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PHARMACY / MEDICAL POLICY – 5.01.500

Growth Hormone Therapy

BCBSA Ref. Policy:	5.01.06
Effective Date:	Mar. 1, 2025
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Replaces:	5.01.06 & 5.01.505

RELATED MEDICAL POLICIES:

5.01.519 Increlex (mecasermin); Recombinant Human Insulin-Like Growth Factor-1

Select a hyperlink below to be directed to that section.

Clicking this icon returns you to the hyperlinks menu above.

Introduction

Growth hormone is produced by the pituitary gland. It aids cell reproduction and promotes physical growth. Growth hormone is also important in how the body converts food into energy. The level of growth hormone varies during the day and is influenced by sleep, diet, stress, and exercise. During childhood, most children produce enough of this hormone for natural growth and development. Lack of enough growth hormone during childhood can result in a number of conditions. In adults, certain medical conditions can result in too little growth hormone. This policy describes when growth hormone therapy may be considered medically necessary for children and adults.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Subject	Medical Necessity
Children	
Conditions	**Growth hormone* may be considered medically necessary in the treatment of children who meet ALL criteria for the conditions listed below:** • Growth deficiency, secondary to insufficient endogenous growth hormone production • Individuals with a history of intrauterine growth restriction (small for gestational age (SGA)) • Chronic renal failure (without functioning kidney transplant) • Gonadal Dysgenesis (Turner Syndrome) • Noonan Syndrome • Infantile hypoglycemia associated with panhypopituitarism • Prader-Willi Syndrome (PWS) • Short stature due to SHOX (short stature homeobox-containing gene) deficiency **Note:** *Genotropin and Omnitrope are considered first line agents. Use of a second line agent must be preapproved. (See **Second Line Agents** section below.)
Diagnoses	**Growth failure in children who are small for gestational age (SGA), intrauterine growth retardation, the initial request may be approved when ALL of the following criteria are met:** • Birth weight, birth length, or both are more than 2 standard deviations below the mean normal values following the adjustment for age and gender **AND** • For individuals aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open **AND** • Normal height range (height >10th percentile for current age) is not reached by two years of age. (See **Appendix**) **Note:** No biochemical testing is required. Approve for 12 months of treatment.

Subject	Medical Necessity
Children	
	Growth failure in children who are small for gestational age (SGA), intrauterine growth retardation, continued treatment may be approved when ALL of the following criteria are met: • The individual must have grown 2.5 centimeters over the previous year with growth hormone therapy **AND** • If aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open **Note:** Approve for an additional 12 months of treatment. **Chronic renal failure (without functioning kidney transplant), the initial request may be approved when at least ONE of the following criteria is met:** • Undergoing dialysis two or more times per week **OR** • Serum creatinine > 2.0 mg/dL **Note:** No biochemical testing is required. Initial approval will be 12 months. For continued approval for another 12 months, confirmation that the member still meets the above coverage criteria must be received. **Note:** Growth hormone is not medically indicated for children with chronic renal failure following functioning renal transplantation **Gonadal Dysgenesis (Turner Syndrome) or Noonan Syndrome, the initial treatment may be approved when ALL of the following criteria are met:** • For individuals aged 10 years or older, bone age must be less than 18 years or epiphysis are confirmed to be open **AND** • Height < 25th percentile for age (see **Appendix**) **Note:** No biochemical testing is required. Approve for 12 months of treatment.

Subject	Medical Necessity
Children	
	Gonadal Dysgenesis (Turner Syndrome) or Noonan Syndrome may be approved for continued treatment when ALL of the following criteria are met: • For individuals aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open **AND** • Height is < 25th percentile for age (see **Appendix**) **AND** • Has grown at least 2.5 centimeters over the previous year with growth hormone therapy **Note:** Approve for an additional 12 months of treatment, or may approve until age 14 and annually thereafter, as long as the above criteria are met. **Infantile hypoglycemia associated with panhypopituitarism may be approved when:** • Demonstrated blood sugar is < 40 mg/dL **AND** • Serum growth hormone level is < 10 ng/ml on all samples obtained during a hypoglycemic episode **OR** during one appropriate stimulation study **Note:** Approve for 12 months of treatment. In emergent situations, treatment may be started before test results are available; approve for 1 month. **Prader-Willi Syndrome (PWS), the initial request may be approved when the following criteria are met:** • Individual has height velocity (<10th percentile for age/sex) (see **Appendix**) **AND** • For individuals aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open. **Note:** No biochemical testing is required. Initial approval for 12 months of treatment.

Subject	Medical Necessity
Children	
	Prader-Willi Syndrome (PWS) may be approved for <u>continued</u> treatment when ALL of the following criteria are met: • The individual has grown at least 2.5 centimeters over the previous year with growth hormone **AND** • For individuals aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open. **Note:** Approve for an additional 12 months of treatment. **Short stature due to SHOX (short stature homeobox-containing gene) deficiency the <u>initial</u> request may be approved when ALL of the following criteria are met:** • Diagnosis is confirmed by genetic testing **AND** • Height < 25th percentile for age (See **Appendix**) **AND** • For individuals aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open **Note:** Approve for 12 months of treatment. **Short stature due to SHOX deficiency may be approved for <u>continued</u> treatment when ALL of the following criteria are met:** • The individual must have grown 2.5 centimeters over the previous year with growth hormone therapy **AND** • Height is < 25th percentile for age **AND** • For individuals aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open

Subject	Medical Necessity
Children	
	Note: Approve for an additional 12 months of treatment.
Initial evaluation of new individuals with diagnosis of growth hormone deficiency	**Treatment of growth deficiency in children (including panhypopituitarism), secondary to insufficient endogenous growth hormone production, may be approved when ALL of the following criteria are present:** • Height velocity <25th percentile for bone age (see **Appendix**) **AND** • For individuals aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open **AND** • Height is below the 3rd percentile on growth charts for individual age or >2.25 SD below the mean for the individual age (see **Appendix**) ○ Exceptions to this height requirement include known acute onset GHD, such as after pituitary surgery or high dose radiation therapy. **AND** • Chronic disease has been ruled out (except renal failure), including liver failure, malnutrition, malabsorption, and hypothyroidism (unless hyperthyroidism is being treated with the appropriate thyroid hormone treatment) **AND** • Serum growth hormone levels of < 10 ng/mL on all samples obtained, utilizing **TWO** separate appropriate (l-dopa, clonidine, arginine, glucagon, insulin-induced hypoglycemia) stimulation studies **OR** serum insulin-like growth factor (IGF-1) level less than the lower limit of normal for individual age. **Note:** Approve for 12 months of treatment.
Subsequent evaluation/reauthorization for children with diagnosed growth hormone deficiency	**Additional treatment may be authorized when the following criteria are met:** • Height velocity while on growth hormone must be ≥ 2.5cm over the previous year **AND**

Subject	Medical Necessity
Children	
	• For individuals aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open (e.g., through wrist film evaluation). **Note:** Approve for an additional 12 months of treatment. **Note:** Adolescents and young adults with severe long-standing multiple pituitary hormone deficiencies (MPHD or panhypopituitarism), those with genetic defects, and those with severe organic GHD can be excluded from GH retesting.

Subject	Medical Necessity
Adults	
Conditions	**Growth hormone* may be considered medically necessary in the treatment of adults who meet ALL criteria for the conditions listed below:** • AIDS wasting syndrome • Severe growth hormone deficiency • Short bowel syndrome **Note:** Baseline lipid panel or bone density scan required for approval. **Note:** *Genotropin and Omnitrope are considered first line agents. Use of a second line agent must be preapproved. (See **Second Line Agents** section below.)
Absolute contraindications	**Growth hormone therapy is considered not medically necessary in individuals for whom it is contraindicated:** • Children with Prader-Willi Syndrome who are severely obese or have severe respiratory impairment • Individuals with acute critical illness, cancer, and active or severe diabetic retinopathy (see manufacturers' labeling for details).
Other non-medically necessary uses	**Growth hormone is considered not medically necessary in the treatment of idiopathic short stature without growth hormone deficiency.**

Subject	Medical Necessity
Adults	
Adults with AIDS wasting syndrome	**Initial requests of treatment with the growth hormone Serostim (somatropin) will be approved when ALL of the following criteria are met:** • There is a diagnosis of AIDS wasting syndrome/cachexia **AND** • The individual is ≥ 18 years of age **AND** • Is not currently receiving treatment with Serostim **AND** • Weight loss is not resulting from underlying treatable conditions (e.g., depression, bacterium avium complex, chronic infectious diarrhea, or malignancy with the exception of Kaposi's sarcoma limited to skin or mucous membranes) **AND** • Has unintentionally lost ≥ 10% of body weight or is 90% or less than their ideal body weight (see chart in the **Appendix**) **Note:** Approve for 6 weeks of initial treatment. Baseline lipid panel or bone density scan required for approval. **Requests for continued treatment with the growth hormone Serostim somatropin beyond the first 6 weeks (for a maximum of 12 weeks of treatment) will be approved when the following criterion is met:** • Clinical benefit is present after the first 6 weeks of treatment (e.g., stabilization of weight or weight gain). **Note:** Approve for an additional 6 weeks of treatment, for a total of 12 weeks.
Adult growth hormone deficiency	**Growth hormone therapy, initial requests must meet the following criterion:** • Adult growth deficiency must be confirmed by a negative response to a growth hormone stimulation test (e.g., serum GH levels of <5 ng/ml on stimulation testing with either of the following: glucagon or insulin). **OR**

Subject	Medical Necessity
Adults	
	• Growth hormone deficiency may be assumed without a stimulation test if individual has had the pituitary removed or destroyed or has had panhypopituitarism since birth. **AND** • Growth hormone therapy is prescribed by or in consultation with an endocrinologist **Note:** Approve for 12 months of initial treatment. Baseline lipid panel or bone density scan required for approval. **Growth hormone therapy may be approved for continued treatment beyond the first 12 months when one or more of the following criteria is met:** • Improvement in bone mineral density (BMD) • Improvement in lipid profile (LDL, TChol) • Serum IGF-1 levels are within 2 standard deviations from normal **Note:** Approve for 12 months of continued treatment.
Adults with short bowel syndrome	**Treatment may be approved when ALL of the following criteria are met:** • There must be documented diagnosis of short bowel syndrome **AND** • The individual must have at least 50 cm residual bowel **AND** • Must be receiving specialized nutritional support. **Note:** Approve for 4 weeks of treatment. Baseline lipid panel or bone density scan required for approval. **Medical necessity of growth hormone treatment is limited to one four-week course of therapy for short bowel syndrome. This is a lifetime maximum, as there are currently no studies showing that additional benefit is conferred by further treatment beyond four weeks.**

Treatment	Investigational
Growth hormone, for conditions not specifically addressed	**Due to the lack of scientific evidence concerning health outcomes, the use of growth hormone for conditions not specifically addressed in this policy is considered investigational, including, but not limited to the following conditions:** • Anabolic therapy, except for AIDS, provided to counteract acute or chronic catabolic illness (e.g., surgery outcomes, trauma, cancer, chronic hemodialysis) producing catabolic (protein wasting) changes in both adult and pediatric individuals • Anabolic therapy to enhance body mass or strength for professional, recreational, or social reasons • Constitutional delay (lower than expected height percentiles when compared with target height percentiles and delayed skeletal maturation when growth velocities and rates of bone age advancement are within the normal range) • Geriatric individual therapy • Glucocorticoid-induced growth failure • Non-GH-deficient short stature, except for Turner's syndrome, Noonan syndrome and Prader-Willi Syndrome • Post-polio syndrome • Short stature after functional renal transplantation • Short stature associated with Lupron therapy • Short stature due to Down's syndromes

Note: Mecasermin (Increlex) is not a growth hormone product and is addressed separately in another medical policy (see **Related Policies**).

Second Line Agents

Second line agents may be considered medically necessary ONLY under the following conditions after the individual has already tried Genotropin or Omnitrope and it didn't work:

- Humatrope: Growth hormone deficiency (GHD), Turner Syndrome, idiopathic short stature (ISS), short stature homeobox-containing gene (SHOX) deficiency, small for gestational age (SGA)

- Ngenla (somatrogon-ghla): Growth hormone deficiency (GHD)
- Norditropin: Growth hormone deficiency (GHD), Noonan Syndrome, Turner Syndrome, born small for gestational age (SGA), idiopathic short stature (ISS), and Prader-Willi Syndrome
- Nutropin, Nutropin AQ: Growth hormone deficiency (GHD), idiopathic short stature (ISS), Turner Syndrome, chronic renal failure (without functioning kidney transplant)
- Saizen: Growth hormone deficiency (GHD)
- Skytrofa (lonapegsomatropin-tcgd): Growth hormone deficiency (GHD)
- Sogroya (somapacitan-beco): Growth hormone deficiency (GHD) in adults
- Zomacton: Growth hormone deficiency (GHD), Turner Syndrome, idiopathic short stature (ISS), short stature homeobox-containing gene (SHOX) deficiency, and born small for gestational age (SGA)
- Any non-preferred product if member either:
    - Has been previously stabilized on non-preferred therapy AND suffers cognitive deficiency of such severity that they cannot be trained to use a preferred product's injection device AND were previously self-administering growth hormone independently
    - Has experienced a documented therapeutic failure on a preferred product

Other diagnoses will be considered on a case-by-case basis.

Chronic Renal Insufficiency

Chronic renal insufficiency is defined as a serum creatinine of greater than 1.5 mg/dL (or 1.4 for women, 1.7 for men) or a creatinine clearance of 75 mL/min per 1.73 m^2 or less. In individuals with chronic renal failure undergoing transplantation, GH therapy is discontinued at the time of transplant or when the growth velocity is less than 2 cm per year, when epiphyseal fusion has occurred, or when the height reaches the 5th percentile of adult height.

Drug	Investigational
As listed	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.** **All other uses of the drugs listed in this policy are considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Non-formulary exception reviews for drugs listed in this policy may be approved up to 12 months.**
Re-authorization criteria	**Non-formulary exception reviews for drugs listed in this policy may be approved up to 12 months.**

Coding

Code	Description
HCPCS	
J2941	Injection, somatropin (use to report: Omnitrope, Zomacton, Nutropin, Serostim, Saizen, Genotropin, Humatrope, Norditropin), 1mg
J3590	Unclassified biologics (use to report: Sogroya, Skytrofa and Ngenla)

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Consideration of Age

The ages stated in this policy for which growth hormone drugs are considered medically necessary is based on the ages approved in the FDA labeling.

Benefit Application

Individual enrollees receiving synthetic growth hormone should be reviewed on at least an annual basis to assure proper application of benefits.

Growth hormone may be covered under the pharmacy or medical benefit, according to the member contract.

Most member contracts specifically exclude coverage of growth hormone for idiopathic short stature syndrome (ISS).

Evidence Review

Description

Synthetic growth hormone has been shown to increase growth rate and eventual adult height when given to children who are growth hormone-deficient. It has also been shown to increase strength, muscle mass, exercise capacity, and quality of life when given to growth hormone-deficient adults. Growth hormone is an anabolic and anti-catabolic agent which results in an increase in lean body mass (LBM), a decrease in body fat, and an overall significant increase in body weight due to the dominant effect of LBM gain.

The U.S. Food and Drug Administration (FDA) has approved this drug for the long-term treatment of growth failure in children due to:

1. Lack of adequate endogenous growth hormone secretion;
2. Chronic renal failure prior to transplantation;
3. Turner's Syndrome or Noonan Syndrome; and
4. Prader-Willi Syndrome

It is also indicated for the treatment of children with short stature born small for gestational age (SGA) with no catch-up growth by age two- to four-years; and idiopathic short stature (ISS), also called non-growth hormone-deficient short stature. The FDA has also approved this drug for adult individuals with somatotropin-deficiency or AIDS wasting syndrome.

Rationale

2008 Update

Several reviews of growth hormone (GH) therapy addressing specific issues were found.

In 2005, Deijen et al. reported a meta-analysis of studies of individual-reported outcomes (PRO) of growth hormone therapy in adults based on a search of PubMed and PiCarta between 1985 and 2004. Eligible studies reported quantitative data about the effect of GH therapy on PRO in GH deficient adults and were placebo-controlled or cross-over/parallel or open clinical trials with endpoints documented by validated questionnaires. Case reports, review articles and studies in which the psychometric quality of the used questionnaire was unknown were excluded, as were studies on GH therapy for other diseases (Turner's syndrome, Prader-Willi Syndrome, fibromyalgia, etc.). Fifteen studies totaling 830 individuals met the inclusion criteria. The authors divided PROs into three categories: quality of life (QOL), health status and wellbeing. Of the three, wellbeing endpoints had the largest effect size, the other two being small. The authors concluded that it is difficult to evaluate the psychological effects of GH in adults, but the QOL impact in this population may frequently be overrated.

A recent systematic review of GH studies in HIV-associated cachexia indexed in MEDLINE through August 2007 was conducted by Gelato et al. In evaluating articles for inclusion, preference was given to clinical studies (including randomized clinical studies), meta-analyses, and guidelines. Review articles that focused on HIV-associated wasting were evaluated and their reference lists examined for additional relevant publications. Statistically significant weight gains were reported, but the average increase was only three kg. Offsetting side effects included hyperglycemia, arthralgia, myalgia and peripheral edema. Subjective improvements in PRO were reported, but the overall value of GH therapy in this population remains to be determined.

A Cochrane review of GH treatment of idiopathic short stature syndrome (ISS) was published in 2007. These children are very short for their age but have normal GH levels and no known cause of their shortness. Ten RCTs were found with final height as primary endpoint. These were meta-analyzed when appropriate, using a random effects model. Incremental increases in final height were modest (1.5-4 inches). One study reported health related QOL and showed no significant improvement in GH treated children compared with those in the control group, while another found no significant evidence that GH treatment impacts psychological adaptation or self-perception in children with ISS.

Practice Guidelines and Position Statements

Pediatric Endocrine Society (PES)

The PES (2015) published an evidence-based report focusing on the risk of neoplasia in individuals receiving growth hormone (GH) therapy.[55] The report concluded that GH therapy can be administered without concerns about the impact on neoplasia in children without known risk factors for malignancy. For children with medical conditions associated with an increased risk of future malignancies, individuals should be evaluated on an individual basis and decisions made about the tradeoff between a possible benefit of GH therapy and possible risks of neoplasm.

As an addendum to the 2015 guidelines, Grimberg and Allen (2017), coauthors, published a historical review of the use of GH.[60] They asserted that although the guidelines did not find an association between GH and neoplasia, the use of GH should not necessarily be expanded. While the use of GH for individuals with growth hormone deficiency (GHD) was recommended, evidence gaps persist in the use of GH for other indications such as idiopathic short stature and partial isolated GHD.

The PES (2016) published guidelines for GH and insulin-like growth factor-1 treatment for children and adolescents with GHD, idiopathic short stature, and primary insulin-like growth factor-1 deficiency.[58] The guidelines used the GRADE approach (grading of recommendations, assessment, development, and evaluation). The following recommendations were made:

- "We recommend the use of GH to normalize adult height and avoid extreme shortness in children and adolescents with GHD. (Strong recommendation, high-quality evidence)"
- "We suggest a shared decision-making approach to pursuing GH treatment for a child with idiopathic short stature. The decision can be made on a case-by-case basis after assessment of physical and psychological burdens, and discussion of risks and benefits. We recommend against the routine use of GH in every child with height SDS [standard deviation score] ≤ -2.25. (Conditional recommendation, moderate-quality evidence)"

The PES (2017) published practice guidelines on the management of Turner syndrome based on proceedings of the International Turner Syndrome Meeting.[59] PES recommended initiating GH treatment early, around 4 to 6 years of age, and preferably before 12 to 13 years if the child had evidence of growth failure (<50th percentile height velocity) or had a strong likelihood of short stature (moderate quality of evidence).

Endocrine Society

Endocrine Society (2011) practice guidelines on adult GHD included the following recommendation.[52]

- GH therapy for GHD adults offers significant clinical benefits in body composition and exercise capacity.
- GH therapy for GHD adults offers significant clinical benefits in skeletal integrity.
- After documentation of persistent GHD, GH therapy should be continued after completion of adult height to obtain full skeletal/muscle maturation during the transition period.

National Institute of Health and Care Excellence

The National Institute of Health and Care Excellence (2010) issued guidance on human GH for growth failure in children.[50] The Institute recommended GH as a possible treatment for children with growth failure with any of the following conditions:

- GHD
- Turner syndrome
- Prader-Willi syndrome
- Chronic renal insufficiency
- Small for gestational age and have growth failure at four years
- Short stature homeobox-containing gene (*SHOX*) deficiency.

American Association of Clinical Endocrinologists

The American Association of Clinical Endocrinologists (2009) updated its guidelines on GH use in GHD adults and transition patients.[46] Evidence-based recommendations included the following:

- GHD is a well-recognized clinical syndrome in adults that is associated with significant comorbidities if untreated

- GH should only be prescribed to patients with clinical features suggestive of adult GHD and biochemically proven evidence of adult GHD
- No data are available to suggest that GH has beneficial effects in treating aging and age-related conditions and the enhancement of sporting performance; therefore, GH treatment was not recommended for any reason other than the well-defined approved uses of the drug.

Growth Hormone Research Society et al

The Growth Hormone Research Society (GHRS), Lawson Wilkins Pediatric Endocrine Society, and the European Society for Paediatric Endocrinology Workshop (2008) published a consensus statement on the diagnosis and treatment of children with idiopathic short stature.[45] The statement indicated that the appropriate height below which GH treatment should be considered ranged from -2 to -3 standard deviation score. The optimal age for treatment was thought to be between five years and early puberty. The group noted that psychological issues should be considered (e.g., GH therapy should not be recommended for short children who are unconcerned about stature). The statement also mentioned that "psychological counseling is worthwhile to consider instead of or as an adjunct to hormone treatment."

The GHRS (2013) issued consensus guidelines on human GH therapy for Prader-Willi syndrome (PWS).[54] The following recommendations were made:

- "After genetic confirmation of the diagnosis of PWS, rhGH [recombinant human growth hormone] treatment should be considered and, if initiated, should be continued for as long as demonstrated benefits outweigh the risks."
- "GH stimulation testing should not be required as part of the therapeutic decision-making process in infants and children with PWS."
- "Exclusion criteria for starting rhGH in patients with PWS include severe obesity, uncontrolled diabetes, untreated severe obstructive sleep apnea, active cancer, and active psychosis."
- Scoliosis and cognitive impairment should not be considered exclusion criteria.

In 2016, results from the Growth Hormone Safety Workshop were published in the European Journal of Endocrinology.[56] The workshop was convened by GHRS and other medical societies. The workshop reappraised the safety of human GH. The position statement concluded:

- After following children and adults for tens of thousands of person-years, the safety profile of rhGH remains good when rhGH is used for approved indications and at recommended doses. There is no evidence supporting an association between rhGH and overall mortality, risk of new primary cancer, risk of recurrence of primary cancer, risk of stroke, or risk of cardiovascular disease.
- A carefully designed cohort study, providing continued long-term surveillance of individuals treated with rhGH, would address the current limitations of safety data (e.g., inconsistent definitions of outcomes, low incidence outcomes, and lack of dose-specific assessments).

American Academy of Pediatrics

The American Academy of Pediatrics (2016) published guidelines on the evaluation and referral of children with signs of early puberty.[57] The use of gonadotropin-releasing hormone analogues was discussed as treatment options, but GH as a treatment option was not discussed.

2009 Update

The 2006 Endocrine Society guidelines for treatment of GH deficiency in adults were reviewed to update the policy guidelines for adults. Key recommendations of this panel include:

- Individuals with childhood-onset growth hormone deficiency (GHD) who are appropriate candidates for GH) therapy should be retested for GHD as adults unless they have known mutations, embryopathic lesions, or irreversible structural lesions/damage (level of evidence, high).
- Adult individuals with evidence of structural hypothalamic/pituitary disease, surgery or irradiation to these areas, or other pituitary hormone deficiencies should be considered for evaluation for acquired GHD (level of evidence, high).
- The insulin tolerance test (ITT) or the growth hormone releasing hormone (GHRH)-arginine test is the preferred test for establishing the diagnosis of GHD. However, in those with clearly established recent hypothalamic causes of suspected GHD (e.g., irradiation) testing with GHRH-arginine may be misleading (level of evidence, high).
- Because of the irreversible nature of the cause of the GHD in children with structural lesions with multiple hormone deficiencies and those with proven genetic causes, a low insulin-like

growth factor I (IGF-I) level at least one month off GH therapy is sufficient documentation of persistent GHD without additional provocative testing (level of evidence, moderate).

The criteria for initiation and continuation of GH in children were revised by comparison with the Lawson Wilkins Society pediatric GH guidelines as updated in 2003. Normal Height velocities for normal boys and girls were obtained from the growth charts available at **www.cdc.gov**.

2010 Update

A literature search of the MEDLINE database did not identify any additional published studies that would prompt reconsideration of the policy statements, which remain unchanged.

2011 Update

A literature search of the MEDLINE database did not identify any additional published studies that would substantively change the policy statements. Policy reformatted and revised for administrative simplification.

2012 Update

A literature search of the MEDLINE database did not identify any additional published studies that would prompt reconsideration of the policy statements, which remain unchanged. The 2009 update on the AACE guidelines for growth hormone use for growth hormone-deficient adults was added to the reference section.

2013 Update

Literature search of PUBMED database did not identify any additional published studies that would prompt policy change. Added that stimulation test is not necessary in adults who are known to not have a functioning pituitary.

2014 Update

Literature search of PUBMED database did not identify any additional published studies that would prompt medical change. Added that growth hormone may be approved up to age 14 and annually thereafter in individuals with Turner or Noonan syndromes.

2018 Update

A literature search conducted from 1/1/2015 through 09/10/2018 found no new evidence that would change this policy. Added notes clarifying requirement for lipid labs in adult individuals. An indication was added for Zomacton for the treatment of short stature or growth failure associated with SHOX deficiency.

2019 Update

A literature search of PUBMED database found no new evidence that would change this policy. References added. Position statements added.

2020 Update

Changes reflect new 2019 AACE practice guidelines which recommend against the use of arginine, levodopa, and clonidine testing as methods for diagnosing adult-onset growth hormone deficiency, due to low sensitivity and specificity in stimulating growth hormone secretion in adults. A new treat-to-target of age-adjusted, mean serum IGF-1 within 2 standard deviations from the norm was also included in the re-authorization criteria. A literature search of PUBMED found no other evidence impacting coverage.

2021 Update

Reviewed prescribing information and updated the list of absolute contraindications to growth hormone therapy. For absolute contraindications removed reference to individuals with acute third-degree burns, multiple traumas, and chronic illness and added children with Prader-Willi Syndrome who are severely obese or have severe respiratory impairment and individuals with active or severe diabetic retinopathy. Removed from second-line agents Saizen and Zomacton,

the requirement individual is using a needless injector and has a documented fear of needles. Conducted a literature search on use of growth hormone stimulation studies in children. Added glucagon to list of appropriate stimulation tests as evidence documents it is less risky than insulin-induced hypoglycemia and is a good choice for infants and young children.

2022 Update

Reviewed prescribing information for all drugs listed in policy. No new evidence was identified that would change coverage criteria.

2023 Update

Reviewed prescribing information for all drugs listed in policy. Added Ngenla (somatrogon-ghla) as a second-line agent for the treatment of GHD.

2024 Update

Reviewed prescribing information for all drugs listed in policy. No new evidence was identified that would change coverage criteria.

2025 Update

Reviewed prescribing information for all drugs listed in policy. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

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Appendix

Link to CDC Clinical Growth Charts: https://www.cdc.gov/growthcharts/clinical_charts.htm

Height and Weight Table for Men*			
Height (feet/inches)	**Small Frame**	**Medium Frame**	**Large Frame**
5′ 2″	128 – 134	131 – 141	138 – 150
5′ 3″	130 – 136	133 – 143	140 – 153
5′ 4″	132 – 138	135 – 145	142 – 156
5′ 5″	134 – 140	137 – 148	144 – 160
5′ 6″	136 – 142	139 – 151	146 – 164
5′ 7″	138 – 145	142 – 154	149 – 168
5′ 8″	140 – 148	145 – 157	152 – 172
5′ 9″	142 – 151	148 – 160	155 – 176
5′ 10″	144 – 154	151 – 163	158 – 180
5′ 11″	146 – 157	154 – 166	161 – 184
6′ 0″	149 – 160	157 – 170	164 – 188
6′ 1″	152 – 164	160 – 174	168 – 192
6′ 2″	155 – 168	164 – 178	172 – 197
6′ 3″	158 – 172	167 – 182	176 – 202
6′ 4″	162 – 176	171 – 187	181 – 207

Weights at ages 25-59 based on lowest mortality. Weight in pounds according to frame (in indoor clothing weighing 5 lbs.; shoes with 1″ heels).

Height and Weight Table for Women*			
Height (feet/inches)	**Small Frame**	**Medium Frame**	**Large Frame**
4′ 10″	102 – 111	109 – 121	118 – 131

Height and Weight Table for Women*			
Height (feet/inches)	**Small Frame**	**Medium Frame**	**Large Frame**
4′ 11″	103 – 113	111 – 123	120 – 134
5′ 0″	104 – 115	113 – 126	122 – 137
5′ 1″	106 – 118	115 – 129	125 – 140
5′ 2″	108 – 121	118 – 132	128 – 143
5′ 3″	111 – 124	121 – 135	131 – 147
5′ 4″	114 – 127	124 – 138	134 – 151
5′ 5″	117 – 130	127 – 141	137 – 155
5′ 6″	120 – 133	130 – 144	140 – 159
5′ 7″	123 – 136	133 – 147	143 – 163
5′ 8″	126 – 139	136 – 150	146 – 167
5′ 9″	129 – 142	139 – 153	149 – 170
5′ 10″	132 – 145	142 – 156	152 – 173
5′ 11″	135 – 148	145 – 159	155 – 176
6′ 0″	138 – 151	148 – 162	158 – 179

Weights at ages 25-59 based on lowest mortality. Weight in pounds according to frame (in indoor clothing weighing 3 lbs.; shoes with 1″ heels).

* Source: Metropolitan Life Insurance Company, Copyright 1996, 1999.

History

Date	Comments
10/01/97	Add to Prescription Drug Section - New Policy
04/14/98	Replace Policy - Reviewed with changes.
06/01/99	Replace Policy - Changed criteria for adults
12/21/00	Replace Policy - Policy reformatted; no criteria changes.
03/15/02	Replace Policy - Policy updated to reflect current consensus guidelines.
02/11/03	Replace Policy - Policy guidelines updated; policy statement unchanged.
05/11/04	Replace Policy - Policy reviewed and updated, with policy statement and guidelines updated for clarification purposes. Now considered medically necessary for

Date	Comments
	intrauterine growth restriction/ SGA. Crohn's Disease and cystic fibrosis added list of investigational uses.
09/01/04	Replace Policy - Policy renumbered from PR.5.01.100. No changes to dates.
09/14/04	Replace Policy - Policy statement changed; Idiopathic short stature changed from investigational to not medically necessary.
10/12/04	Replace Policy - Policy updated with Aids Wasting Syndrome—in order to delete policy PR.5.01.505.
05/10/05	Replace Policy - Policy updated with literature search. Reviewed and approved by P&T on March 22, 2005; policy statement is changed to include adults with short bowel syndrome as medically necessary.
02/06/06	Codes updated - No other changes.
07/11/06	Replace Policy - Policy updated with literature search; baseline study requirements removed from criteria for adult patient growth hormone therapy; policy statement unchanged; Scope and Disclaimer updated.
07/25/06	Replace Policy - Policy reviewed by the Pharmacy and Therapeutic Committee; recommended without changes.
12/12/06	Update Cross Reference - No other changes.
03/13/07	Replace Policy - Clarification added under Policy Guidelines indicating the continuation of treatment for pituitary dwarfism without additional testing. No other changes.
03/21/07	Codes Updated - No other changes.
05/08/07	Replace Policy - Policy updated with a statement added to the Policy section indicating that medical necessity determination is not required for Mecasermin (Iplex Incrilex).
10/9/07	Replace Policy - Policy updated with a statement added to the Policy section indicating that a benefit advisory is not required for Mecasermin replacing "Medical necessity determination is not a requirement for this indication". Under Policy guidelines "No biochemical testing is required" was added and section title was clarified.
08/12/08	Replace Policy - Policy updated with literature search; no change to the policy statement. A note was included at the end of the policy statement referencing the Mecasermin policy. Policy reviewed by the Pharmacy and Therapeutic Committee; recommended no changes. Rationale updated and references added.
10/14/08	Code Update - J9225 and J9226 removed, no other changes.
11/11/08	Code Update - J1675 removed, no other changes.
07/29/09	Update Benefit Application - No other changes.
08/11/09	Replace Policy - Policy updated with literature search. Policy statement updated to include Medically necessary indication (2 bullets) under the "Children" section. P&T reviewed on July 28, 2009.

Date	Comments
12/14/10	Replace Policy - Policy updated with literature review; no change in policy statements. Reviewed by P&T November 2010.
03/08/11	Replace Policy - Policy updated with literature review; no change in policy statements. Policy re-written and reformatted for improved clarity and administrative simplification.
09/11/12	Replace policy. Policy updated with literature review through July 2012. Reference #45 added. Other references renumbered. Policy statement unchanged.
10/15/12	Replace policy. Policy guidelines revised with addition of clarifying statement "For patients aged 10 years or older, bone age must be less than 18 years or epiphyses are confirmed to be open". Policy statement unchanged. Medco replaced with Express Scripts within Benefit Application.
11/13/12	Replace policy. Genotropin and Omnitrope added as first line agents as referenced in the existing medically necessary policy statement. Second line agents have been addressed in the Policy Guidelines, with outlining conditions for which they may be approved.
10/14/13	Replace policy. Policy Guidelines section updated with the addition that stimulation test is not necessary in adults who are known to not have a functioning pituitary.
12/03/13	Coding Updating. Add ICD-10 codes.
11/10/14	Annual review. Policy updated with literature review; no change to policy statement. Added that growth hormone may be approved up to age 14 and annually thereafter in patients with Turner or Noonan syndromes within the Policy Guidelines section.
06/09/15	Interim update. Replace name of Tev-Tropin with Zomacton – name change by manufacturer.
04/01/16	Coding Update. Removed HCPCS J2940.
10/01/16	Annual Review, approved September 13, 2016. Update of the re-authorization criteria for adult GH use.
10/21/16	Minor edit. Removed an example of clinical benefit in Adult Growth Hormone Deficiency section.
10/01/17	Annual Review, approved September 21, 2017. Clarified criteria for reauthorization of adult growth hormone. Removed CPT codes 77072, 77073, and 96372. Removed ICD-10 codes.
12/01/17	Interim Review, approved, November 9, 2017. Clarified criteria for pediatric growth hormone deficiency.
09/01/18	Minor update. Re-added Consideration of Age information, which was inadvertently removed during a previous update.
12/01/18	Annual Review, approved November 21, 2018. Added an indication for Zomacton for the treatment of short stature or growth failure associated with SHOX deficiency

Date	Comments
01/01/20	Annual Review, approved December 10, 2019. Policy updated with literature review; references added. Added short stature due to SHOX gene deficiency to list of conditions for which growth hormone for children is considered medically necessary; otherwise policy statements unchanged.
01/01/21	Annual Review, approved December 17, 2020. Omitted arginine, levodopa, and clonidine testing as approved methods for diagnosing adult-onset growth hormone deficiency (AO-GHD). Included age-adjusted serum IGF-1 within 2 SDs of mean as approved criterion for re-authorization in AO-GHD. Removed HCPC code S9558 due to low utilization.
03/01/21	Interim Review, approved February 18, 2021. Added Sogroya (somapacitan-beco) as a second-line agent for the treatment of GHD in adults. Added HCPCS code J3590.
09/01/21	Annual Review, approved August 3, 2021. Removed from the second-line agents Saizen and Zomacton the requirement patient is using a needless injector and has a documented fear of needles. Updated the list of absolute contraindications to include children with Prader-Willi Syndrome who are severely obese or have severe respiratory impairment and patients with active or severe diabetic retinopathy. Added glucagon to list of appropriate stimulation tests in children.
10/01/21	Interim Review, approved September 23, 2021. For adult growth hormone deficiency added requirement growth hormone therapy is prescribed by or in consultation with an endocrinologist.
01/01/22	Interim Review, approved December 21, 2021. Added Skytrofa (lonapegsomatropin-tcgd) as a second-line agent for the treatment of GHD.
01/01/23	Annual Review, approved December 23, 2022. No changes to policy statements. Changed the wording from "patient" to "individual" throughout the policy for standardization.
07/01/23	Annual Review, approved June 26, 2023. No changes to policy statements.
12/01/23	Interim Review, approved November 14, 2023. Added Ngenla (somatrogon-ghla) as a second-line agent for the treatment of GHD. Added Ngenla to HCPCS code J3590.
08/01/24	Annual Review, approved July 8, 2024. No changes to policy statements.
03/01/25	Annual Review, approved February 24, 2025. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.