease and that the benefit of treatment outweighs the member's risk
AND
3. Prescriber attestation that thyroid function (TSH) tests are within normal range for member's age.

G. PRADER-WILLI SYNDROME (PWS):

NOTE TO REVIEWER: GH Provocative Stimulation Test: NOT required

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

H. SHORT STATURE HOMEBOX-CONTAINING GENE (SHOX) DEFICIENCY [Humatrope, Zomacton ONLY]:

NOTE TO REVIEWER:GH Provocative Stimulation Test: NOT required for SHOX deficiency

1. Diagnosis of pediatric growth failure with SHOX gene deficiency as confirmed by molecular or genetic testing. Documentation of lab result confirming SHOX mutation is required. [DOCUMENTATION REQUIRED]
2. Prescriber attestation that thyroid function (TSH) tests are within normal range for member's age

I. NEONATAL HYPOGLYCEMIA RELATED TO GH DEFICIENCY:

1. 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 disorder 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. Imaging: 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

FOR ALL ADULT INDICATIONS (MEMBERS 18 YEARS OF AGE OR GREATER):

A. SHORT BOWEL SYNDROME (SBS) [Zorbtive Only]:

NOTE TO REVIEWER: Stimulation testing requirements not applicable for diagnosis of SBS. Zorbtive may only be authorized for one 4-week course. GH treatment of SBS for more than 4 weeks will NOT be authorized since administration of GH for more than 4 weeks duration has not been adequately studied for SBS.

1. Prescriber attests that member has not previously received 4 weeks of treatment with growth hormone
AND
2. Documentation of diagnosis of short bowel syndrome (SBS) by a gastroenterologist
AND
3. Documentation that member is receiving specialized nutritional support (e.g. enteral feedings, fluids, micronutrient supplements) AND dependent on intravenous parenteral nutrition (IPN) for nutritional support

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AND

4. Prescriber attestation that member does not have active malignancy, an acute critical illness, active proliferative or severe non-proliferative diabetic retinopathy.

B. HIV/AIDS-ASSOCIATED WASTING AND CACHEXIA [Serostim only]:

NOTE TO REVIEWER: 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 (1) of the following, not attributable to other concurrent illness(es) or medical condition(s)
[DOCUMENTATION REQUIRED]:
 - i. Unintentional weight loss of at least 10% of baseline weight within the past 12 months
OR
 - ii. BMI < 20 kg/m², not attributable to other concurrent illness(es) or medical condition(s)
OR
 - iii. Weighs less than 90% Ideal Body Weight
OR
 - iv. Baseline bioelectrical impedance analysis (BIA) or total body DEXA showing body cell mass (BCM) below 40% in males and 35% in females
2. Prescriber attestation that 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, intolerance, 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): 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. Prescriber attests that other underlying treatable conditions that may potentially cause weight loss to have been ruled out, including ALL of the following:
 - i. Presence of significant anxiety and/or depression affecting food intake,
AND
 - ii. Growth inhibiting medication, chronic disease or chronic infectious diarrhea or endocrine disorders
AND
 - iii. Opportunistic infections (i.e. Mycobacterium avium, Pneumocystis carinii, esophageal candidiasis, cryptosporidiosis, microsporidiosis, Salmonella, Shigella, cytomegalovirus, tuberculosis)
AND
 - iv. Evidence of other causes of wasting and cachexia have been ruled out, such as: hypothyroidism, chronic systemic disease, nutritional/emotional deprivation, intracranial malignancy or tumor, growth-inhibiting medication(s), and endocrine disorders,
AND
6. Prescriber attestation that member does not have active malignancy, either newly diagnosed or recurrent. Any preexisting malignancy treatment must be completed with evidence of remission for at least the past 12 months. Member should be free of recurrence prior to initiating GH therapy.
AND
7. Prescriber attestation that member does not have an acute critical illness, active proliferative or severe non-proliferative diabetic neuropathy.
AND
8. 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.

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AND

9. Documentation of the following baseline measurements:
 - i. Height, weight, ideal body weight, body mass index (BMI)
AND
 - ii. Body cell mass (BCM) by bioelectrical impedance analysis (BIA)
AND
 - iii. Weekly weight measurements

C. 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. Prescriber attestation that 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. For members with a history of malignancy: Documentation that anti-malignancy treatment has been completed AND evidence of complete remission for at least 12 months free of recurrence
AND
6. Member meets criteria for persistent growth hormone deficiency by meeting [ONE] #1 or #2 [DOCUMENTATION REQUIRED]:
 1. 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/m²
 - Macimorelin: ≤ 2.8 mcg/L
 - Arginine: ≤ 0.4 mcg/L
 - Arginine/GHRH: ≤ 4.1 mcg/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/mL if BMI ≥ 30 kg/m²;
 - Arginine/L- Dopa (peak GH < 1.7 mcg/mL)
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.
 - 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
 2. 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

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- 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 OR GREATER):

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.
AND
3. Prescriber attestation that 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, infections of the central nervous system, genetic syndromes, skeletal disorders, or other organic causes]
AND
4. Prescriber attestation that 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. Prescriber attestation that member's nutritional status has been optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum
AND
6. History of malignancy: Documentation that anti-malignancy treatment has been completed AND evidence of complete remission for at least 12 months free of recurrence
AND
7. 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
8. ANY DIAGNOSIS/INDICATION SPECIFIC CRITERIA BELOW (D-F)

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

1. Adult GHD is due to or the result of 1 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

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iv. Head trauma, OR

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/m²
 - Macimorelin: ≤ 2.8 mcg/L
 - Arginine: ≤ 0.4 mcg/L
 - Arginine/GHRH: ≤ 4.1 mcg/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/mL if BMI ≥ 30 kg/m²)
 - Arginine/L- Dopa (peak GH < 1.7 mcg/mL)
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)

E. PANHYPOPITUITARISM:

NOTE TO REVIEWER: Growth hormone stimulation testing is not required for panhypopituitarism.

1. 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.

F. 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/m²
 - Macimorelin: ≤ 2.8 mcg/L
 - Arginine: ≤ 0.4 mcg/L
 - Arginine/GHRH: ≤ 4.1 mcg/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/mL if BMI ≥ 30 kg/m²)
 - Arginine/L- Dopa (peak GH < 1.7 mcg/mL)
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-Willis syndrome, Short Stature Homeobox-Containing Gene deficiency

1. Member is 18 years or younger

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AND

2. Compliance with GH therapy as verified by Prescriber and member's medication fill history
AND
3. Open epiphyses confirmed by bone age X-ray of the left hand and wrist (required for 12 years of age and older only) at least once annually. Males: not to exceed 16 0/12 years of age; Females: not to exceed 14 0/12 years of age. X-ray required annually and must be taken within 6 months of request. 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. Expected adult height has not been reached (calculated using mid-parental height); 5th percentile for adults (65 inches for men and 60 inches for women); 50th percentile for height based on age
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:
 - i. First year of therapy: A doubling of pre-treatment growth, OR Growth velocity while on therapy is $\geq 2.5\text{cm/year}$
 - ii. After the first year of therapy: Growth velocity remains above 2.5 cm/year (Not applicable to children with prior documented hypopituitarism)
 - iii. For PWS only: Body composition: Increase in lean body mass and decreases in fat mass. Documentation required.
 - iv. 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. Prescriber attests that thyroid function (TSH) tests are within normal range for member's age
AND
7. Prescriber attests that member's nutritional status has been re-evaluated and optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum
AND
8. Provider attests that 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 SHORT BOWEL SYNDROME:

NO CONTINUATION OF THERAPY- Treatment with Zorbtive is limited to 4 weeks

C. ADULT HIV-ASSOCIATED WASTING AND CACHEXIA

1. Documentation members who received a 3-month (12-week) course of 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 $< 20\text{ kg/m}^2$, 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 from ONE of the following baseline measures:
 - i. Body mass index (BMI)
OR

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- ii. Body cell mass (BCM) by bioelectrical impedance analysis (BIA)
OR
- iii. 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 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

D. NOONAN SYNDROME (NS):

1. Compliance with GH therapy is verified by Prescriber and member's medication fill history
AND
2. Expected adult height has not been reached based on NS growth chart
AND
3. 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 twenties is possible (DYSCERNE— Noonan Syndrome Guideline Development Group, 2011; NIH, 2022)
AND
4. 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 that 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

E. 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 or older OR is an adolescent whose epiphyses have closed
AND
2. Documentation of compliance with GH therapy as verified by Prescriber and member's medication fill history
AND
3. Prescriber attestation that thyroid function tests are within normal range (TSH 0.4 - 4.0 mIU/L)
AND
4. Prescriber attestation that nutritional status has been optimized, metabolic abnormalities have been corrected, and steroid usage has been reduced to a minimum
AND
5. For members with a history of malignancy: Documentation that anti-malignancy treatment must be completed AND evidence of complete remission for at least 12 months free of recurrence
AND
6. 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
7. Documentation of continual clinical benefit from growth hormone therapy [e.g. improvements in cardiovascular risk markers, improvement in body composition; weight loss; bone mineral density; increase bone mass; Improvement on lipid profile; serum cholesterol; Increase in physical or muscle strength; Improvement in 'Quality of Life Assessment

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of Growth Hormone Deficiency in Adults' (QoL-AGHDA) score]
AND

8. Provider attests that 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:

SHORT BOWEL SYNDROME (SBS):

Initial authorization: 4 weeks of therapy based on FDA-approved dosage

Continuation of therapy: No additional authorizations after 4 weeks of therapy

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)

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 children diagnoses), endocrinologist (for adult diagnoses) or infectious disease specialist (for AIDs only) or gastroenterologist (for Short Bowel Syndrome 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

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renal transplantation, Small for Gestational Age (SGA), Turner Syndrome (TS), Noonan Syndrome (NS), Prader-Willi syndrome (PWS), Short Stature Homeobox-Containing Gene (SHOX) Deficiency

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, Short-bowel syndrome (SBS), HIV Wasting

Ngenla (somatrogen-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).

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.

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

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resulting in various degrees of malabsorption depending on the area and site of resection and persistence of damage to the remaining bowel.

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.

ABBREVIATIONS:

Adrenocorticotropin hormone (ACTH)

Thyroid stimulating hormone (TSH)

Leutinizing hormone (LH)

Follicle stimulating hormone (FSH)

Arginine vasopressin (AVP)

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

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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. Somatotropin 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):

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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 somatotrophic 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 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 GH are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Other contraindications include: History of hypersensitivity to somatotropin 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, Prader-Willi Syndrome: Individuals who are severely obese or have severe respiratory impairment (reports of sudden death); Uncontrolled diabetes; History of upper airway obstruction or severe respiratory impairment; Untreated severe obstructive sleep apnea; Active cancer; Active psychosis obstructive sleep apnea; Active cancer; Active psychosis, CRI: Renal transplantation (GH therapy must be discontinued at the time of renal transplantation) DISCONTINUATION

For pediatric indications with associated with growth failure:

1. Epiphyseal closure (Bone age \geq 16 years (male), or \geq 14 years (female) is reached); or
2. Attained any of the following height goals (at any age): [ANY]
 - 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
8. EXCLUSIONS - 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

OTHER SPECIAL CONSIDERATIONS:

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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.

AVAILABLE DOSAGE FORMS

AVAILABLE DOSAGE FORMS:

Genotropin CART 12MG	Serostim SOLR 5MG
Genotropin CART 5MG	Serostim SOLR 6MG
Genotropin MiniQuick PRSY 0.2MG	Skytrofa CART 11MG
Genotropin MiniQuick PRSY 0.4MG	Skytrofa CART 13.3MG
Genotropin MiniQuick PRSY 0.6MG	Skytrofa CART 3.6MG
Genotropin MiniQuick PRSY 0.8MG	Ngenla 24mg/1.2mL Prefilled Pen
Norditropin FlexPro SOPN 5MG/1.5ML	Ngenla 60mg/1.2mL Prefilled Pen
Nutropin AQ NuSpin 10 SOPN 10MG/2ML	Norditropin FlexPro SOPN 10MG/1.5ML
Nutropin AQ NuSpin 20 SOPN 20MG/2ML	Norditropin FlexPro SOPN 15MG/1.5ML
Nutropin AQ NuSpin 5 SOPN 5MG/2ML	Skytrofa CART 3MG
Omnitrope SOCT 10MG/1.5ML	Skytrofa CART 4.3MG
Omnitrope SOCT 5MG/1.5ML	Skytrofa CART 5.2MG
Genotropin MiniQuick PRSY 1.2MG	Skytrofa CART 6.3MG
Genotropin MiniQuick PRSY 1.4MG	Norditropin FlexPro SOPN 30MG/3ML
Genotropin MiniQuick PRSY 1.6MG	Skytrofa CART 7.6MG
Genotropin MiniQuick PRSY 1.8MG	Skytrofa CART 9.1MG
Genotropin MiniQuick PRSY 1MG	Sogroya SOPN 5MG/1.5ML
Genotropin MiniQuick PRSY 2MG	Sogroya SOPN 10MG/1.5ML
Humatrope CART 12MG	Sogroya SOPN 15MG/1.5ML
Humatrope CART 24MG	Zomacton (for Zoma-Jet 10) SOLR 10MG
Humatrope CART 6MG	Zomacton SOLR 10MG
Humatrope SOLR 5MG	Zomacton SOLR 5MG
Omnitrope SOLR 5.8MG	Zorbtive SOLR 8.8MG
Saizen SOLR 5MG	
Saizen SOLR 8.8MG	
Saizenprep SOLR 8.8MG	
Serostim SOLR 4MG	

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Drug and Biologic Coverage Criteria

SUMMARY OF REVIEW/REVISIONS	DATE
Off-cycle updates: Required Medical Information – removed required trial of Oxandrin (oxandrone)	07/2024
ANNUAL REVIEW - Notable revisions: Products Affected Required Medical Information Continuation of Therapy FDA-Approved Uses Contraindications/Exclusions/Discontinuation Available Dosage Forms References	01/2024
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	04/2023