BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

GROWTH HORMONE THERAPY:
GENOTROPIN® (somatropin) subcutaneous injection
HUMATROPE® (somatropin) subcutaneous injection
NGENLA® (somatrogon-ghla) subcutaneous injection
NORDITROPIN® (somatropin) subcutaneous injection
NUTROPIN AQ® (somatropin) subcutaneous injection
OMNITROPE® (somatropin) subcutaneous injection
SAIZEN® (somatropin) subcutaneous injection
SEROSTIM® (somatropin) subcutaneous injection
SKYTROFA™ (lonapegsomatropin-tcgd) subcutaneous injection
SOGROYA® (somapacitan-beco) subcutaneous injection
ZOMACTON® (somatropin) subcutaneous injection
ZORBTIVE® (somatropin) subcutaneous injection

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

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PHARMACY COVERAGE GUIDELINE

GROWTH HORMONE THERAPY

Criteria:

Section A. Applies for all indications and uses:

- **Criteria for initial therapy:** Growth Hormone injection is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in or is in consultation with an Endocrinologist, Nephrologist, Infectious Disease, or Trauma/Burn Surgery depending upon indication or use

  2. Individual meets **other initial criteria** per indication or use as described below in Sections B-G below
     a. See section B – Growth Hormone Deficiency under 18 years of age
     b. See section C – Growth Hormone Deficiency 18 years of age and older
     c. See section D – Burns
     d. See section E – HIV/AIDS Wasting Syndrome
     e. See section F – Short Bowel Syndrome
     f. See section G – Small for Gestational Age
     g. See section H – Idiopathic Short Stature

  3. Age of individual is consistent with requested FDA product label

  4. Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for **ALL** of the following:
     a. Genotropin
     b. Norditropin
     c. Omnitrope

  5. Growth hormone and growth hormone analogs will not be used in combination with each other or in combination with Increlex (mecasermin)

  6. There are **NO** FDA-label contraindications (see Definitions section)

- **Criteria for continuation of coverage (renewal request):** Growth Hormone injection is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

  1. Individual continues to be seen by a physician specializing in or is in consultation with an Endocrinologist, Nephrologist, Infectious Disease, or Trauma/Burn Surgery depending upon indication or use

  2. Meets other continuation criteria per indication or use as described in Sections B-G below
     a. See section B – Growth Hormone Deficiency under 18 years of age
     b. See section C – Growth Hormone Deficiency 18 years of age and older
     c. See section D – Burns
     d. See section E – HIV/AIDS Wasting Syndrome
     e. See section F – Short Bowel Syndrome
     f. See section G – Small for Gestational Age
     g. See section H – Idiopathic Short Stature

3. Individual has been adherent with the medication

4. Growth hormone and growth hormone analogs will not be used in combination with each other or in combination with Increlex (mecasermin)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Section B. Growth Hormone Deficiency for Individuals *Under* 18 Years of Age:

- **Criteria for initial therapy:** Initial course of treatment of Growth Hormone injection therapy for **individuals under 18 years of age** may be considered ***medically necessary*** with documentation of the following:

1. Individual meets **other initial criteria** as described in Section A above

2. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Individual with ***suspected growth hormone deficiency*** (GHD) with **ALL** of the following:
        i. There is documentation of **ONE** of the following:
            1. Individual has no evidence of other pituitary deficiency (**Note:** documentation requires two subnormal growth hormone stimulation tests for diagnosis)
            2. Individual has one subnormal growth hormone stimulation test **AND** has IGF-1 levels below normal for age and gender matched individual below (see Definitions section)
            3. Individual has a hypothalamic pituitary defect (such as a major congenital malformation, tumor, surgery, irradiation, or trauma) **AND** has a deficiency in at least **one** additional pituitary hormone
        ii. There is marked short stature (more than 2.5 standard deviations [SD] below the mean)
        iii. There is marked growth failure (height velocity less than the 25th percentile for age) or there is more moderate degrees of short stature and growth failure **with** decelerating growth
        iv. There is moderately or severely reduced IGF-1 (e.g., SD <-2) **with** delayed bone age (bone age is less than individual's chronological age)

    b. Individual with ***proven growth failure due to growth hormone deficiency (GHD)*** as documented by **ALL** of the following:
        i. Bone age is less than the individual's chronological age and gender (14 years for females, 16 years for males)
        ii. Insulin-like growth factor 1 (IGF-1) is subnormal for age as indicated by the table in the Description Section

iii. The individual growth/height velocity is 2 SD below age-appropriate mean less than for age and gender
iv. **ONE** of the following:
1. There is documentation of destructive pituitary lesion or GHD is a result of treatment (e.g., irradiation, surgery), congenital anomaly, central nervous system pathology of the pituitary or hypothalamus, tumor, or multiple pituitary hormone deficiencies
2. Has at least **one** provocative growth hormone (GH) stimulation tests with a peak serum growth hormone value of less than 5 ng/mL after GH stimulation (**Note: This is not needed in an** infant or young child with congenital and severe GHD with extreme short stature (e.g., height < -3 SD), significantly reduced IGF-1 (e.g., < -2 SD) and IGFBP-3, and delayed bone age)

c. Growth Hormone Deficiency due to congenital hypopituitarism in a *newborn* with **ALL** of the following:
i. Documentation of hypoglycemia associated with growth hormone levels <5 ng/mL
ii. **ONE** of the following:
1. Documentation of deficiency of at least **one** additional pituitary hormone
2. Imaging to support a pituitary defect (such as ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk)

d. Individual with growth failure/short stature and **ALL** of the following**:**
i. Diagnosis is **ONE** of the following**:**
1. Noonan Syndrome
2. Short stature homeobox-containing gene (SHOX) deficiency
3. Turners Syndrome (defined as 45, XO genotype)
ii. Has a recent (within the last 12 months) radiographic evidence of open epiphyses
iii. Height is at least two standard deviations below the mean for individual's chronologic age and gender
iv. Growth velocity for at least 6 months is abnormal

e. Individual with chronic kidney disease (CKD) and **ALL** of the following:
i. Growth failure/short stature (height velocity Z-score less than -1.88 or height velocity for age less than 3rd percentile persisting beyond 3-months)
ii. Has stage 3 to 5 CKD, is on dialysis, or has undergone kidney transplantation
iii. Has a recent (within the last 12 months) radiographic evidence of open epiphyses

f. Individual with growth failure/short stature due to ***Prader-Willi Syndrome*** in the absence of severe obesity, uncontrolled diabetes, upper airway obstruction or sleep apnea or severe respiratory impairment by sleep study

Initial approval duration: If approved, may be authorized for a maximum of 12 months

- **Criteria for continuation of coverage (renewal request):** Continuing or repeat courses of treatment of Growth Hormone injection therapy for individuals **under 18 years of age** are considered ***medically necessary*** with documentation that the individual has been compliant with treatment **and** documentation of the following **(samples are not considered for continuation of therapy)**:

1. Individual meets other continuation criteria as described in Section A above

2. Individual's condition responded while on therapy with response defined as the following:
   a. For proven GHD, Noonan syndrome, Prader-Willi syndrome, short stature in CKD, SHOX deficiency, or Turner's syndrome:
   b. Height has increased at least 2-5 cm/year over the previous year (previous height and date test was done and current height and date test was done must be sent)
   c. Has not reached expected adult height (expected height goal must be sent)
   d. Recent (within the last 12 months) radiographic evidence epiphyses have not closed

Renewal duration: If approved, may be authorized for a maximum of 12 months per request

Section C. Growth Hormone Deficiency for Individuals 18 Years of Age and Older:

- **Criteria for initial therapy: Initial course of treatment** Growth Hormone injection therapy for individuals **18 years of age and older** may be considered ***medically necessary*** with documentation of the following:

1. Meets **other initial criteria** as described in Section A above

2. Individual has a confirmed diagnosis of **ONE** of the following:
   a. Individual with ***suspected adult-onset GHD*** where GHD is a result of an **unknown etiology** **and** individual has **BOTH** of the following:
      i. Individual has a serum insulin-like growth factor 1 (IGF-1) less than the lower limit of normal for the assay that was used
      ii. Individual has subnormal response to **two** growth hormone stimulation tests

   b. Individual with ***suspected adult-onset GHD*** where GHD is the result of a **defined etiology** such as destructive hypothalamic or pituitary disease, radiation therapy, surgery or trauma **and** individual has **BOTH** of the following:
      i. Individual has a serum insulin-like growth factor 1 (IGF-1) less than the lower limit of normal for the assay that was used
      ii. Individual has subnormal response to **one** growth hormone stimulation tests

   c. Individual with ***proven childhood-onset GHD*** (acquired or idiopathic) and received growth hormone during childhood who is transitioning to adulthood there is documentation of **ALL** of the following:
      i. GHD is **ONE** of the following:
         1. GHD was caused by genetic defect, structural cause, organic cause (surgery, radiation, tumor, or multiple (3 or more) pituitary hormone deficiency), no further growth hormone stimulation retesting needed
         2. GHD was **NOT** due to genetic defect, structural cause, organic cause (surgery, radiation, tumor, or multiple (3 or more) pituitary hormone deficiency), **and** individual has subnormal response to **one** growth hormone stimulation tests to determine if on-going replacement therapy is needed
      ii. Serum insulin-like growth factor 1 (IGF-1) is below -2 standard deviations from the mean, which was done while **off growth hormone for 1-month**

d. Individual with ***congenital/genetic growth hormone deficiency*** such as Noonan syndrome, Prader-Willi Syndrome, short stature homeobox-containing gene (SHOX) deficiency, or Turner's syndrome **and** whose epiphyses have **NOT** closed, no growth hormone stimulation testing required

e. Individual with ***multiple (3 or more) pituitary hormone deficiencies other than growth hormone*** (i.e., TSH, ACTH, LH, FSH, AVP), no growth hormone stimulation testing needed

Initial approval duration: If approved, may be authorized for a maximum of 12 months.

- **Criteria for continuation of coverage (renewal request): Continuing or repeat courses of treatment** of Growth Hormone injection therapy for individuals **18 years of age and older** are considered ***medically necessary*** with documentation that the individual has been compliant with treatment **and** documentation of the following **(samples are not considered for continuation of therapy)**:

1. Individual meets other continuation as described in Section A above

2. Individual's condition has responded while on therapy with response defined as **ONE** of the following:
   a. Individual with proven childhood-onset GHD (acquired or idiopathic or received growth hormone in childhood) or suspected adult-onset GHD and historical documentation in the clinical record of **two** abnormal provocative stimulation tests
   b. Individual with surgery, irradiation or trauma involving the hypothalamus or pituitary gland or other diseases of the pituitary or hypothalamus and has historical clinical records of **one** abnormal provocative stimulation test
   c. Individual with multiple pituitary hormone deficiencies other than growth hormone (i.e., TSH, ACTH, LH and/or FSH, AVP) **and** serum insulin-like growth factor 1 (IGF-1) level is within but not higher than the age and gender-specific range of normal to avoid over-replacement
   d. Individual with congenital/genetic growth hormone deficiency such as Noonan syndrome, Prader-Willi Syndrome, short stature homeobox-containing gene (SHOX) deficiency, or Turner's syndrome

3. Clinical records document that without ongoing treatment with growth hormone (GH), signs or symptoms of GH deficiency would reappear, or if a gap in treatment occurred, low GH levels or signs and symptoms of GH deficiency reappeared

Renewal duration: If approved, may be authorized for a maximum of 12 months per request

Section D. Burns:

- **Criteria for initial therapy:** Growth Hormone injection therapy is considered ***medically necessary*** for the treatment of severe burns with documentation of **ALL** the following:

1. Meets **other initial criteria** per indication or use as described in Section A above

2. Individual has a confirmed diagnosis of **ONE** of the following:
   a. Individual with extensive 3rd degree burns showing difficulty with wound healing

b. To prevent growth delay in a child with severe burns that cover at least 40% of total body surface area

Approval duration: For up to 1 year after the burn

Section E. HIV/AIDS Wasting (Serostim only):

- **Criteria for initial therapy: Serostim** for the treatment of HIV/AIDS wasting syndrome or cachexia is considered ***medically necessary*** with documentation of **ALL** of the following:

1. Individual meets **other initial criteria** as described in Section A above
2. There is **ONE** of the following:
   a. Unintentional/involuntary weight loss of at least 10% of ideal (standard) body weight for height and weight (See women's/men's weight at different ages charts in Definitions section) within the last 12 months.)
   b. Unintentional/involuntary weight loss to a BMI of < 20 kg/m^2
3. Individual's weight loss is **not** explained by another concurrent illness other than HIV/AIDS infection
4. Individual has continued weight loss despite adequate nutrition and other measures
5. Individual is currently receiving optimal antiretroviral drug therapy for HIV/AIDS
6. Agent will not be used as intermittent therapy for maintenance
7. Individual has failure, contraindication per FDA label, intolerance, or not a candidate for megestrol or dronabinol

Initial approval duration: 12 weeks

- **Criteria for continuation of coverage (renewal request): Serostim** for the treatment of HIV/AIDS wasting syndrome or cachexia is considered ***medically necessary*** with documentation of **ALL** of the following **(samples are not considered for continuation of therapy)**:

1. Individual meets other continuation criteria as described in Section A above
2. Individual's condition has responded while on therapy with response defined as weight loss has improved, or weight has stabilized during the initial 12 weeks but target body mass index or target weight has not been achieved and needs continued therapy
3. Individual is currently receiving optimal antiretroviral drug therapy for HIV/AIDS
4. Agent will not be used as intermittent therapy for maintenance

Renewal duration: Total course: 48 weeks (includes the duration of use under Initial approval)

Section F. Short Bowel Syndrome (Zorbtive only):

- **Criteria for therapy: Zorbtive** for the treatment of short bowel syndrome is considered ***medically necessary*** with documentation of **ALL** of the following:

  1. Individual meets **other initial criteria** as described in Section A above

  2. Individual has documentation of **ONE** of the following:
     a. At least 50% of the small intestine has been removed
     b. Individual has malabsorption, diarrhea, fluid and electrolyte disturbances, and malnutrition due to short bowel syndrome

  3. Individual is on concurrent specialized nutritional support (i.e., high-carbohydrate, low-fat diet adjusted for individual patient requirements, enteral feedings, parenteral nutrition, fluid, and micronutrient supplements)

  4. There is **NO** history of previous use of Zorbtive for 4 weeks for short bowel syndrome

  Approval duration: Single 4-week course only

Section G. Small for Gestational Age (SGA):

- **Criteria for initial therapy:** Growth Hormone injection therapy is considered ***medically necessary*** for the treatment of individuals 2 years of age who are small for gestational age with documentation of **ALL** the following:

  1. Individual meets **other initial criteria** as described in Section A above

  2. Individual's diagnosis must be confirmed by weight and/or length *at birth* that is 2 standard deviations or more below the mean for gestational age and gender (See WHO Growth Charts Definitions section)

  3. Individual at age 2 years has not manifested catch-up growth documented by a current height remaining at 2 standard deviations or more below the mean for age and gender

  4. For individuals over the age of 12 years there is recent (within the last 12 months) radiographic evidence that the epiphyses are still open

  5. Individual has documentation of goal for expected height

  Initial approval duration: If approved, may be authorized for a maximum of 12 months

- **Criteria for continuation of coverage (renewal request):** Growth Hormone injection therapy is considered ***medically necessary*** for the treatment of individuals 2 years of age who are small for gestational age with documentation of **ALL** the following **(samples are not considered for continuation of therapy)**:

  1. Individual meets other continuation criteria as described in Section A above

2. Individual's condition has responded while on therapy with response defined as **BOTH** of the following:
    a. Height has increased at least 2 cm/year over the previous year (date previous height was reached and date current was height reached must be sent)
    b. Individual has not reached expected adult height (expected height goal must be sent)

3. For individuals over the age of 12 years there is recent (within the last 12 months) radiographic evidence that the epiphyses are still open

Renewal duration: If approved, may be authorized for a maximum of 12 months per request

Section H. Idiopathic Short Stature (ISS):

- **Growth Hormone injection therapy for treatment of *idiopathic short stature***, without documentation of growth hormone deficiency or underlying pathology is a ***benefit plan exclusion*** and ***not eligible for coverage***.

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

    1. **Off-Label Use of Non-Cancer Medications**

    2. **Off-Label Use of Cancer Medications**

Description:

Somatropin is a synthetically produced growth hormone (GH). Somatropin is indicated for the treatment of growth hormone deficiency (GHD), short stature associated with Turner syndrome (TS) or Noonan syndrome (NS), short-stature homeobox (SHOX) gene deficiency, growth failure due to Prader-Willi syndrome (PWS), short stature in children born small for gestational age (SGA), growth failure in children with chronic renal insufficiency (CRI) or chronic kidney disease (CKD) up to the time of transplant, idiopathic short stature (ISS), to promote wound healing in burns, short bowel syndrome (SBS) in patients receiving specialized nutritional support, and HIV-associated wasting. Somatropin is also indicated for replacement of endogenous growth hormone in adults with confirmed GHD. Short stature, such as in idiopathic short stature (ISS) and in small for gestational age (SGA), in the absence of defined pathology is not a sickness or injury; growth hormone is not a covered health service for these indications.

Growth Hormone Deficiency (GHD) is defined as the inadequate secretion of endogenous growth hormone. GHD may be idiopathic or organic and can occur in childhood or adulthood. Pathophysiology differs between the two onsets. GHD is diagnosed through a combination of clinical and biochemical examination, testing and analysis.

Children with GHD generally present with short stature and growth velocity that is two (2) standard deviations below the mean for chronologic age, sex and pubertal stage. Often the etiology is isolated idiopathic GHD.

GHD in adults often results from conditions affecting the hypothalamus or pituitary gland including surgery and radiation therapy. Adults frequently report symptoms such as unintentional weight gain or difficulty losing weight, low energy, reduced physical performance, decreased libido, impaired psychological well-being and a feeling that

things are not right. Physical findings may include increased fat mass, decreased lean body and muscle mass, decreased bone density as well as reduced muscle strength and exercise capacity. There is however no single symptom or sign that is pathognomonic for GHD in adults. In addition, some adults with GHD may be entirely asymptomatic.

Growth Hormone (GH) provocative stimulation test is one of the procedures that may be performed to diagnose growth hormone deficiency (GHD). A provocative agent is used to stimulate the pituitary gland to secrete GH. The intent is to determine the maximum peak GH response from the provocative agent. The peak is the value used to determine whether the response is considered normal or abnormal for the purpose of supporting the diagnosis of GHD. Serum levels may be measured by radioimmunoassay (RIA) or immunoradiometric assay (IRMA).

GH secretion is pulsatile. There are approximately 10 pulses of GH secretion per day, lasting approximately 90 minutes and separated by roughly 128 minutes. Nearly 50% of samples collected during the day in normal subjects have undetectable serum GH concentrations. In addition, GH is undetectable in over 95% of samples in obese or older subjects.

Baseline testing is performed prior to administration of the provocative agent and frequent blood sampling is done thereafter. Sampling occurs approximately 30, 60, 90, 120 and 180 minutes after provocative agent administration. Sampling defines the “curve” of the response (going from a lower GH value prior to provocation to the highest, or peak, GH value after provocation and then a drop from peak) and must provide sufficient information to determine a peak value.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Adult: Age 18 years and older

Growth hormone and growth hormone analogs:
- Human growth hormone (hGH):
  - Somatropin products:
    - Genotropin – preferred product
    - Humatrope
    - Ngenla (somatrogon-ghla)
    - Norditropin – preferred product
    - Nutropin AQ
    - Omnitrope – preferred product
    - Saizen
    - Serostim
    - Skytrofa (lonapegsomatropin-tcgd) – pegylated prodrug of hGH
    - Sogroya (somapacitan-beco)
    - Zomacton
    - Zorbtive

Contraindications to use of hGH and hGH analogs include:
- Active malignancy
- Active proliferative or severe non-proliferative diabetic retinopathy

- Acute critical illness in response to open heart surgery, abdominal surgery, multiple accidental trauma, or acute respiratory failure
- Growth promotion in pediatric individuals with closed epiphysis
- Pediatric individuals with Prader-Willi syndrome who are severely obese or have history of upper airway obstruction or sleep apnea or have severe respiratory impairment by determined by sleep study
- Known hypersensitivity to the drug or any diluent (benzyl alcohol, m-cresol) or any other ingredient of the formulation

Growth Hormone (GH) Provocative Stimulation Tests:
- Arginine HCL Test
- Arginine/L-Dopa Test
- Clonidine Test
- Glucagon Stimulation Test
- Growth Hormone Releasing Hormone Test (GHRH)
- Insulin Tolerance Test (ITT) or Insulin Induced Hypoglycemic Test
- L-Dopa Test
- Propranolol / Glucagons Test
- Physiological: sleep-induced or exercise-induced stimulation
- Macimorelin: a ghrelin agonist

Insulin-Like Growth Factor 1 (IGF-1):
A hormone created mainly by the liver that mediates most of the effects of growth hormone. IGF-1 blood tests may be used in the diagnosis of growth hormone deficiency.

AGE	SUBNORMAL RESULT
7 years [1]	Less than 52 ng/mL
8 through 10 years	Less than 75 ng/mL
11 through 12 years	Less than 127 ng/mL
13 through 17 years	Less than 212 ng/mL

[1] Limited safety and efficacy data are available below the age of 7.

Insulin-Like Growth Factor Binding Protein (IGFBP-3):
The transport protein for IGF-1 and IGF-2 in the circulation. It modulates IGF activity and inhibits cell growth. Its levels increase in the presence of IGF-I, insulin and other growth-stimulating factors such as growth hormone. IGFBP-3 blood tests may be used in the diagnosis of growth hormone deficiency.

AGE	SUBNORMAL RESULT	AGE	SUBNORMAL RESULT
7 years [1]	Less than 1.4 mg/L	13 years	Less than 3.1 mg/L
8 years	Less than 1.6 mg/L	14 years	Less than 3.1 mg/L
9 years	Less than 1.8 mg/L	15 years	Less than 3.5 mg/L
10 years	Less than 2.1 mg/L	16 years	Less than 3.4 mg/L
11 years	Less than 2.4 mg/L	17 years	Less than 3.2 mg/L
12 years	Less than 2.7 mg/L		

[1] Limited safety and efficacy data are available below the age of 7.

Functional Impairment:
A state in which the normal or proper action (function) of any body part or organ is damaged or deficient because of growth hormone deficiency.

Burn evaluation:
Extent of total body surface area expressed as a percent
- Rule of 9s for adult:
  - Head 9%

  - Each arm 9%
  - Anterior chest and abdomen 18%
  - Posterior chest and back 18%
  - Each leg 18%
  - Perineum 1%
- Rule of 9s for child:
  - Head 18%
  - Each leg 13.5%
  - Then the rest as above

Depth of burn, estimates the depth of burn affecting the outer epidermis and dermis:

- First degree: superficial, only involves the epidermis
- Second degree: partial thickness, extends through the epidermis and into the dermis
- Third degree: full thickness, extends through the epidermis, into the dermis and into the subcutaneous fat
- Fourth degree: damage the underlying bones, muscles, and tendons

Short Bowel Syndrome:
A malabsorption syndrome resulting from surgical removal of at least 50% of the small intestine. According to the American Gastroenterological Association, SBS is a disorder that is defined clinically as malabsorption, diarrhea, fluid and electrolyte disturbances, and malnutrition. In SBS there is functional or anatomical loss of extensive segments of the small intestines, with resultant compromised absorptive capacity.

Idiopathic Short Stature (ISS):
ISS (also known as non-growth hormone-deficient short stature) is extreme short stature that does not have a diagnostic explanation after a growth evaluation documenting normal physical function and normal lab tests. ISS includes short stature without documentation of growth hormone deficiency and children are identified as being abnormally short. ISS may also be referred to as short stature of undefined cause.

Small for gestational age (SGA):
A term used to describe a baby who is smaller than the usual amount for the number of weeks of pregnancy. SGA is commonly defined as a weight below the 10th percentile for the gestational age.

Abnormally Short:
Boys: Height predicted to be shorter than 5 feet 3 inches
Girls: Height predicted to be shorter than 4 feet 11 inches

Z-height score:
A conversion of height/length that represents the number of standard deviations (SD) from the mean height for age and gender. A child with a height Z-score <-1.88 has short stature.

Growth or height velocity:
Growth or height velocity, the change in growth over time, a more sensitive index of growth than a single measurement. Current height/length measures are compared with previous growth points to determine the interval growth/height velocity.

PHARMACY COVERAGE GUIDELINE

GROWTH HORMONE THERAPY

WHO Growth Charts and Calculators:

Weight-for-length/height

https://reference.medscape.com/guide/medical-calculators

Body weight for height charts for women and men:

WEIGHT FOR WOMEN AT DIFFERENT AGES									
	Age 18 to 29			Age 30 to 44			Age 45 to 65		
Height	25%		40%	25%		40%	25%		40%
	UW	SW	OW	UW	SW	OW	UW	SW	OW
4'11"	85	113	158	89	119	167	95	126	176
5'0"	86	114	160	92	122	171	97	129	181
5'1"	87	116	162	93	124	174	99	132	185
5'2"	89	118	165	95	127	178	101	135	189
5'3"	92	122	171	98	131	183	104	139	195
5'4"	94	125	175	101	134	188	107	143	200
5'5"	96	128	179	104	139	195	111	148	207
5'6"	99	132	185	107	143	200	114	152	213
5'7"	101	135	189	110	147	206	116	155	217
5'8"	105	140	196	113	151	211	119	159	223
5'9"	108	144	202	116	155	217	123	164	230
5'10"	110	147	206	119	159	223	126	168	235
5'11"	112	149	209	122	163	228	129	172	241
6'0"	113	151	211	125	167	234	132	176	246
6'1"	115	153	214	127	169	237	135	180	252
6'2"	116	155	217	128	171	239	138	184	258

Legend: UW: underweight SW: standard weight OW: overweight

WEIGHT FOR MEN AT DIFFERENT AGES									
	Age 18 to 29			Age 30 to 44			Age 45 to 65		
Height	25%		40%	25%		40%	25%		40%
	UW	SW	OW	UW	SW	OW	UW	SW	OW
5'0"	94	125	175	98	131	183	101	134	188
5'1"	95	126	176	99	132	185	102	136	190
5'2"	96	128	179	100	133	186	104	138	193
5'3"	98	131	183	102	136	190	106	141	197
5'4"	101	135	189	105	140	196	109	145	203
5'5"	104	138	193	107	143	200	112	149	209
5'6"	107	142	199	110	147	206	115	153	214
5'7"	110	147	206	114	152	213	119	158	221
5'8"	113	151	211	118	157	220	122	163	228
5'9"	116	155	217	122	162	227	126	168	235
5'10"	119	159	223	125	167	234	130	173	242
5'11"	123	164	230	130	173	242	134	178	249
6'0"	128	170	238	134	179	251	137	183	256
6'1"	133	177	248	139	185	259	142	189	264
6'2"	138	184	258	145	193	270	146	194	272
6'3"	143	190	266	149	198	277	150	200	280
6'4"	147	196	274	152	203	284	155	206	288
6'5"	151	201	281	155	207	290	158	211	295
6'6"	155	206	288	158	211	295	162	216	302
6'7"	157	209	293	161	215	301	166	221	309

PHARMACY COVERAGE GUIDELINE

GROWTH HORMONE THERAPY

6'8"	161	214	300	164	219	307	170	226	316

Legend: UW: underweight SW: standard weight OW: overweight

Summary of FDA-approved indications: Growth hormone and Growth hormone analogs

	Genotropin	Humatrope	Ngenla	Norditropin	Nutropin AQ	Omnitrope	Saizen	Serostim	Skytrofa	Sogroya	Zomacton †
Condition											
Adult GHD [a]	✓	✓		✓	✓	✓	✓			✓	✓
Pediatric GHD [b]	✓	✓	✓	✓	✓	✓	✓		✓		✓
Growth failure with CKD [c]					✓						
Idiopathic short stature (ISS) [d]	✓	✓		✓	✓	✓					✓
Noonan syndrome (NS)				✓							
Prader-Willi syndrome (PWS)	✓			✓		✓					
Short bowel syndrome (SBS)											
SHOX deficiency [e]		✓									✓
Turner syndrome (TS)	✓	✓		✓	✓	✓					✓
Small for gestational age (SGA)	✓ [g]	✓ [h]		✓ [h]		✓ [g]					✓
Wasting or cachexia in adults with HIV [f]								✓			

[a] Adult Growth hormone deficiency **(GHD) may be either**: (1) ***adult-onset*** (patients who have GHD, either alone or associated with multiple hormone deficiencies [hypopituitarism], as a result of pituitary disease, hypothalamic disease, surgery, radiation, or trauma) or (2) ***childhood-onset*** (patients who were GHD during childhood as a result of congenital, genetic, acquired, or idiopathic causes). *Patients who were treated with somatropin for GHD in childhood and whose epiphyses are closed should be reevaluated before continuation of somatropin* therapy at the reduced dose level recommended for GHD adults. According to current standards, confirmation of the diagnosis of adult growth hormone deficiency in **both** of the above **groups** involves an appropriate growth hormone provocative test with **two exceptions**: (1) patients with multiple other pituitary hormone deficiencies due to organic disease (ex., damage to the hypothalamic-pituitary region by lesions, surgery and/or radiation); and (2) patients with congenital/genetic growth hormone deficiency

[b] Caused by an inadequate secretion of endogenous growth hormone

[c] CKD = chronic kidney disease. Use until time of renal transplantation & in conjunction with optimal management of CKD.

[d] Also called non-growth hormone-deficient short stature (defined by height standard deviation score [SDS] less than or equal to −2.25) and associated with growth rates unlikely to permit attainment of adult height in the normal range in pediatric patients whose epiphyses are not closed and for whom diagnostic evaluation excludes other causes associated with short stature that should be observed or treated by other means.

[e] SHOX = short stature homeobox-containing gene

[f] Concomitant antiretroviral therapy is necessary

[g] For children who fail to manifest catch-up growth by 2 years of age

[h] For children with no catch-up growth by 2 to 4 years of age

† Brand Tev-Tropin was renamed to Zomacton

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