Drug Coverage Policy

Effective Date.....10/01/2025
Coverage Policy Number.....IP0375
Policy Title.....Skytrofa

Growth Disorders – Skytrofa

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview
Skytrofa, a weekly human growth hormone (hGH) product, is indicated for the treatment of pediatric patients ≥ 1 year of age who weigh at least 11.5 kg and have **growth failure due to an inadequate secretion of endogenous growth hormone (GH)**.[1] Skytrofa is also indicated for the replacement of endogenous GH in adults with GH deficiency (GHD).

Disease Overview

GHD in Children and Adolescents

Lonapegsomatropin is a prodrug of somatropin.[1] In children with GH deficiency (GHD), somatropin is effective for increasing final adult height.[2] Somatropin therapy is recommended to normalize adult height and avoid extreme shortness in children and adolescents with GHD.[2] In addition to congenital causes, hypopituitarism may also be caused by radiation therapy; somatropin may be used to improve final height of children who have undergone radiation.[3,4]

GHD in Adults or Transition Adolescents

Somatropin is indicated for the replacement of endogenous GH in adults with GH, which may present in adults or children as GHD.[11] Patients with other anterior pituitary hormone deficiencies are likely to have GHD. In adults, the diagnosis of GHD usually is made in patients with signs and symptoms of hypothalamic-pituitary disease (endocrine, structural, and/or genetic causes); those who have received cranial irradiation or tumor treatment; or those with traumatic brain injury or subarachnoid hemorrhage.[11,12] Onset may be in adulthood or childhood. In childhood, the goal of somatropin therapy is primarily for statural growth. When final adult height is attained, somatropin therapy is no longer required for statural growth. Transition is used to describe the period in adolescence after growth is completed and the need for continued replacement into adulthood is assessed. Confirmatory GH stimulation testing may not be required in patients, such as those with congenital/genetic GHD or multiple pituitary hormone deficiencies. When persistent GHD is documented after completion of adult height, somatropin therapy should be continued to attain full skeletal and muscle maturation during the transition period from childhood to adulthood.[11] In adults with GHD, somatropin replacement therapy improves abnormalities in substrate metabolism, body composition, and physical and psychosocial function.[11,12] GH is not approved by the FDA for the treatment of other conditions in adults who may have a low GH response to GH provocative testing (such as obesity, aging, or depression) or to improve athletic performance.[3,5]

Macrilen (macimorelin oral solution) was the most recently approved test for the diagnosis of adult GHD. Patients in the pivotal trial were 18 to 66 years of age and the BMI ranged from 16 to 40 kg/m^2.[26] Safety and diagnostic performance have not been established in patients with BMI > 40 kg/m^2. Clinical studies established that a maximally stimulated serum growth hormone level of < 2.8 ng/mL (i.e., at the 30, 45, 60, and 90 minute time points) after Macrilen administration confirms the presence of adult GHD. Novo Nordisk no longer commercializes Macrilen. As of May 2023, Aeterna Zentaris/Cosciens Biopahrma regained the rights to macimorelin in the United States and is engaged in business development efforts to secure a new development and commercialization partner.[27]

Guidelines

A consensus statement from international experts was recently published (2025) regarding long-acting GH therapy.[12] The authors note that lonapegsomatropin, somapacitan, and somatrogon have all demonstrated noninferiority to daily somatropin for efficacy (i.e., annualized height velocity) in pediatric GHD. They also state that the safety profile of long-acting products is comparable to that of daily somatropin. It is noted that given the unique pharmacokinetic and pharmacodynamic profile and molecular weight of each formulation, the weight-based dosing calculation is different for each product and direct milligram dose comparisons are not appropriate. Some guidelines do not specifically address Skytrofa. Neither the Pediatric Endocrine Society guidelines for children and adolescents with GHD[2] (2016) nor the GH Research Society guidelines on children with short stature[11] (2019) recommend a specific GH product for GHD. Guidelines recommend the use of GH to normalize adult height and avoid extreme shortness in pediatric patients with GHD.

The American Association of Clinical Endocrinologists and the American College of Endocrinology guidelines for management of GHD in adults and patients transitioning from pediatric to adult care[16] (2019) also do not prefer one GH agent over another. These guidelines state that when the clinician is suspicious of adult GHD, establishing a diagnosis is essential before replacement with GH. Adult GHD is associated with numerous adverse metabolic abnormalities (abdominal obesity, reduced lean body mass, increased peripheral insulin resistance, impaired cardiac performance) which may contribute to increased cardiovascular morbidity and mortality.

Coverage Policy

Policy Statement
Prior Authorization is required for benefit coverage of Skytrofa. All reviews will be directed to a clinician (i.e., pharmacist or nurse) for verification of criteria. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Skytrofa as well as monitoring required for adverse events and long-term efficacy, initial approval requires the medication to be prescribed by or in consultation with a physician who specializes in the condition being treated. hGH is FDA-approved for treatment of a limited number of conditions. The FDA has not approved the use of human growth hormone as therapy for anti-aging, longevity, cosmetic or performance enhancement. Federal law prohibits the dispensing of human growth hormone for non-approved purposes. A pharmacy's failure to comply with that law could result in significant criminal penalties to the pharmacy and its employees. Accordingly, a pharmacy may decline to dispense prescriptions for human growth hormone when written by a physician or other authorized prescribers who they believe may be involved in or affiliated with the fields of anti-aging, longevity, rejuvenation, cosmetic, performance enhancement, or sports medicine.

Documentation: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes, laboratory tests, claims records, and/or other information.

Skytrofa is considered medically necessary when the following criteria is met:

1. **Growth Hormone Deficiency in a Pediatric Patient (≥ 1 year of age) .** Individual meets **ALL** of the following criteria:
    A. At least 1 year of age but less than 18 years of age
    B. **ONE** of the following:
        1. Documentation of **BOTH** of the following:
            a. Diagnostic evaluation including **BOTH** of the following:
                I. Other pituitary hormone deficiencies (for example, thyroid, cortisol or sex steroids) have been ruled out and/or corrected prior to time of testing
                II. At least **TWO** growth hormone stimulation tests performed with any of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon **AND** both tests show a growth hormone response of less than 10 ng/mL
            b. Auxologic evaluation (stature and growth velocity data) including **ONE** of the following:
                a. Height is more than two [2] standards of deviation (SD) below average for the population mean height for age and sex , and **ONE** of the following:

1) One-year height velocity more than one standard of deviation (SD) below the mean for chronological age
2) 2 years of age or older, and there is a decrease in height of more than 0.5 standards of deviation (SD) over one year

b. One-year height velocity is more than two standards of deviation (SD) below the mean for age and sex
c. Height velocity is more than 1.5 standards of deviation (SD) below the mean sustained over two years

2. Cranial or Whole Body irradiation

3. **BOTH** of the following:
   a. **ONE** of the following:
      I. Defined central nervous system pathology (for example, empty sella syndrome, interruption of pituitary stalk, hypoplasia of the pituitary gland, craniofacial developmental defects, pituitary or hypothalamic tumors)
      II. undergone tumor resection
   b. **ONE** of the following:
      I. **ONE** growth hormone stimulation test with any of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon **AND** the test shows a growth hormone response of less than 10 ng/mL
      II. Deficiency in at least **ONE** other pituitary hormone (for example, adrenocorticotropic hormone, thyroid-stimulating hormone, gonadotropin [luteinizing hormone and/or follicle stimulating hormone deficiency are counted as one deficiency], or prolactin)

4. Congenital hypopituitarism

5. Multiple pituitary hormone deficiencies and **BOTH** of the following:
   a. **THREE** or more of the following pituitary hormone deficiencies: somatropin (growth hormone), adrenocorticotropic hormone, thyroid-stimulating hormone, gonadotropin (luteinizing hormone and/or follicle stimulating hormone deficiency are counted as one deficiency), and prolactin
   b. **ONE** growth hormone stimulation test with any of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon **AND** the test shows a growth hormone response of less than 10 ng/mL

   Note: If the individual has had one growth hormone stimulation test and the peak growth hormone response was less than 10 ng/mL, this would satisfy criteria for an approval.

6. Hypophysectomy (surgical removal of pituitary gland)

C. The medication has been prescribed by, or in consultation with, an endocrinologist
D. Preferred product criteria is met for the products listed in the below table(s)

2. Growth Hormone Deficiency in an Adult or Transition Adolescent. Approve for 1 year if the patient meets ALL of the following (A, B, C, D and E):

A. The endocrinologist must certify that growth hormone therapy is not being prescribed for anti-aging therapy or to enhance athletic ability or for body building; AND

B. Patient must have a diagnosis of growth hormone deficiency that is ONE of the following (i or ii): **[documentation required for all elements]**

i. Childhood onset; OR

ii. Adult onset that results from one of the following: growth hormone deficiency alone or multiple hormone deficiencies (hypopituitarism) resulting from pituitary disease, hypothalamic disease, pituitary surgery, cranial radiation therapy, tumor treatment, traumatic brain injury, or subarachnoid hemorrhage; AND

C. Patient meets at least ONE of the following (i, ii, or iii):

i. Patient (adult or transition adolescent) has known perinatal insults OR congenital or genetic defects; **[documentation required]** OR

ii. Patient meets ALL of the following (a, b, and c):

a. Patient (adult onset or transition adolescent) has or had three or more of the following pituitary hormone deficiencies prior to hormone replacement therapy (if hormone therapy is required): Adrenocorticotropic hormone , thyroid-stimulation hormone, gonadotropin deficiency (luteinizing hormone and/or follicle stimulating hormone deficiency are counted as one deficiency), and prolactin **[documentation required]**; AND

b. The age and gender adjusted serum insulin-like growth factor-1 is or was below the lower limit of the normal reference range for the reporting laboratory **[documentation required]**, prior to growth hormone therapy; AND

c. Other causes of low serum insulin-like growth factor-1 have been excluded (e.g., malnutrition, prolonged fasting, poorly controlled diabetes mellitus, hypothyroidism, hepatic insufficiency, oral estrogen therapy); OR

iii. Patient meets at least ONE of the following (a or b):

a. Adult. Patient has had a negative response to at least ONE of the following standard growth hormone stimulation tests (1, 2, 3, 4, 5, or 6) **[documentation required for all elements]**:

Note: If the patient has had a previous trial of an arginine test with a peak response of ≤ 0.4 mcg/L, this would meet the criteria for a negative response to a growth hormone stimulation test.

1. Insulin tolerance test (obtaining at least 3 growth hormone levels in at least a 60 minute timeframe [not including a level at timeframe zero], with adequate hypoglycemia being achieved) with peak response ≤ 5.0 mcg/L; OR

2. Glucagon stimulation test (obtaining at least 3 growth hormone levels in at least 180 minute timeframe [not including a level at timeframe zero]) with peak response ≤ 3.0 mcg/L AND the patient's body mass index (BMI) is < 25 kg/m^2; OR

3. Glucagon stimulation test (obtaining at least 3 growth hormone levels in at least 180 minute timeframe [not including a level at timeframe zero]) with a peak response ≤ 3.0 mcg/L AND the patient's BMI is ≥ 25 kg/m^2 and ≤ 30 kg/m^2 with, according to the prescriber, a high pretest probability of growth hormone deficiency; OR

4. Glucagon stimulation test (obtaining at least 3 growth hormone levels in at least 180 minute timeframe [not including a level at timeframe zero]) with a peak response ≤ 1.0 mcg/L AND the patient's BMI is ≥ 25 kg/m^2 and ≤ 30 kg/m^2 with, according to the prescriber, a low pretest probability of growth hormone deficiency; OR
5. Glucagon stimulation test (obtaining at least 3 growth hormone levels in at least 180 minute timeframe [not including a level at timeframe zero]) with peak response ≤ 1.0 mcg/L AND the patient's BMI is > 30 kg/m^2; OR
6. Macrilen (macimorelin oral solution) test (obtaining at least 4 growth hormone levels in at least a 90 minute timeframe [not including a level at timeframe zero]) with peak responses < 2.8 ng/mL (2.8 mcg/L) AND the patient's BMI is ≤ 40 kg/m^2; OR

   Note: The following formula can be used to calculate BMI: BMI equals body weight in kg divided by height meters squared (m^2) [i.e., BMI = kg/m^2]

b. Transition adolescent. Patient meets BOTH of the following (1 and 2): **[documentation required for all elements]**:

Note: The transition period is the time from late puberty to establishment of adult muscle and bone composition, and encompasses attainment of adult height.

Note: If the patient has had a trial of a Macrilen test with a peak response of < 2.8 ng/mL (mcg/L), this would meet the criteria for a negative response to a growth hormone stimulation test.

1. Patient has been off growth hormone therapy for at least 1 month before retesting with a growth hormone stimulation test; AND
2. Patient meets at least ONE of the following responses to growth hormone stimulation testing (i, ii, iii, iv, v or vi):
   - **i.** Insulin tolerance test (obtaining at least 3 growth hormone levels in at least a 60 minute timeframe [not including a level at timeframe zero], with adequate hypoglycemia being achieved) with peak response ≤ 5.0 mcg/L; OR
   - **ii.** Glucagon stimulation test (obtaining at least 3 growth hormone levels in at least 180 minute timeframe [not including a level at timeframe zero]) with peak response ≤ 3.0 mcg/L AND the patient's body mass index (BMI) is < 25 kg/m^2; OR
   - **iii.** Glucagon stimulation test (obtaining at least 3 growth hormone levels in at least 180 minute timeframe [not including a level at timeframe zero]) with a peak response of ≤ 3.0 mcg/L AND the patient's BMI is ≥ 25 kg/m^2 and ≤ 30 kg/m^2 with, according to the prescriber, a high pretest probability of growth hormone deficiency; OR
   - **iv.** Glucagon stimulation test (obtaining at least 3 growth hormone levels in at least 180 minute timeframe [not including a level at timeframe zero]) with a peak response ≤ 1.0 mcg/L AND the patient's BMI is ≥ 25 kg/m^2 and ≤ 30 kg/m^2 with, according to the prescriber, a low pretest probability of growth hormone deficiency; OR
   - **v.** Glucagon stimulation test (obtaining at least 3 growth hormone levels in at least 180 minute timeframe [not including a level at timeframe zero]) with peak response ≤ 1.0 mcg/L AND the patient's BMI is > 30 kg/m^2; OR
   - **vi.** If both the insulin tolerance test AND glucagon stimulation test are contraindicated, the arginine test can be used (obtaining at least 3

growth hormone levels in at least 120 minute timeframe [not including a level at timeframe zero]) with a peak response ≤ 0.4 mcg/L; AND

d. The medication was prescribed by or in consultation with an endocrinologist.

e. Preferred product criteria is met for the products listed in the below table(s)

Employer Drug Lists:

Product	Criteria
Skytrofa (lonapegsomatropin)	**Advantage/Value/Total Savings Drug List Plans:** Patients ≥ 2.5 years of age to < 18 years of age and meets ONE of the following (A or B): **A.** Patient has been able to adhere to somatropin product(s) administered daily AND has experienced inadequate efficacy (i.e., patient has tried for 12 months and has a growth rate of less than 2 cm per year) **[documentation required]** with ONE product from the following list: Genotropin or Omnitrope; OR **B.** Patient meets BOTH of the following (i and ii): **i.** Patient has tried ONE of the following products: Genotropin and Omnitrope **[documentation required]**; AND **ii.** Patient cannot continue to use the product due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**. Note: Meeting the criteria above with a trial of any daily growth hormone product(s) would count toward meeting the requirements regardless of formulary status Patients ≥ 18 years of age and meets BOTH of the following (A and B): **A.** Patient has tried ONE of the following products: Genotropin and Omnitrope **[documentation required]**; AND **B.** Patient cannot continue to use the product due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**. Note: Meeting the criteria above with a trial of any daily growth hormone product(s) would count toward meeting the requirements regardless of formulary status **Standard/Performance Drug List Plans:** Patient meets ONE of the following (1, 2 or 3): **1.** Patient is < 3 years of age; OR **2.** Patient is ≥ 3 years of age to < 18 years of age and meets ONE of the following (a or b): **a.** Patient has tried Ngenla for 6 months **[documentation required]**; OR

Product	Criteria
	b. Patient has experienced an intolerance with Ngenla **[documentation required]** **3.** Patient is ≥ 18 years of age

Individual and Family Plans:

Product	Criteria
Skytrofa (lonapegsomatropin)	Patients ≥ 2.5 years of age to < 18 years of age and meets ONE of the following (A or B): **A.** Patient has been able to adhere to somatropin product(s) administered daily AND has experienced inadequate efficacy (i.e., patient has tried for 12 months and has a growth rate of less than 2 cm per year) **[documentation required]** with ONE product from the following list: Genotropin or Omnitrope; OR **B.** Patient meets BOTH of the following (i and ii): **i.** Patient has tried BOTH of the following products: Genotropin and Omnitrope **[documentation required]**; AND **ii.** Patient cannot continue to use each of the TWO pruducts due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**. Note: Meeting the criteria above with a trial of any daily growth hormone product(s) would count toward meeting the requirements regardless of formulary status Patients ≥ 18 years of age and meets BOTH of the following (A and B): **A.** Patient has tried BOTH of the following products: Genotropin and Omnitrope **[documentation required]**; AND **B.** Patient cannot continue to use each of the TWO products due to a formulation difference in the inactive ingredient(s) [e.g., differences in stabilizing agent, buffering agent, and/or surfactant] which, according to the prescriber, would result in a significant allergy or serious adverse reaction **[documentation required]**. Note: Meeting the criteria above with a trial of any daily growth hormone product(s) would count toward meeting the requirements regardless of formulary status.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Continuation of lonapegsomatropin (Skytrofa) is considered medically necessary For **Growth Hormone Deficiency in a Pediatric Patient (≥ 1 year of age)** when the above medical necessity criteria are met AND beneficial response is demonstrated by **ONE** of the following:

1. Less than 12 years of age: Height has increased by at least 2 cm/year in the most recent year
2. 12 years of age to 17 years of age AND **BOTH** of the following:
    a. Height has increased by at least 2 cm/year in the most recent year
    b. Epiphyses are open

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Skytrofa for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Acute Critical Illness Due to Complications Following Surgery, Multiple Accidental Trauma, or with Acute Respiratory Failure.**[1] Skytrofa is contraindicated in acute critical illness after open-heart surgery, abdominal surgery, multiple accidental trauma, or those with acute respiratory failure because of the risk of increased mortality.

2. **Aging (i.e., Anti-Aging), to Improve Functional Status in an Elderly Patient, and Somatopause.**[13,14,17,18] Somatropin is not FDA-approved for anti-aging therapy, to improve functional status in elderly patients, or to treat somatopause. Federal law prohibits the distribution or dispensing of somatropin for non-FDA approved uses. There are no long-term studies assessing somatropin efficacy and safety for anti-aging therapy. Short-term therapy with somatropin may improve some measures of body composition, including increased muscle mass, reduced total body fat, improved skin elasticity, and reduced rate of bone demineralization, but somatotropin does not have positive effects on strength, functional capacity, or metabolism. Somatropin is associated with considerable adverse effects in non-growth hormone deficient adults (e.g., carpal tunnel syndrome, soft tissue edema, arthralgias, glucose intolerance, increased serum lipids). Another concern is the possible increased risk of cancer with long-term use of somatropin and the potentiating effects of insulin growth factor (IGFs) on cancer. Somatropin is not indicated for the age-related decrease in growth hormone/IGF-1 status.[12]

3. **Athletic Ability Enhancement.**[5] Somatropin and related agents are not FDA-approved for athletic performance enhancement or for body building in non-athletes. Federal law prohibits the distribution or dispensing of somatropin or related agents for non-FDA approved uses.

4. **Central Precocious Puberty.** Children with precocious puberty are often treated with gonadotropin releasing hormone (GnRH) agonists (Lupron® [leuprolide acetate injection]) to suppress pituitary gonadal activity, to slow the advancement of bone age (prevent premature fusion of the epiphyseal growth plates), and to improve adult height. In some patients GnRH

agonist therapy may result in marked deceleration of bone velocity and may result in adult height that is less than the mid-parental height. Small and nonrandomized studies have demonstrated a significant improvement in final adult height over pre-treated predicted adult height in patients treated with GnRH agonist and growth hormone as compared with patients treated with GnRH agonist alone. However, larger randomized studies are lacking, and routine use of growth hormone in this setting is not recommended.[6,7]

5. **Chronic Fatigue Syndrome.** There is no evidence of GHD in chronic fatigue syndrome.[19]

6. **Congenital Adrenal Hyperplasia (CAH).**[8,9] The Endocrine Society clinical practice guidelines on CAH due to steroid 21-hydroxylase deficiency recommend against the use of experimental treatment approaches outside of formally approved clinical trials.[9] Children with predicted adult height standard deviation ≤ -2.25 may be considered for growth-promoting treatments in appropriately controlled trials.

7. **Constitutional Delay of Growth and Puberty.** These children have delayed skeletal maturation and pubertal development. Administering somatropin does not increase adult height (which is usually normal). Short-term androgen therapy accelerates growth and the rate of pubertal advancement in boys.

8. **Corticosteroid-Induced Short Stature.** This includes a variety of chronic glucocorticoid-dependent conditions, such as asthma, Crohn's disease, juvenile rheumatoid arthritis, as well as after renal, heart, liver, or bone marrow transplantation. Short-term improvement in growth velocity in children with glucocorticoid-induced suppression has been reported with somatropin therapy. Long-term data are not available. Children being considered for treatment with somatropin should be enrolled in studies that allow careful monitoring and data analysis.

9. **Fibromyalgia.** In one placebo-controlled study, 120 non-GHD adult women with severe fibromyalgia and low levels of IGF-1 were randomized to somatropin 0.006 mg/kg/day for 12 months (dose was adjusted) or placebo for 6 months.[20] Patients receiving placebo initially were switched to somatropin from Months 6 to 12 (open label). Standard therapy for fibromyalgia was continued. After 6 months, there were no differences between somatropin and placebo in the percentage of patients with fewer than 11 positive tender points, mean number of tender points, intensity of pain in every point evaluated, and other measures. After 12 months of somatropin therapy, 53% of patients had less than 11 positive tender points compared with 33% of patients who received placebo and then somatropin for 6 months ($P < 0.05$). At 18 months follow-up evaluation when somatropin was discontinued, impairment in pain perception worsened in both groups but to a lesser extent in the patients on somatropin for 12 months. Further controlled trials are needed with a longer duration,[21] with different doses, and using the 2010 American College of Rheumatology criteria for fibromyalgia. Some patients with fibromyalgia may have adult GHD.

10. **Human Immunodeficiency Virus (HIV)-Infected Patients with Alterations in Body Fat Distribution** (e.g., increased abdominal girth, lipodystrophy and excess abdominal fat, buffalo hump). Somatropin is not indicated for the treatment of HIV-associated adipose redistribution syndrome (HARS). HARS is a subset of HIV lipodystrophy and is defined as maldistribution of body fat characterized by central fat accumulation (lipohypertrophy) with or without lipoatrophy. In HARS, fat may also accumulate in the upper body subcutaneous area such as the dorsocervical area (buffalo hump). These changes may be associated with metabolic disturbances (insulin resistance, glucose intolerance, dyslipidemia) and belly image distress. Safety and efficacy are not established.

11. **Infertility**. Some trials have demonstrated that GH intervention is associated with improved in-vitro fertilization (IVF) reproductive outcome, but others have concluded there is no evidence of an increased chance of a live birth with use of somatropin. More randomized controlled clinical trials with rigorous methodology are needed to confirm the beneficial effects of GH on assisted reproductive technology outcomes.[23] A 2025 phase III open-label study showed that empiric adjuvant GH therapy in GnRH antagonist cycles does not improve IVF stimulation results or reproductive outcomes, including implantation, miscarriage, and clinical pregnancy rates.[22]

12. **Obesity.**[24,25] Somatropin is not indicated for the treatment of obesity. Low growth hormone levels are a consequence of central obesity and not a cause. Obesity is associated with decreased basal and pulsatile release of growth hormone and decreased stimulated growth hormone release. Somatropin therapy does not have significant beneficial effects on obesity in persons without GHD and does not produce significant overall weight loss. Supraphysiologic doses of somatropin have been used to treat obesity. Effects of long-term therapy with somatropin are unknown.

13. **Osteoporosis.**[13,14] Guidelines for treatment or prevention of osteoporosis do not include recommendations for use of somatropin. In one double-blind trial, 80 postmenopausal women with osteoporosis (56% of patients [n = 45/80] had a history of fractures) were randomized to somatropin 0.33 mg/day or 0.83 mg/day or to placebo for 3 years.[13] The double-blind phase was 18 months and patients on somatropin continued drug for another 18 months and patients on placebo stopped at 18 months. Patients were compared with an age-matched random population sample of women (n = 120). All patients received calcium 750 mg, vitamin D 400 units, and hormone replacement therapy. All women were followed for 10 years total. Bone mineral density increased in the patients receiving somatropin at Years 4 and 5, and after 10 years, had decreased to similar levels as before treatment. At 10 years, 28% of women (n = 22/80) had fractures. In the control group, fractures increased from 8% of patients at baseline to 32% of patients after 10 years. At 10 years, 41% of patients (n = 33/80) had stopped hormone replacement therapy; 23% had started bisphosphonates due to fractures, and 3% had received Forteo® (teriparatide injection). Larger studies are needed to determine the effects of somatropin therapy on bone mineral density and fractures in non-growth hormone deficient persons.

14. **Other Off-label Uses [for example, celiac disease, chromosomal anomalies unless otherwise specified as covered (for example, but not limited to, deletion of chromosome 18q), Crohn's disease, cystic fibrosis, Down syndrome, hypophosphatemic rickets, juvenile rheumatoid arthritis, muscular dystrophy, primary or idiopathic IGF-1 deficiency, skeletal dysplasias, spinal cord defects].** There is insufficient evidence in the peer-reviewed published scientific literature to support the safety and efficacy of growth hormone therapy in these conditions. Additionally, federal law prohibits the distribution or dispensing of somatropin for non-FDA approved uses.

References

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Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	Removed preferred product requirements from the Standard, Value and Legacy formularies.	03/15/2024
Selected Revision	Updated Individual and Family plan preferred product requirements.	01/01/2025
Selected Revision	Updated the Employer Plans preferred product requirements.	07/01/2025
Annual Revision	The following statement in the Policy Statement was updated to include a clinician nurse: "All reviews will be directed to a clinician (i.e., pharmacist or nurse) for verification of criteria." **Growth Hormone Deficiency in a Pediatric Patient (≥ 1 year of age)**: The wording "at least" was added to the requirement for two growth hormone stimulation tests < 10 ng/mL. Added criterion related to continuation of therapy if the patient's mid-parenteral height has not been obtained. **Growth Hormone Deficiency in an Adult or Transition Adolescent:** Added criterion for this diagnosis. Documentation requirements were also added for this diagnosis.	10/01/2025

	Conditions Not Covered: Updated Acute Critical Illness Due to Complications Following Surgery, Multiple Accidental Trauma, or with Acute Respiratory Failure, Central Precocious Puberty and Infertility information **Updated** preferred product tablet for Employer Plans and Individual and Family Plans	

The policy effective date is in force until updated or retired.