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## DRUG POLICY

# Growth Hormone

### NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

### BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

### DESCRIPTION

The intent of the Growth Hormone drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies. The criteria will require the use one of the health plan's preferred growth hormones, Norditropin and Genotropin, prior to the use of non-preferred growth hormones unless requesting Nutropin/Nutropin AQ and Humatrope for chronic kidney disease (CKD), and short stature homeobox-containing gene (SHOX) deficiency, respectively. Serostim and Zorbtive are excluded from preferred growth hormone requirement. Growth hormone therapy must be prescribed by or in consultation with a specialist (endocrinologist, geneticist, pediatric nephrologist, gastroenterologist/nutritional support specialist, or an infectious disease specialist) and the patient must not have an active malignancy or history of malignancy in the past 12 months.

#### FDA-Approved Indications

- Pediatric patients with growth failure due to any of the following:
  - Growth hormone (GH) deficiency
  - Turner syndrome
  - Noonan syndrome
  - Small for gestational age (SGA)
  - Prader-Willi syndrome
  - Chronic kidney disease (CKD)
  - Short stature homeobox-containing gene (SHOX) deficiency
  - Idiopathic short stature (ISS)
- Adults with childhood-onset or adult-onset GH deficiency
- Short bowel syndrome (SBS)
- Human immunodeficiency virus (HIV)-associated wasting/cachexia

Growth Hormone	Generic Name	FDA Approved Indications
<b>Genotropin®</b>	somatropin	Pediatric GHD, adult GHD, TS, ISS, SGA, PWS
<b>Humatrope®</b>	somatropin	Pediatric GHD, adult GHD, TS, ISS, SGA, SHOXD
<b>Norditropin®</b>	somatropin	Pediatric GHD, adult GHD, TS, ISS, SGA, PWS, NS
<b>Nutropin/Nutropin AQ®</b>	somatropin	Pediatric GHD, adult GHD, TS, ISS, CKD
<b>Omnitrope®</b>	somatropin	Pediatric GHD, adult GHD, TS, ISS, SGA, PWS
<b>Saizen®</b>	somatropin	Pediatric GHD, adult GHD
<b>Serostim®</b>	somatropin	HIV-associated wasting/cachexia
<b>Skytrofa</b>	lonapegsomatropin-tcgd	Pediatric GHD (1 year and older who weight at least 11.4kg)
<b>Sogroya®</b>	somapacitan-beco	Adult GHD
<b>Zomacton®</b>	somatropin	Pediatric GHD, SGA, adult GHD, SHOXD, TS, ISS
<b>Zorbtive®</b>	somatropin	SBS

## POLICY

### REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for both initial and continuation of therapy requests (where applicable):

- Medical records supporting the diagnosis of neonatal growth hormone (GH) deficiency
- Pretreatment growth hormone provocative test result(s) (laboratory report or medical record documentation)
- Growth Chart
- Pretreatment and/or current IGF-1 level (laboratory report or medical record documentation)\*
- The following laboratory test reports must be provided:
  - Diagnostic karyotype results in Turner syndrome
  - Diagnostic genetic test results in Prader-Willi syndrome
  - Diagnostic molecular or genetic test results in SHOX deficiency
- The following information must be provided for all continuation of therapy requests:
  - Total duration of treatment (approximate duration is acceptable)
  - Date of last dose administered
  - Approving health plan/pharmacy benefit manager
  - Date of prior authorization/approval
  - Prior authorization approval letter
- Body mass index (BMI) documentation may be required for review of adult growth hormone deficiency

\* IGF-1 levels vary based on the laboratory performing the analysis. Laboratory-specific values must be provided to determine whether the value is within the normal range.

### PRESCRIBER SPECIALTIES

For all diagnoses excluding HIV-associated wasting/cachexia, therapy must be prescribed by or in consultation with any of the following specialists:

- Endocrinologist
- Pediatric endocrinologist
- Geneticist
- Pediatric nephrologist (CKD only)
- Gastroenterologist/Nutritional support specialist (SBS only)

#### **INITIAL CRITERIA FOR APPROVAL**

\* The criteria will require the use one of the health plan's preferred growth hormones, Norditropin and Genotropin, prior to the use of non-preferred growth hormones unless requesting Nutropin/Nutropin AQ and Humatrope for chronic kidney disease (CKD), and short stature homeobox-containing gene (SHOX) deficiency, respectively. Serostim, and Zorbtive are excluded from preferred growth hormone requirement. Sogroya will only be covered for adult growth hormone deficiency when criteria are met. Skytrofa will only be covered for pediatric growth hormone deficiency in patients 1 year of age and older when criteria are met. Skytrofa and Sogroya will not be covered for any other indication.

- I. Growth hormone may be considered **medically necessary** for the treatment of pediatric growth hormone deficiency when the following criteria are met:
  - a. Patient is a neonate, unless the request drug is Skytrofa, or was diagnosed with GH deficiency as a neonate. Medical records must be available to support the diagnosis of neonatal GH deficiency (e.g., hypoglycemia with random GH level, evidence of multiple pituitary hormone deficiency, chart notes, or magnetic resonance imaging [MRI] results).

**OR**

- b. Patient meets ALL of the following:
  - i. Patient has EITHER:
    1. Two pretreatment pharmacologic provocative GH tests with both results demonstrating a peak GH level < 10 ng/mL, OR
    2. A documented pituitary or CNS disorder (refer to Appendix A) and a pretreatment IGF-1 level > 2 standard deviations (SD) below the mean
  - ii. For patients < 2.5 years of age at initiation of treatment:
    1. Pretreatment height is > 2 SD below the mean and growth velocity is slow
  - iii. For patients ≥ 2.5 years of age at initiation of treatment:
    1. Pretreatment height is > 2 SD below the mean and 1-year height velocity is >1 SD below the mean, OR
    2. Pretreatment 1-year height velocity is > 2 SD below the mean.
  - iv. Epiphyses are open

**Approval is for 12 months.**

- II. Growth hormone may be considered **medically necessary** for the treatment of Turner Syndrome when ALL of the following criteria are met:
  - a. Diagnosis was confirmed by karyotyping
  - b. Patient's pretreatment height is less than the 5<sup>th</sup> percentile for age
  - c. Epiphyses are open

**Approval is for 12 months.**

- III. Growth hormone may be considered **medically necessary** for the treatment of Noonan Syndrome when ALL of the following criteria are met:

- a. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
- b. Epiphyses are open

**Approval is for 12 months.**

- IV. Growth hormone may be considered **medically necessary** for the treatment of growth failure associated with chronic kidney disease when ALL of the following criteria are met:
  - a. For patients < 2.5 years of age at initiation of treatment:
    - i. Pretreatment height is > 2 SD below the mean and growth velocity is slow.
  - b. For patients ≥ 2.5 years of age at initiation of treatment
    - i. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
    - ii. Pretreatment 1-year height velocity is > 2 SD below the mean
  - c. Epiphyses are open

**Approval is for 12 months.**

- V. Growth hormone may be considered **medically necessary** for the treatment of short children born small for gestational age when ALL of the following criteria are met:
  - a. Patient meets at least one of the following:
    - i. Birth weight < 2500 g at gestational age > 37 weeks
    - ii. Birth weight or length less than 3<sup>rd</sup> percentile for gestational age
    - iii. Birth weight or length ≥ 2 SD below the mean for gestational age
  - b. Pretreatment age is ≥ 2 years
  - c. Patient failed to manifest catch-up growth by age 2 (i.e., pretreatment height is > 2 SD below the mean)
  - d. Epiphyses are open

**Approval is for 12 months.**

- VI. Growth hormone may be considered **medically necessary** for the treatment of Prader-Willi Syndrome when the following criteria are met:
  - a. The diagnosis of Prader-Willi syndrome was confirmed by genetic testing demonstrating any of the following:
    - i. Deletion in the chromosomal 15q11.2-q13 region
    - ii. Maternal uniparental disomy in chromosome 15
    - iii. Imprinting defects, translocations, or inversions involving chromosome 15

**Approval is for 12 months.**

- VII. Growth hormone may be considered **medically necessary** for the treatment of Idiopathic Short Stature when ALL of the following criteria are met:
  - a. Pretreatment height is > 2.25 SD below the mean
  - b. Predicted adult height is < 5'3" for boys and < 4'11" for girls
  - c. Pediatric growth hormone (GH) deficiency has been ruled out with a provocative GH test (peak GH level ≥ 10 ng/mL)
  - d. Epiphyses are open

**Approval is for 12 months.**

VIII. Growth hormone may be considered **medically necessary** for the treatment of Short Stature Homeobox-Containing Gene (SHOX) deficiency when ALL of the following criteria are met:

- a. The diagnosis of SHOX deficiency was confirmed by molecular or genetic analyses
- b. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean
- c. Epiphyses are open

**Approval is for 12 months.**

IX. Growth hormone may be considered **medically necessary** for the treatment of adult growth hormone deficiency when ANY of the following criteria are met:

- a. The patient meets both of the following:
  - i. The patient has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated deficient GH responses defined as the following:
    1. Insulin tolerance test (ITT) with a peak GH level  $\leq 5$  ng/mL
    2. Macrilen with a peak GH level less than 2.8 ng/mL
    3. Glucagon stimulation test with a peak GH level  $\leq 3$  ng/mL in patients with a body mass index (BMI) less than or equal to 30 kg/m<sup>2</sup> and a high pretest probability (e.g., acquired structural abnormalities) OR a BMI less than 25 kg/m<sup>2</sup>
    4. Glucagon stimulation test with a peak GH level  $\leq 1$  ng/mL in patients with a BMI  $\geq 25$  kg/m<sup>2</sup> and a low pretest probability (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m<sup>2</sup>
  - ii. The patient has a low pre-treatment IGF-1 (between 0 to 2 SD below the mean for age and gender)
- b. The patient meets both of the following:
  - i. The patient has had 1 pretreatment pharmacologic provocative GH test that demonstrated deficient GH responses defined as one of the following:
    1. Insulin tolerance test (ITT) with a peak GH level  $\leq 5$  ng/mL
    2. Macrilen with a peak GH level less than 2.8 ng/mL
    3. Glucagon stimulation test with a peak GH level  $\leq 3$  ng/mL in patients with a body mass index (BMI) less than or equal to 30 kg/m<sup>2</sup> and a high pretest probability (e.g., acquired structural abnormalities) OR a BMI less than 25 kg/m<sup>2</sup>
    4. Glucagon stimulation test with a peak GH level  $\leq 1$  ng/mL in patients with a BMI  $\geq 25$  kg/m<sup>2</sup> and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m<sup>2</sup>
  - ii. The patient has a pretreatment IGF-1 level that is more than 2 SD below the mean for age and gender
- c. The patient has organic hypothalamic-pituitary disease (e.g., suprasellar mass with previous surgery and cranial irradiation) with  $\geq 3$  documented pituitary hormone deficiencies [refer to Appendix B] and a low pre-treatment IGF-1 more than 2 standard deviations below the mean for age and gender
- d. The patient has documented genetic or structural hypothalamic-pituitary defects (refer to Appendix A)
- e. The patient has childhood-onset GH deficiency and a documented congenital abnormality of the CNS, hypothalamus or pituitary (refer to Appendix A)

**Approval is for 12 months.**

X. Growth hormone may be considered **medically necessary** for the treatment of HIV-Associated Wasting/Cachexia when ALL of the following criteria are met:

- a. Patient is diagnosed with HIV-associated wasting/cachexia

- b. Patient has tried and had a suboptimal response to alternative therapies (e.g., cyproheptadine, dronabinol, megestrol acetate or testosterone if hypogonadal) unless the patient has a contraindication or intolerance to alternative therapies
- c. Patient is currently on antiretroviral therapy
- d. Pretreatment BMI is less than 18.5 kg/m<sup>2</sup> prior to initiating therapy with growth hormone (see Appendix D)

**Approval is for 12 weeks.**

- XI. Growth hormone may be considered **medically necessary** for the treatment of Short Bowel Syndrome (SBS) when ALL of the following criteria are met:
- a. Patient is dependent on intravenous parenteral nutrition for nutritional support
  - b. GH will be used in conjunction with optimal management of SBS unless requesting Zorbtive
  - c. Patient has not previously received GH therapy for more than 8 weeks (4 weeks for Zorbtive)

**Approval is for 8 weeks (4 weeks for Zorbtive).**

### CONTINUATION OF THERAPY

- I. The continuation of growth hormone therapy may be considered **medically necessary** for the treatment of pediatric growth hormone deficiency, Turner Syndrome, Noonan Syndrome, CKD, SGA, ISS, and SHOX deficiency when ALL of the following criteria are met:
- i. Epiphyses are open (confirmed by X-ray or X-ray is not available)
  - ii. Patient's growth rate is > 2 cm/year unless there is documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing adult final height/late stages of puberty)

**Approval is for 12 months.**

- II. The continuation of growth hormone therapy may be considered **medically necessary** for the treatment of Prader-Willi Syndrome when ALL body composition and psychomotor function have improved or stabilized in response to GH therapy

**Approval is for 12 months.**

- III. The continuation of growth hormone therapy may be considered **medically necessary** for the treatment of adult growth hormone deficiency when ANY of the following are met:
- a. The patient meets all of the following:
    - i. The patient has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated deficient GH responses defined as the following:
      - 1. Insulin tolerance test (ITT) or another provocative GH test with a peak GH level  $\leq$  5 ng/mL
      - 2. Macrilen with a peak GH level less than 2.8 ng/mL
      - 3. Glucagon stimulation test with a peak GH level  $\leq$  3 ng/mL in patients with a body mass index (BMI) less than or equal to 30 kg/m<sup>2</sup> and a high pretest probability (e.g., acquired structural abnormalities) OR a BMI less than 25 kg/m<sup>2</sup>
      - 4. Glucagon stimulation test with a peak GH level  $\leq$  1 ng/mL in patients with a BMI  $\geq$  25 kg/m<sup>2</sup> and a low pretest probability (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m<sup>2</sup>
    - ii. The patient has a low pre-treatment IGF-1 (between 0 to 2 SD below the mean for age and gender)
    - iii. Current IGF-1 level is not elevated for age and gender
  - b. The patient meets all of the following:

- i. The patient has had 1 pretreatment pharmacologic provocative GH test that demonstrated deficient GH responses defined as one of the following:
  - 1. Insulin tolerance test (ITT) or another provocative GH test with a peak GH level  $\leq$  5 ng/mL
  - 2. Macrilen with a peak GH level less than 2.8 ng/mL
  - 3. Glucagon stimulation test with a peak GH level  $\leq$  3 ng/mL in patients with a body mass index (BMI) less than or equal to 30 kg/m<sup>2</sup> and a high pretest probability (e.g., acquired structural abnormalities) OR a BMI less than 25 kg/m<sup>2</sup>
  - 4. Glucagon stimulation test with a peak GH level  $\leq$  1 ng/mL in patients with a BMI  $\geq$  25 kg/m<sup>2</sup> and a low pretest probability (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m<sup>2</sup>
- ii. The patient has a pretreatment IGF-1 level that is more than 2 SD below the mean
- iii. Current IGF-1 level is not elevated for age and gender
- c. The patient meets both of the following:
  - i. The patient has organic hypothalamic-pituitary disease (e.g., suprasellar mass with previous surgery and cranial irradiation) with  $\geq$  3 documented pituitary hormone deficiencies [refer to Appendix B] and a low pre-treatment IGF-1 more than 2 standard deviations below the mean for age and gender
  - ii. Current IGF-1 level is not elevated for age and gender
- d. The patient has documented genetic or structural hypothalamic-pituitary defects (refer to Appendix A) and current IGF-1 level is not elevated for age and gender
- e. The patient has childhood-onset GH deficiency and a documented congenital abnormality of the CNS, hypothalamus or pituitary (refer to Appendix A) and current IGF-1 level is not elevated for age and gender

XII. The continuation of growth hormone therapy may be considered **medically necessary** for the treatment of HIV-Associated Wasting/Cachexia when ALL of the following criteria are met:

- a. Patient is diagnosed with HIV-associated wasting/cachexia
- b. Patient is currently on antiretroviral therapy
- c. Current BMI is less than 27 kg/m<sup>2</sup>

**Approval is for 12 weeks.**

Growth Hormone Therapy is considered **not medically necessary** for patients who do not meet the criteria set forth above.

Quantity Limits Apply

Product	Quantity Limit
Sogroya 1.5 mL prefilled pen	4 per 28 days

**APPENDIX**

**Appendix A: Examples of Hypothalamic/Pituitary/CNS Disorders**

- 1. Congenital genetic abnormalities
  - a. Transcription factor defects (PIT-1, PROP-1, LHX3/4, HESX-1, PITX-2)
  - b. Growth hormone releasing hormone (GHRH) receptor gene defects
  - c. GH secretagogue receptor gene defects
  - d. GH gene defects
  - e. GH receptor/post receptor defects



2. Congenital structural abnormalities
  - a. Optic nerve hypoplasia/septo-optic dysplasia
  - b. Agenesis of corpus callosum
  - c. Empty sella syndrome
  - d. Ectopic posterior pituitary
  - e. Pituitary aplasia/hypoplasia
  - f. Pituitary stalk defect
  - g. Holoprosencephaly
  - h. Encephalocele
  - i. Hydrocephalus
  - j. Anencephaly or prosencephaly
  - k. Arachnoid cyst
  - l. Other mid-line facial defects (e.g., single central incisor, cleft lip/palate)
  - m. Vascular malformations
3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
  - a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma/astrocytoma, pituitary adenoma, germinoma)
  - b. Cysts (Rathke cleft cyst or arachnoid cleft cyst)
  - c. Surgery
  - d. Radiation
  - e. Chemotherapy
  - f. CNS infections
  - g. CNS infarction (e.g., Sheehan's syndrome)
  - h. Inflammatory processes (e.g., autoimmune hypophysitis)
  - i. Infiltrative processes (e.g., sarcoidosis, histiocytosis)
  - j. Head trauma/traumatic brain injury
  - k. Aneurysmal subarachnoid hemorrhage
  - l. Perinatal or postnatal trauma
  - m. Surgery of the pituitary or hypothalamus

#### **Appendix B: Pituitary Hormones (Other than Growth Hormone)**

1. Adrenocorticotropic hormone (ACTH)
2. Antidiuretic hormone (ADH)
3. Follicle stimulating hormone (FSH)
4. Luteinizing hormone (LH)
5. Thyroid stimulating hormone (TSH)
6. Prolactin

#### **Appendix C: Requirements for GH-Stimulation Testing in Adults**

1. Testing for adult GHD is not required
  - a. Three or more pituitary hormone deficiencies and low IGF-1
  - b. Congenital structural abnormalities
    - i. Transcription factor defects (PIT-1, PROP-1, LHX3/4, HESX-1, PITX-2)
    - ii. GHRH receptor-gene defects
    - iii. GH-receptor/post-receptor defects
    - iv. GH-gene defects associated with brain structural defects
    - v. Single central incisor
    - vi. Cleft lip/palate
  - c. Acquired causes such as perinatal insults
2. Testing for adult GHD is required
  - a. Acquired
    - i. Skull-base lesions
    - ii. Pituitary adenoma



- iii. Craniopharyngioma
- iv. Rathke's cleft cyst
- v. Meningioma
- vi. Glioma/astrocytoma
- vii. Neoplastic sellar and parasellar lesions
- viii. Chordoma
- ix. Hamartoma
- x. Lymphoma
- xi. Metastases
- xii. Other brain injury
- xiii. Traumatic brain injury
- xiv. Sports-related head trauma
- xv. Blast injury
- xvi. Infiltrative/granulomatous disease
- xvii. Langerhans cell histiocytosis
- xviii. Autoimmune hypophysitis (primary or secondary)
- xix. Sarcoidosis
- xx. Tuberculosis
- xxi. Amyloidosis
- b. Surgery to the sella, suprasellar, and parasellar region
- c. Cranial irradiation
- d. Central nervous system infections (bacteria, viruses, fungi, parasites)
- e. Infarction/hemorrhage (e.g., apoplexy, Sheehan's syndrome, subarachnoid hemorrhage, ischemic stroke, snake bite)
- f. Empty sella
- g. Hydrocephalus
- h. Idiopathic

#### Appendix D: Calculation of BMI

$$\text{BMI} = \frac{\text{Weight (pounds)} \times 703}{[\text{Height (inches)}]^2} \quad \text{OR} \quad \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}$$

BMI classification:	Underweight	< 18.5 kg/m <sup>2</sup>
	Normal weight	18.5 – 24.9 kg/m <sup>2</sup>
	Overweight	25 – 29.9 kg/m <sup>2</sup>
	Obesity (class 1)	30 – 34.9 kg/m <sup>2</sup>
	Obesity (class 2)	35 – 39.9 kg/m <sup>2</sup>
	Extreme obesity (class 3)	≥ 40 kg/m <sup>2</sup>

#### PROCEDURES AND BILLING CODES

**To report provider services, use appropriate CPT\* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD-CM diagnostic codes.**

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