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Subject: Growth Hormone Therapy

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Growth hormone (GH) is an anterior pituitary hormone that directly influences protein, carbohydrate, and lipid metabolism and controls the rate of skeletal and visceral growth by stimulating the release of Insulin like Growth Factor 1 (IGF-1) from the liver. IGF-1 acts directly on many cell types to stimulate growth. Their secretion of GH is in part controlled by the hypothalamus. Pharmaceutical preparations are referred to as somatropins.

Somatropin is a pharmaceutical preparation of growth hormone, prepared by recombinant means.

POSITION STATEMENT:

Certificate of Medical Necessity

Submit a completed Certificate of Medical Necessity (CMN) along with your request to expedite the medical review process.

1. Click the link Growth Hormone Therapy under Certificates of Medical Necessity in the side navigation of this page to access the form.
2. Complete all fields on the form thoroughly.
3. Print and submit a copy of the form with your request.

Note: Florida Blue regularly updates CMNs. Ensure you are using the most current copy of a CMN before submitting to Florida Blue.

Growth hormone therapy (recombinant or biosynthetic) **meets the definition of medical necessity** when administered for the following indications **AND** indication specific criteria are met (**SEE TABLE 1 FOR SPECIFIC CRITERIA**):

- Growth failure due to growth hormone deficiency (GHD) in children under the age of 21 years
- Growth hormone therapy in children with chronic renal failure (before renal transplantation)
- Growth hormone therapy with Turner's syndrome
- Growth hormone therapy with Noonan's syndrome
- Growth hormone therapy in children with Short Stature Homeobox Gene (SHOX) deficiency
- Growth hormone therapy with Prader-Willi syndrome
- Growth hormone therapy with Small for Gestational Age (SGA)
- Growth hormone deficiency in adults 21 years of age and older **OR** adolescents whose epiphyses have closed
- Growth hormone therapy in members with HIV-associated wasting or cachexia
- Growth hormone therapy in members with Short Bowel syndrome.

Growth hormone is an effective treatment for conditions that may or may not be related to a deficiency of growth hormone. Growth hormone meets the definition of medical necessity when used for the indications listed in Table 1; conversely, the use of growth hormone to manage linear growth in the absence of one of the above conditions is considered cosmetic.

NOTE: Norditropin is the preferred growth hormone product.

SPECIFIC CRITERIA FOR GROWTH HORMONE THERAPY	
INDICATION	**COVERAGE CRITERIA**
Growth failure due to growth hormone deficiency (GHD) in children under the age of 21 **NOTE:** For adolescents whose epiphyses have closed please also refer to criteria in section below "Growth hormone deficiency in adults 21 years of age and older or adolescents whose epiphyses have closed documentation must indicate all of the following:"	**Meets the definition of medical necessity** when **ALL** of the following are met: 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Other causes of growth failure (e.g. cranial tumors, cranial irradiation, hypothyroidism, chronic systemic disease, infections of the central nervous system, genetic syndromes, skeletal disorders, or other organic causes) have been considered and appropriately excluded. 3. Demonstration of growth hormone (GH) deficiency by **ONE** of the following: a. Members must have two abnormal growth hormone (GH) provocative stimulation tests with results of 10 ng/ml or less – laboratory documentation must be provided (Examples of stimulation tests: arginine, clonidine, glucagon, insulin, or L-dopa.) b. For children with multiple ≥ 3 anterior pituitary hormone

	deficiencies, subnormal insulin-like growth factor (IGF-1) level for age, gender and tanner development stage may be used instead of stimulation tests – laboratory and medical record documentation must be provided c. One abnormal GH provocative stimulation test is sufficient if the child has a documented history of GHD as a result of destructive lesions of the pituitary or treatment (e.g. ablative pituitary irradiation) – laboratory and medical record documentation must be provided d. GH deficiency due to congenital hypopituitarism can be diagnosed without provocative stimulation testing in a newborn with hypoglycemia who does not attain a serum GH concentration above 5 mcg/L in the first week of life and has deficiency of at least one additional pituitary hormone or a congenital malformation (ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk) 4. Other pituitary hormone deficiencies, e.g., thyroid, cortisol or sex steroids, have been ruled out and/or corrected prior to time of testing 5. The epiphyses have not closed, as determined by x-ray* 6. Member meets **ONE** of the following: a. Pretreatment height at least 3 Standard Deviations (SD) below the population mean for age and gender – documentation from the medical record must be provided b. Pretreatment height less than 3rd percentile or 2 Standard Deviations (SD) below the population mean for age and gender **AND** Growth velocity of 4 cm/year or less or growth velocity below the 25th percentile for chronological age – documentation from the medical record must be provided Approval duration: 1 year **Continuation of Therapy for GHD in children:** After the initial 12 months of GH treatment **ALL** of the following criteria must be documented to demonstrate the medical necessity of continued therapy. 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Insulin-like Growth Factor I must be within normal levels for age, gender and tanner development stage – laboratory and medical record documentation must be provided 3. **ONE** of the following must be met: a. Doubling of pre-treatment growth rate in first year of

	therapy – documentation from the medical record must be provided b. Increase in growth rate of 3 cm/year or more in first year of therapy – documentation from the medical record must be provided c. Growth rate remains above 2 cm/year after the first year of therapy – documentation from the medical record must be provided 4. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only). – documentation from the medical record must be provided* 5. Expected adult height has not been reached (calculated using mid-parental height) – documentation from the medical record must be provided 6. **ONE** of the following: a. The member has been previously approved for growth hormone therapy by Florida Blue in the past 2 years b. The member has been previously approved for growth hormone therapy by another health plan in the past 2 years AND historical documentation of GH deficiency is provided (e.g., provocative stimulation test results, medical history of ablative pituitary irradiation) c. The member has previously met all initiation criteria for coverage Approval duration: 1 year
Growth hormone therapy in children with chronic renal failure (before renal transplantation)	**Meets the definition of medical necessity** when **ALL** of the following are met: 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Chronic renal insufficiency showing reduction in the glomerular filtration rate (GFR) or creatinine clearance (CrCL) to below 25% of normal level (decline of 30 ml/min/1.73 m2) for at least 3 months (See Table 3 for normal CrCl values) 3. Nutritional status has been optimized, metabolic abnormalities such as acidosis, secondary hyperparathyroidism, and under nutrition corrected. 4. Steroid usage has been reduced to a minimum. 5. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* Approval duration: 1 year **Continuation of Therapy for CRF:**

	After the initial 12 months of GH treatment **ALL** of the following criteria must be documented to demonstrate the medical necessity of continued therapy. 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Growth response of at least 4 cm/yr in the first year of GH therapy or 2 cm/yr thereafter must occur for continuation of coverage – documentation from the medical record must be provided 3. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* 4. In members with chronic renal failure undergoing transplantation, GH therapy is discontinued at the time of transplant and will not be continued until at least 1 year after the transplant to allow for evaluation of the functionality of the grafted organ and catch-up growth. 5. The member has been previously approved for growth hormone therapy by Florida Blue or another health plan in the past 2 years, or the member has previously met all initiation criteria for coverage Approval duration: 1 year
Growth hormone therapy with Turner's syndrome	**Meets the definition of medical necessity** when **ALL** of the following are met: 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Peripheral blood karyotype showing a 45, XO genotype – laboratory documentation must be provided 3. Member meets **ONE** of the following: a. Pretreatment height less than 3rd percentile or 2 Standard Deviations (SD) below the population mean for age and gender – documentation from the medical record must be provided b. Growth velocity below the 50th percentile for chronological age over 6 months– documentation from the medical record must be provided 4. X-ray report showing that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* Approval duration: 1 year **Continuation of Therapy for Turner's syndrome:**

	After the initial 12 months of GH treatment **ALL** of the following criteria must be documented to demonstrate the medical necessity of continued therapy. 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* 3. Growth velocity of >4 cm in the first year and >2 cm thereafter – documentation from the medical record must be provided 4. The member has been previously approved for growth hormone therapy by Florida Blue or another health plan in the past 2 years, or the member has previously met all initiation criteria for coverage Approval duration: 1 year
Growth hormone therapy with Noonan's syndrome	**Meets the definition of medical necessity** when **ALL** of the following are met: 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Member has no serious heart failure 3. IGF-1 levels and cardiac function are monitored regularly 4. Pretreatment height less than 3rd percentile or 2 Standard Deviations (SD) below the population mean for age and gender – documentation from the medical record must be provided 5. Growth velocity (GV) measured over one year prior to initiation of therapy of 1 or more standard deviations below the mean for age and gender – documentation from the medical record must be provided 6. X-ray report showing that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* Approval duration: 1 year **Continuation of Therapy for Noonan syndrome:** After the initial 12 months of GH treatment **ALL** of the following criteria must be documented to demonstrate the medical necessity of continued therapy. 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. IGF-1 levels and cardiac function are monitored regularly

	3. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* 4. Growth velocity of >4 cm in the first year and >2 cm thereafter – documentation from the medical record must be provided 5. The member has been previously approved for growth hormone therapy by Florida Blue or another health plan in the past 2 years, or the member has previously met all initiation criteria for coverage Approval duration: 1 year
Growth hormone therapy in children with Short Stature Homeobox Gene (SHOX) Deficiency	**Meets the definition of medical necessity** when **ALL** of the following are met: 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* Approval duration: 1 year **Continuation of Therapy for Short Stature Homeobox Gene (SHOX) Deficiency:** After the initial 12 months of GH treatment **ALL** of the following criteria must be documented to demonstrate the medical necessity of continued therapy. 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* 3. Growth velocity of >4 cm in the first year and >2 cm thereafter – documentation from the medical record must be provided 4. The member has been previously approved for growth hormone therapy by Florida Blue or another health plan in the past 2 years, or the member has previously met all initiation criteria for coverage Approval duration: 1 year
Growth hormone therapy with Prader-Willi syndrome **NOTE:** Those with Prader-	**Meets the definition of medical necessity** when **ALL** of the following are met: 1. Endocrinologist evaluation must be submitted to Florida Blue for

Willi syndrome suffer from centripetal obesity and growth hormone therapy can result in fluid retention in the lungs which can be life threatening.	review documenting the need or continued need for growth hormone therapy 2. Normal sleep study is required prior to initiation of therapy – documentation from the medical record must be provided 3. Micro-deletion in the long arm of chromosome 15 or 2 maternal chromosome 15 and no paternal chromosome 15, or nonfunctional paternal chromosome 15 – documentation from the medical record must be provided 4. Pretreatment height less than 5th percentile or 1.6 Standard Deviations (SD) below the population mean for age and gender – documentation from the medical record must be provided 5. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* Approval duration: 1 year **Continuation of Therapy for Prader-Willi syndrome:** After the initial 12 months of GH treatment **ALL** of the following criteria must be documented to demonstrate the medical necessity of continued therapy. 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. A growth response of >2cm/yr must occur for continuation of coverage – documentation from the medical record must be provided 3. Documentation of improvement in body composition: increase in lean body mass and decreases in fat mass – documentation from the medical record must be provided 4. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* 5. The member has been previously approved for growth hormone therapy by Florida Blue or another health plan in the past 2 years, or the member has previously met all initiation criteria for coverage Approval duration: 1 year
Growth hormone therapy with Small for Gestational Age (SGA)	**Meets the definition of medical necessity** when **ALL** of the following are met: 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. A child with short stature associated with SGA who is at least 2

	years of age 3. Documentation of birth weight less than 5th percentile for gestational age and birth height < 10% for gestational age – documentation from the medical record must be provided 4. At 24 months of age has failed to demonstrate catch up growth and is below the 3rd percentile in height and weight for chronological age or height and weight < 2 SD below the mean for chronological age – documentation from the medical record must be provided Approval duration: 1 year **Continuation of Therapy for SGA:** After the initial 12 months of GH treatment **ALL** of the following criteria must be documented to demonstrate the medical necessity of continued therapy. 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Insulin-like Growth Factor I (IGF-I) is considered medically necessary to determine adequacy of GH therapy and must be within normal levels for age, gender and tanner development stage – laboratory documentation must be provided (Ranges more than 2 SD below the mean for IGF-I strongly suggests abnormality in the GH axis if other causes of low IGF have been excluded.) 3. Doubling of pre-treatment growth rate or increase in growth rate of 3 cm/year or more in first year of therapy – documentation from the medical record must be provided 4. Growth rate remains above 2 cm/year after the first year – documentation from the medical record must be provided 5. Bone age x-ray of the left hand and wrist to determine that epiphyses have not yet closed (children over 10 years of age only) – documentation from the medical record must be provided* 6. The member has been previously approved for growth hormone therapy by Florida Blue or another health plan in the past 2 years, or the member has previously met all initiation criteria for coverage Approval duration: 1 year
Growth hormone deficiency in adults 21 years of age and older OR adolescents whose epiphyses have closed	Meets the definition of medical necessity when **ALL** of the following are met: 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy

	2. Member meets **ONE** of the following: a. For those adults with childhood onset deficiency **OR** adult growth hormone deficiency due to organic disease presenting with 0, 1, or more anterior pituitary hormone deficiency(s) treated with replacement therapy and **ONE** of the following: i. An abnormal response as indicated by **TWO** of the following standard growth hormone provocative stimulation tests: • ITT - Peak GH ≤ 5 ng/ml – laboratory documentation must be provided • Glucagon - Peak GH ≤ 3 ng/ml BMI ≤ 25 kg/m2 – laboratory documentation must be provided • Glucagon - Peak GH ≤ 1 ng/ml BMI > 25 kg/m2 – laboratory documentation must be provided • Arginine - Peak GH ≤ 0.4 ng/ml – laboratory documentation must be provided • GHRH/ARG - Peak GH ≤ 11 ng/ml BMI < 25 kg/m2 – laboratory documentation must be provided • GHRH/ARG - Peak GH ≤ 8 ng/ml BMI ≥25 kg/m2 and <30kg/m2 – laboratory documentation must be provided • GHRH/ARG - Peak GH ≤ 4 ng/ml BMI ≥ 30 kg/m2 – laboratory documentation must be provided • Macimorelin - Peak GH ≤ 2.8 ng/ml – laboratory documentation must be provided ii. Baseline pretreatment Serum IGF-1 is low for age and gender as established per the laboratory's reference range (laboratory documentation must be provided) **AND** the member has an abnormal response to **ONE** of the following standard growth hormone provocative stimulation tests: • ITT - Peak GH ≤ 5 ng/ml – laboratory documentation must be provided • Glucagon - Peak GH ≤ 3 ng/ml BMI ≤ 25 kg/m2 – laboratory documentation must be provided • Glucagon – Peak GH ≤ 1 ng/ml BMI > 25 kg/m2 – laboratory documentation must be provided • Arginine - Peak GH ≤ 0.4 ng/ml –

	laboratory documentation must be provided • GHRH/ARG - Peak GH ≤ 11 ng/ml BMI < 25 kg/m2 – laboratory documentation must be provided • GHRH/ARG - Peak GH ≤ 8 ng/ml BMI ≥25 kg/m2 and <30kg/m2 – laboratory documentation must be provided • GHRH/ARG - Peak GH ≤ 4 ng/ml BMI ≥ 30 kg/m2 – laboratory documentation must be provided • Macimorelin - Peak GH ≤ 2.8 ng/ml – laboratory documentation must be provided **NOTE:** Insulin Tolerance Test (ITT) is considered the gold standard, but alternatives such as the Glucagon or Arginine tests are also acceptable b. Adult GH deficiency as a result of pituitary disease or hypothalamic disease (e.g. panhypopituitarism, multiple pituitary hormone deficiency (MPHD), pituitary tumor, surgical damage, cranial irradiation, Sheehan's syndrome, autoimmune hypophysitis, or sarcoidosis trauma) presenting with ≥ 3 anterior pituitary hormone deficiencies (e.g. corticosteroid, thyroid hormone, sex steroid(s)), and **ALL** of the following: i. Existing anterior pituitary hormone deficiencies are being treated with replacement therapy – documentation from the medical record must be provided ii. Baseline pretreatment Serum IGF-1 is low for age and gender as established per the laboratory's reference range – documentation from the medical record must be provided Approval duration: 1 year **Continuation of Therapy for adult GHD:** After the initial 12 months of GH treatment all of the following criteria must be documented to demonstrate the medical necessity of continued therapy. 1. Endocrinologist evaluation must be submitted to Florida Blue for review documenting the need or continued need for growth hormone therapy 2. Members on GH therapy have achieved a serum IGF-I concentration in the normal range for age and gender – laboratory documentation must be provided 3. The member has been previously approved for growth hormone therapy by Florida Blue or another health plan in the past 2

	years, or the member has previously met all initiation criteria for coverage Approval duration: 1 year
Growth hormone therapy in members with HIV-associated wasting or cachexia	**Meets the definition of medical necessity** when all of the following are met: 1. Diagnosis of HIV infection 2. Unexplained baseline weight loss of more than 10 percent in the recent past twelve (12) months or a body-mass index (BMI) of less than 20 that cannot be attributed to any other condition other than HIV infection – documentation from the medical record must be provided 3. Concurrent treatment with anti-viral agents 4. Failure of alternative appetite stimulant therapy. 5. The dose does not exceed 6 mg per day Approval duration: 12 weeks **Continuation of Therapy for HIV-associated wasting or cachexia:** After 12 weeks of therapy, all of the following criteria must be documented to demonstrate the medical necessity of continued therapy: 1. Concurrent treatment with anti-viral agents 2. Member has a beneficial response to therapy (e.g., improved BMI, increased body weight, lean body mass) 3. BMI remains less than 20 or at least 10% of baseline body weight has not been gained 4. The dose does not exceed 6 mg per day 5. The member has been previously approved for growth hormone therapy by Florida Blue or another health plan in the past 2 years†, or the member has previously met all initiation criteria for coverage Approval duration: 12 weeks
Growth hormone therapy in members with Short Bowel syndrome	**Meets the definition of medical necessity** when all of the following are met: 1. Documented short bowel syndrome as a result of resected or damaged bowel with chronic diarrhea, weight loss, electrolyte imbalances, malnutrition, dehydration, and malabsorption of fats, vitamins and minerals – documentation from the medical record must be provided 2. Dependence on specialized nutritional support needs including dietary adjustments such as a high carbohydrate, low fat diet, enteral feedings, parenteral nutrition, fluid, and micronutrient supplements – documentation from the medical record must be

	provided 3. Member has not previously received 4 weeks of treatment with growth hormone 4. The dose does not exceed 8 mg per day Approval duration: 4 weeks **Continuation of therapy for Short Bowel syndrome:** 1. Duration of therapy is limited to 4 weeks. Administration for more than 4 weeks has not been adequately studied and will not be authorized.
*X-ray must be taken within 6 months of request †Step therapy requirement does not apply if a prior health plan paid for the medication - documentation of a paid claim within the past 90 days must be submitted	

NOTE: There is no standardization of IGF-1 assays and what is normal is dependent upon the assays method performed at the performing lab.

Growth hormone, a self-administered injectable prescription drug used to increase height or bone growth except for conditions of growth hormone deficiency documented with abnormally low stimulation tests of less than 10 mg/ml and abnormally low growth hormone dependent peptide (IGF-1) or for conditions of growth hormone deficiency associated with loss of pituitary function due to trauma, surgery, tumors, radiation or disease, or for state mandated use as in members with AIDS is not considered medically necessary and therefore not a covered benefit.

Growth hormone is not considered a medical necessity for all other indications, including:

1. Use as an antiaging agent
2. Infertility
3. Crohn's Disease
4. Use in obesity
5. Use in somatopause
6. Use as a performance-enhancing drug for athletes
7. Use for chronic fatigue syndrome, fibromyalgia, or obesity
8. Growth hormone insensitivity (Laron Syndrome)
9. Children with constitutional growth delay
10. Children with idiopathic short stature
11. Children with growth failure caused by glucocorticoids
12. Growth retardation due to amphetamines (e.g., Adderall®, Ritalin®)
13. Children who are not growth hormone deficient but have short stature associated with chronic disease (except chronic renal failure)
14. Children with functioning renal transplants
15. Children with chromosomal and genetic disorders (except Turner's and Prader-Willi Syndrome)

16. Familial short stature
17. Use as an adjunct to ovulation induction in hypogonadotropic hypogonadism, bilateral tubal occlusion, anovulatory or oligo ovulatory infertility or unexplained infertility
18. HIV lipodystrophy or adipose redistribution syndrome

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

Table 2

Clinical Condition	Dose in µ/kg/day	Dose in mg/kg/day
GHD in Children	24 – 34	0.024 – 0.034
GHD in Adolescents	25 – 100	0.025 – 0.100
GHD in Adults	4 – 16	0.004– 0.016
Chronic Renal Insufficiency	50	0.050
Turner's Syndrome	Up to 67	Up to 0.067
Noonan Syndrome	Up to 66	Up to 0.066
Small for Gestational Age	Up to 67	Up to 0.067
Prader Willi Syndrome	35 – 50	0.035 – 0.050
HIV-associated wasting or cachexia	-	0.1 (max 6 mg/day)
Short-bowel syndrome	-	0.1 (max 8 mg/day)

PRECAUTIONS:

Boxed Warning: none

Contraindications:

- Acute Critical Illness
- Children with Prader-Willi syndrome who are severely obese or have severe respiratory impairment - reports of sudden death
- Active Malignancy
- Hypersensitivity to somatropin or excipients
- Active Proliferative or Severe Non-Proliferative Diabetic Retinopathy
- Children with closed epiphyses

Precautions/Warnings:

- Acute Critical Illness: Potential benefit of treatment continuation should be weighed against the potential risk
- Prader-Willi Syndrome in Children: Evaluate for signs of upper airway obstruction and sleep apnea before initiation of treatment for GHD. Discontinue treatment if these signs occur
- Neoplasm: Monitor patients with preexisting tumors for progression or recurrence. Increased risk of a second neoplasm in childhood cancer survivors treated with somatropin - in particular meningiomas in patients treated with radiation to the head for their first neoplasm

- Impaired Glucose Tolerance and Diabetes Mellitus: May be unmasked. Periodically monitor glucose levels in all patients. Doses of concurrent antihyperglycemic drugs in diabetics may require adjustment
- Intracranial Hypertension: Exclude preexisting papilledema. May develop and is usually reversible after discontinuation or dose reduction
- Hypersensitivity: Serious hypersensitivity reactions may occur. In the event of an allergic reaction, seek prompt medical attention.
- Fluid Retention (i.e., edema, arthralgia, carpal tunnel syndrome – especially in adults): May occur frequently. Reduce dose as necessary
- Hypoadrenalism: Monitor patients for reduced serum cortisol levels and/or need for glucocorticoid dose increases in those with known hypoadrenalism
- Hypothyroidism: May first become evident or worsen
- Slipped Capital Femoral Epiphysis: May develop. Evaluate children with the onset of a limp or hip/knee pain
- Progression of Preexisting Scoliosis: May develop
- Pancreatitis: Consider pancreatitis in patients with persistent severe abdominal pain
- Lipoatrophy: Rotate injection sites
- Carpal tunnel syndrome: Discontinue if symptoms do not resolve
- Concomitant antiretroviral therapy: Antiretroviral agents should be continued for patients treated for HIV-associated wasting or cachexia.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J2941	Injection, somatropin, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

B20	Human immunodeficiency virus (HIV) disease
E23.0	Hypopituitarism
E23.1	Drug-induced hypopituitarism
E23.3	Hypothalamic dysfunction, not elsewhere classified
E23.6	Other disorders of pituitary gland
E23.7	Disorder of pituitary gland, unspecified
E89.3	Post-procedural hypopituitarism
E34.3	Short stature due to endocrine disorder
E34.8	Other specified endocrine disorder
E34.9	Endocrine disorder, unspecified
K91.2	Postsurgical malabsorption, not elsewhere classified
N18.9	Chronic kidney disease, unspecified
P05.00 – P05.9	Disorders of newborn related to slow fetal growth and fetal malnutrition
Q85.00	Neurofibromatosis, unspecified
Q85.01	Neurofibromatosis, type 1

Q85.02	Neurofibromatosis, type 2
Q85.03	Schwannomatosis
Q85.09	Other neurofibromatosis
Q87.1	Congenital malformation syndromes predominantly associated with short stature
Q89.2	Congenital malformations of other endocrine glands
Q96.0 – Q96.9	Turner's syndrome, unspecified
R62.50	Unspecified lack of expected normal physiological development in childhood
R62.51	Failure to thrive (child)
R62.52	Short stature (child) [covered for SHOX deficiency in children whose epiphyses are not closed]
R62.7	Adult failure to thrive
R64	Cachexia

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

- Reimbursement for continuation of GH therapy is limited to twelve (12) months, with exceptions: GH therapy for AIDS-wasting syndrome is limited to twelve (12) weeks unless extended pursuant to medical review, **AND**
- GH therapy for Short Bowel Syndrome is limited to 4 weeks.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

DEFINITIONS:

HIV-associated wasting or cachexia: unintentional and progressive weight loss associated with HIV infection

Bone age: estimate of a child's age based on x-ray appearance of the bones.

Chronic fatigue syndrome: an usual illness of uncertain cause, that is characterized by unexplained fatigue, weakness, muscle pain, lymph node swelling, and malaise.

Constitutional growth delay: common normal developmental process, usually in boys who are short, but later catch up to their expected normal height.

Corticosteroid: Any of the steroids secreted by the adrenal cortex of the adrenal gland.

Epiphyses: the ends of certain bones, which come together when final height is reached.

Fibromyalgia: A disorder characterized by muscle pain, stiffness, and easy fatigability.

Growth velocity rate: how fast a child is growing.

Obesity: An increase in body weight greater than the limitation of skeletal and physical requirement, as a result of excessive accumulation of body fat.

Prader-Willi Syndrome: A genetic disorder characterized by obesity, short stature, cognitive disabilities, and small hands and feet.

Provocative stimuli of growth hormone release: lab test where drugs are given in an attempt to increase the growth hormone levels produced by the pituitary gland; used to diagnose growth hormone deficiency.

Short Bowel Syndrome: A syndrome caused by surgical bowel (intestinal) removal or damage resulting in chronic diarrhea, impaired fat, vitamin, mineral and fluid absorption.

Somatopause: A gradual and progressive decrease in growth hormone secretion that occurs normally with increasing age during adult life and is associated with an increase in adipose tissue (body fat) and LDL cholesterol levels and a decrease in lean body mass.

Turner's syndrome: genetic disease in girls where a missing chromosome causes deformity and shortness in height.

RELATED GUIDELINES:

Mecasermin (Increlex®), 09-J0000-57

OTHER:

Table 3

Normal CrCl Values	
Age Group	**CrCl**
Newborn	38 mL/min/1.73 m2
At 1 year of age	77 mL/min/1.73 m2
Between 4 and 10 years	Males: 131 ml/min/1.73 m2 Females: 109 ml/min/1.73 m2

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/13/19.

GUIDELINE UPDATE INFORMATION:

11/15/00	Medical Coverage Guideline reformatted.
01/01/02	Revision to guideline; coding changes.
12/15/02	Reviewed with no revisions.
10/15/05	Reviewed with update to description added short bowel syndrome, small for gestational age and Prader-Willi syndrome. Added idiopathic short stature, infertility use and adipose redistribution syndrome to WHEN SERVICES ARE NOT COVERED.
01/01/06	Annual CPT code update, deleted expired code 90782, added new code 90772. HCPCS update, deleted unclassified code J3490.
09/15/06	Biennial review; reformatted and updated references.
11/15/06	Revised: removed criteria for continuation of therapy for growth hormone deficiency stating “height has not reached the 5th percentile of adult height, added “or adolescents whose epiphyses have closed” to Adults with GHD and added continuation of therapy criteria for AIDS-wasting syndrome.
01/01/07	Revision to include Medicare Part D as program exception.
02/15/07	Revision; revised criteria for growth hormone deficiency in children to allow alternative to

	GH stimulation test (i.e., subnormal IGF-1 and IGFBP-3 levels).
07/15/07	Reviewed: Reformatted guideline, inserted paragraph under description regarding renal impairment, deleted IGF-1 criteria for continuation of therapy for CRF patients, added "growth failure due to GHD" for coverage of GHD, deleted bone age as criteria for GHD, added criteria "by x-ray, the epiphyses have not closed", and updated references.
07/15/08	Review and revision; consisting of updating the description, reformatting, adding 2 new indications, updating dosage and administration section, adding definitions and updating references.
05/15/09	Revision; consisting of adding to criteria requirement a failure of one of the preferred agents.
09/15/09	Review and Revision; consisting of requiring endocrinologist evaluation prior to initiation and continuation of therapy, revision to description section, requiring normal sleep study prior to initiation of therapy for Prader-Willi syndrome, removing IGF-1 reference table and inserting a note stating there is no standardization of IGF-1 assays and updating references.
01/15/10	Revision; consisting of removing endocrinology evaluation for AIDS and SBD and adding contract language statement.
04/01/10	Revision; consisting of removing step therapy and for one preferred product.
11/15/10	Review and revision; consisting of an added requirement that a child has not yet reached predicted adult height for renewal of therapy, addition that any anterior pituitary hormone deficiencies have been treated with replacement therapy, removal of a GH stimulation test requirement for those with greater than or equal to 3 anterior pituitary hormone deficiencies, updated GH definition, removed somatrem (no longer on the market) from the introduction, and updated the administration code.
02/15/11	Revision to guideline; consisting of formatting changes.
11/15/11	Review and revision to guideline consisting of updating the reimbursement section to remove specific brand names, added somatopause to the list of conditions considered not medically necessary, Added definition of somatopause.
11/15/12	Review and revision to guideline; consisting of updating the chart by adding that a correction for other pituitary deficiencies be corrected before initiating GH therapy in children with idiopathic growth hormone deficiency, removed IGFBP-3 as a diagnostic marker in children, added standard deviation below the mean in addition to height percentile and updated this consistently where applicable throughout the document, Updated the adult GH stim response test values according to agent used and BMI. Added obesity, infertility, amphetamine use, and Crohn's disease to the non-medically necessary list.
02/13/13	Review and revision to guideline; consisted of updating formatting and moved the note for required ruling out of other organic cause for growth failure in children to the bulleted section. Updated the use of IGF-1 testing in lieu of growth hormone stimulation tests to apply in children with ≥ 3 anterior pituitary deficiencies.
03/15/14	Review and revision to guideline; consisting of updating the recommendation in Prader Willi to 5th percentile based on summarized growth chart comparison for Prader Willi and the GHD charts. Minor formatting changes.
05/11/14	Revision: Program Exceptions section updated.
12/15/14	Revision to guideline; consisting of position statement, other
05/15/15	Revision: updated billing/coding
11/01/15	Revision: ICD-9 Codes deleted.
03/15/16	Review and revision to guideline; consisting of updating the position statement for use in

	children, adults, Turner Syndrome; updated references.
08/15/16	Revision: update to position statement and coding.
10/01/16	Update to ICD-10 coding.
03/15/17	Review and revision to guideline; consisting of updating dosing, precautions and references.
04/15/17	Revision: update to position statement.
03/15/18	Review and revision to guideline; consisting of updating the position statement; updated dosing, precautions and references.
05/15/18	Review and revision to guideline; consisting of updating the position statement and references.
04/15/19	Review and revision to guideline; consisting of updating references.
01/01/20	Revision to guideline consisting of updating the position statement.