GROWTH HORMONE THERAPY

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:

Somatotropin is a synthetically produced growth hormone (GH). It has been used in the treatment of growth hormone deficiency, Noonan, Turner and Prader-Willi Syndromes, to promote wound healing in burns, for AIDS wasting and for short bowel syndrome. It has also been investigated as a treatment for other conditions.
GROWTH HORMONE THERAPY (cont.)

Description: (cont.)

Growth Hormone Deficiency (GHD):
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:
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.

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:
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. This 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).

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.

Examples of this test are:

- Arginine HCL Test
- Arginine/L-Dopa Test
- Clonidine Test
- Glucagon Stimulation Test
- Growth Hormone Releasing Hormone Test (Geref)
- Insulin Tolerance Test (ITT) or Insulin Induced Hypoglycemic Test
- L-Dopa Test
- Propranolol/Glucagons Test
- Physiological: Sleep-induced or exercise-induced stimulation
GROWTH HORMONE THERAPY (cont.)

Description: (cont.)

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

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. Idiopathic short stature includes short stature without documentation of growth hormone deficiency and children identified as abnormally short. ISS may also be referred to as short stature of undefined cause.

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.

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-1, insulin and other growth-stimulating factors such as growth hormone. IGFBP-3 blood tests may be used in the diagnosis of growth hormone deficiency.

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

Short Bowel Syndrome:
Malabsorption syndrome resulting from surgical removal of at least 50% of the small intestine.

Definitions:

Adult: Age 18 years and older

Preferred Growth Hormone Therapy Medication:
- Nutropin AQ®

Significant Adverse Drug Event:
A significant adverse drug event is when an individual’s outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or permanent change, impairment, damage or disruption in the individuals’ body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.
GROWTH HORMONE THERAPY (cont.)

Criteria:

➢ FDA-approved dosage of Genotropin, Humatrope, Norditropin, Omnitrope, Saizen, and Zomacton are considered **medically necessary** with documentation of **ALL** of the following:

1. Failed response to the preferred growth hormone therapy medication Nutropin AQ (unless otherwise contraindicated or not labeled for the indication being prescribed, (refer to, “Growth Hormone Therapy Chart” Administrative Procedure Guideline) with documentation of **ANY** of the following:
   - Individual’s condition has not improved or has worsened
   - Individual experienced a significant adverse drug event to the preferred GH medication
   - Individual is intolerant to the preferred GH medication
   - Individual is non-adherent to the preferred GH medication

2. Absence of **ALL** of the following contraindications:
   - Active malignancy
   - Active proliferative or severe non-proliferative diabetic retinopathy
   - Acute critical illness
   - Growth promotion in pediatric individuals with closed epiphysis
   - Hypersensitivity to growth hormone
   - Pediatric individuals with Prader-Willi syndrome who are severely obese or have severe respiratory impairment
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Growth Hormone Deficiency for Individuals Under 18 Years of Age:

Initial Course of Treatment:

Initial requests for growth hormone therapy for treatment of growth hormone deficiency will be reviewed by the clinical pharmacist and/or medical director(s) and/or clinical advisor(s) and, if approved, may be authorized for a maximum of 12 months.

➢ An initial course of growth hormone therapy may be considered medically necessary with documentation of ANY of the following:

1. Individual with growth failure due to growth hormone deficiency as documented by ALL of the following:

   • Results of one (1) growth hormone stimulation test demonstrating a peak value of less than 10ng/ml (unless otherwise contraindicated)
   • Bone age is less than chronological age and individual’s chronological age is prior to gender-appropriate mature bone age (14 years for females, 16 years for males)
   • Height at least two (2) standard deviations below the mean for chronologic age
   • IGF-1 with subnormal result for age as indicated by the following table:

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<th>SUBNORMAL RESULT</th>
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</thead>
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<tr>
<td>7 years †</td>
<td>Less than 52 ng/mL</td>
</tr>
<tr>
<td>8 through 10 years</td>
<td>Less than 75 ng/mL</td>
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<tr>
<td>11 through 12 years</td>
<td>Less than 127 ng/mL</td>
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<tr>
<td>13 through 17 years</td>
<td>Less than 212 ng/mL</td>
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   • IGFBP-3 with subnormal result for age as indicated by the following table:

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<th>SUBNORMAL RESULT</th>
</tr>
</thead>
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<tr>
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<td>Less than 1.6 mg/L</td>
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<td>Less than 1.8 mg/L</td>
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<tr>
<td>10 years</td>
<td>Less than 2.1 mg/L</td>
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<tr>
<td>11 years</td>
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<td>Less than 3.1 mg/L</td>
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<td>16 years</td>
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<tr>
<td>17 years</td>
<td>Less than 3.2 mg/L</td>
</tr>
</tbody>
</table>
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Growth Hormone Deficiency for Individuals Under 18 Years of Age: (cont.)

Initial Course of Treatment: (cont.)

- An initial course of growth hormone therapy may be considered medically necessary with documentation of ANY of the following: (cont.)

  1. Individual with growth failure due to growth hormone deficiency as documented by ALL of the following: (cont.)
     - Diagnostic tests have ruled out treatable causes. These tests include:
       - Cranial MRI and T4
       - FSH
       - Cortisol

  2. Individual with height less than the 3rd percentile for chronological age secondary to chronic renal insufficiency up to the time of renal transplantation

  3. Individual 3 through 17 years of age with growth failure due to Noonan's Syndrome with documented short stature

  4. Individual with Turner's Syndrome

  5. Individual with growth failure due to Prader-Willi Syndrome with documented absence of upper airway obstruction or sleep apnea by sleep study

  6. Individuals with short stature due to short stature homeobox-containing gene (SHOX) deficiency.

- If the above criteria are not met, the initial course of treatment of growth hormone therapy for growth hormone deficiency is considered experimental or investigational due to:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and

  2. Insufficient evidence to support improvement of the net health outcome.
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Growth Hormone Deficiency for Individuals Under 18 Years of Age: (cont.)

Continuing and Repeat Courses of Treatment:

Requests for continuing or repeat courses of growth hormone therapy will be reviewed annually to determine if growth hormone therapy continues to be medically necessary and, if approved, may be authorized for a maximum of 12 months per request. Requests not meeting criteria below will be reviewed by the clinical pharmacist and/or medical director(s) and/or clinical advisor(s).

- Continuing or repeat courses of growth hormone therapy are considered medically necessary with documentation that the individual has been compliant with treatment and documentation of ANY of the following:

  1. Individual with growth failure due to growth hormone deficiency as documented by ALL of the following:
     - Historical clinical records include results of one (1) growth hormone stimulation test demonstrating a peak value of less than 10 ng/ml with appropriate timing of provocative agent administration (unless otherwise contraindicated) (see Description section)
     - Growth velocity is 5 cm or greater over the year (i.e. past 12 months) of treatment and individual’s growth plates have not fused

  2. Individual with height less than the 3rd percentile for chronological age secondary to chronic renal insufficiency up to the time of renal transplantation

  3. Individual 3 through 17 years of age with growth failure due to Noonan’s Syndrome with documented short stature

  4. Individual with Turner’s Syndrome

  5. Individual with growth failure due to Prader-Willi Syndrome with documented absence of upper airway obstruction or sleep apnea by sleep study

  6. Individuals with short stature due to short stature homeobox-containing gene (SHOX) deficiency.

- If the above criteria are not met, continuing or repeat courses of treatment of growth hormone therapy for growth hormone deficiency are considered experimental or investigational due to:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and

  2. Insufficient evidence to support improvement of the net health outcome.
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

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

Initial Course of Treatment:

Initial requests for growth hormone therapy for treatment of growth hormone deficiency will be reviewed by the clinical pharmacist and/or medical director(s) and/or clinical advisor(s) and, if approved, may be authorized for a maximum of 12 months.

- An initial course of growth hormone therapy may be considered medically necessary with documentation of ANY of the following:

1. Growth hormone deficiency (GHD) with documentation of ALL of the following:
   - Individual with proven childhood-onset GHD retested to determine if on-going replacement therapy is needed or individual with suspected adult-onset GHD
   - Results of two (2) provocative stimulation tests demonstrating peak value less than 5ng/ml when measured by RIA, or peak value less than 2.5ng/ml when measured by IRMA
   - Time of administration of the provocative agent
   - Number of minutes elapsed between provocative agent administration time and drawing of serum GH level

2. Individual with surgery, irradiation or trauma involving the hypothalamus or pituitary gland or other diseases of the pituitary or hypothalamus with documentation of ALL of the following:
   - Results of one (1) provocative stimulation test demonstrating peak value less than 5ng/ml when measured by RIA, or peak value less than 2.5ng/ml when measured by IRMA
   - Time of administration of the provocative agent
   - Number of minutes elapsed between provocative agent administration time and drawing of serum GH level
   - Clinical records document that without treatment, low GH levels result and/or signs and symptoms of growth hormone deficiency reappear

3. Individual with multiple pituitary hormone deficiencies other than growth hormone (i.e., TSH, ACTH, LH and/or FSH, AVP) or serum insulin-like growth factor 1 (IGF-1) less than 84 ng/mL

4. Individual with Turner’s Syndrome

- If the above criteria are not met, the initial course of growth hormone therapy for the treatment of growth hormone deficiency is considered experimental or investigational due to:

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome.
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Continuing and Repeat Courses of Treatment:

Requests for continuing or repeat courses of growth hormone therapy will be reviewed annually to determine if growth hormone therapy continues to be medically necessary and, if approved, may be authorized for a maximum of 12 months per request. Requests not meeting criteria below will be reviewed by the clinical pharmacist and/or medical director(s) and/or clinical advisor(s).

- Continuing or repeat courses of growth hormone therapy are considered medically necessary with documentation that the individual has been compliant with treatment and documentation of ANY of the following:

1. Individual with historical diagnosis of proven growth hormone deficiency (GHD) with documentation of ALL of the following:
   - ONE of the following historical clinical records:
     - Results of two (2) provocative stimulation tests demonstrating peak value less than 5ng/ml when measured by RIA with appropriate timing of provocative agent administration
     - Results of two (2) provocative stimulation tests demonstrating peak value less than 2.5ng/ml when measured by IRMA with appropriate timing of provocative agent administration
   - 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 had occurred, low GH levels or signs and symptoms of GH deficiency have reappeared

2. Individual with surgery, irradiation or trauma involving the hypothalamus or pituitary gland or other diseases of the pituitary or hypothalamus with documentation of ALL of the following:
   - ONE of the following historical clinical records:
     - Results of one (1) provocative stimulation test demonstrating peak value less than 5ng/ml when measured by RIA with appropriate timing of provocative agent administration (see Description section)
     - Results of one (1) provocative stimulation test demonstrating peak value less than 2.5ng/ml when measured by IRMA with appropriate timing of provocative agent administration (see Description section)
   - 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 had occurred, low GH levels or signs and symptoms of GH deficiency have reappeared
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Growth Hormone Deficiency for Individuals 18 Years of Age and Older: (cont.)

Continuing and Repeat Courses of Treatment: (cont.)

- Continuing or repeat courses of growth hormone therapy are considered medically necessary with documentation that the individual has been compliant with treatment and documentation of ANY of the following: (cont.)

  3. Individual with multiple pituitary hormone deficiencies other than growth hormone (i.e., TSH, ACTH, LH and/or FSH, AVP) or serum insulin-like growth factor 1 (IGF-1) less than 84 ng/mL

  4. Individual with Turner’s Syndrome

- If the above criteria are not met, continuing or repeat courses of treatment of growth hormone therapy for treatment of growth hormone deficiency are considered experimental or investigational due to:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and

  2. Insufficient evidence to support improvement of the net health outcome.
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Growth Failure:

COVERAGE FOR TREATMENT TO CORRECT A CONGENITAL DEFECT OR BIRTH ABNORMALITY IS DEPENDENT UPON BENEFIT PLAN LANGUAGE AND IS SUBJECT TO THE PROVISIONS OF THE RECONSTRUCTIVE BENEFIT AND THE COSMETIC BENEFIT EXCLUSION. REFER TO MEMBER’S SPECIFIC BENEFIT PLAN BOOKLET TO VERIFY BENEFITS AND THE FUNCTIONAL IMPAIRMENT REQUIREMENT.

- Growth hormone therapy for the treatment of children born small for gestational age (SGA), including those who have failed to manifest “catch-up” growth by two years of age, is considered not medically necessary and not eligible for coverage due to lack of an associated functional impairment.

- Growth hormone therapy for treatment of growth failure for all other indications not previously listed is considered experimental or investigational based upon:
  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome, and
  3. Insufficient evidence to support improvement outside the investigational setting.

These indications include, but are not limited to:

- Improvement of neurodevelopmental status (intelligence)
- Prevention of dyslipidemia, insulin resistance and/or metabolic syndrome (diabetes, hypertension, obesity)

Idiopathic Short Stature:

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

Wound Healing for Burns:

- Growth hormone therapy is considered medically necessary for the promotion of wound healing in extensive 3rd degree burns.

- Growth hormone therapy is considered medically necessary for the prevention of growth delay in children with severe burns.
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Other Indications:

- Growth hormone therapy for all other indications not previously listed is considered experimental or investigational based upon:

  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome.

These indications include, but are not limited to:

- Altered body habitus, e.g., buffalo hump, associated with antiviral therapy in individuals with HIV
- Anabolic therapy to counteract acute or chronic illness (surgery outcomes, trauma, cancer, chronic hemodialysis, chronic infectious disease) that produces catabolic (protein wasting) changes in both adults and children, except as specified for AIDS and short bowel syndrome
- Anabolic therapy to counteract the gradual declines in muscle and bone mass that occur with aging
- Anabolic therapy to enhance body mass and strength for professional, recreational or social reasons
- Constitutional delay
- Cystic fibrosis
- Growth failure as the result of glucocorticoids
- Idiopathic dilated cardiomyopathy
- Intrauterine growth retardation
- Juvenile idiopathic or juvenile chronic arthritis
- Obesity
- Precocious puberty in conjunction with gonadotropin releasing hormone (GnRH) analogs
- Short stature after renal transplantation
- Short stature as the result of Down Syndrome
- Treatment of children with "genetic potential" (i.e., lower than expected height percentiles based on parents' height)
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Serostim:

AIDS Wasting:

- Serostim for the treatment of adults with AIDS wasting is considered *medically necessary* for an initial 2-week trial course with documentation of ALL of the following:

  1. Weight loss is greater than or equal to 10% of ideal (standard) body weight for height and weight (see women's/men's weight at different ages charts at end of section) within the last 12 months
  2. Currently receiving triple drug therapy for HIV positive disorder
  3. Continued weight loss despite adequate nutrition and other measures
  4. Absence of ALL of the following contraindications:
     - Active malignancy
     - Acute critical illness
     - Diabetic retinopathy
     - Hypersensitivity to growth hormone

- Additional 10-week course of Serostim for the treatment of adults with AIDS wasting is considered *medically necessary* with documentation of ALL of the following:

  1. Weight loss was arrested during the initial 2-week trial course
  2. Absence of ALL of the following contraindications:
     - Active malignancy
     - Acute critical illness
     - Diabetic retinopathy
     - Hypersensitivity to growth hormone

- Continued 12-week courses of Serostim are considered *medically necessary* with documentation of ALL of the following:

  1. Weight loss was arrested during the 10-week course that followed the initial 2-week trial course
  2. Individual remains on triple drug therapy for HIV positive disorder
  3. Treatment does not exceed a total of 3 continued 12-week courses
  4. Absence of ALL of the following contraindications:
     - Active malignancy
     - Acute critical illness
     - Diabetic retinopathy
     - Hypersensitivity to growth hormone
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Serostim: (cont.)

AIDS Wasting: (cont.)

- The following will be reviewed by the clinical pharmacist and/or medical director(s) and/or clinical advisor(s):

  1. Continuation of Serostim for the treatment of adults with AIDS wasting if weight loss is not arrested during the initial 2-week trial course
  2. Additional courses of Serostim for the treatment of adults with AIDS wasting if weight loss has recurred after receiving a 12-week course of therapy.

- Continuation of Serostim after 48 weeks of therapy for the treatment of adults with AIDS wasting is considered experimental or investigational based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and  
  2. Insufficient evidence to support improvement of the net health outcome.

- Intermittent therapy with Serostim for maintenance in the treatment of adults with AIDS wasting is considered experimental or investigational based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and  
  2. Insufficient evidence to support improvement of the net health outcome.

Other Indications:

- Serostim for all other indications not previously listed is considered experimental or investigational based upon:

  1. Lack of final approval from the Food and Drug Administration, and  
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and  
  3. Insufficient evidence to support improvement of the net health outcome.
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Serostim: (cont.)

WEIGHT FOR WOMEN AT DIFFERENT AGES

| Height | Age 18 to 29 | | Age 30 to 44 | | Age 45 to 65 | |
|--------|-------------|-------------|-------------|-------------|-------------|
|        | 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 | 199 |
| 5'3"   | 92 | 122 | 171 | 98 | 131 | 183 | 104 | 139 | 205 |
| 5'4"   | 94 | 125 | 175 | 101 | 134 | 188 | 107 | 143 | 213 |
| 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: over weight
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Serostim: (cont.)

WEIGHT FOR MEN AT DIFFERENT AGES

<table>
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<tr>
<th>Height</th>
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<th>Age 30 to 44</th>
<th>Age 45 to 65</th>
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</tbody>
</table>

Legend: UW: underweight   SW: standard weight   OW: over weight
GROWTH HORMONE THERAPY (cont.)

Criteria: (cont.)

Zorbtive:

Short Bowel Syndrome:

➢ Zorbtive for the treatment of adults with short bowel syndrome is considered **medically necessary** for a single 4-week course with documentation of **ALL** of the following:

1. Concurrent specialized nutritional support (i.e., enteral feedings, parenteral nutrition, fluid and micronutrient supplements)
2. Absence of **ALL** of the following contraindications:
   • Active malignancy
   • Acute critical illness
   • Hypersensitivity to growth hormone

➢ Additional course of Zorbtive for the treatment of adults with short bowel syndrome is considered **experimental or investigational** based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome.

Other Indications:

➢ Zorbtive for all other indications not previously listed is considered **experimental or investigational** based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome.

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

Refer To:

▪ “Growth Hormone Therapy Chart”, #AP96, BCBSAZ Administrative Procedure Guideline when preferred GH medication Nutropin AQ is otherwise contraindicated or not labeled for the indication being prescribed
GROWTH HORMONE THERAPY (cont.)

Resources:

Literature reviewed 12/06/16. We do not include marketing materials, poster boards and non-published literature in our review.

The BCBS Association Medical Policy Reference Manual (MPRM) policy is included in our guideline review. References cited in the MPRM policy are not duplicated on this guideline.


GROWTH HORMONE THERAPY (cont.)

Resources: (cont.)


GROWTH HORMONE THERAPY (cont.)

Resources: (cont.)


GROWTH HORMONE THERAPY (cont.)

Resources: (cont.)

Genotropin Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>All indications</td>
<td>Administer subcutaneously and rotate injection sites to avoid lipoatrophy.</td>
</tr>
<tr>
<td>Children with growth failure due to growth hormone deficiency (GHD)</td>
<td>0.16 to 0.24 mg/kg/week</td>
</tr>
<tr>
<td>Children with Prader-Willi syndrome</td>
<td>0.24 mg/kg/week</td>
</tr>
<tr>
<td>Children small for gestational age</td>
<td>Up to 0.48 mg/kg/week</td>
</tr>
<tr>
<td>Children with Turner Syndrome</td>
<td>0.33 mg/kg/week</td>
</tr>
<tr>
<td>Children with Idiopathic Short Stature</td>
<td>Up to 0.47 mg/kg/week</td>
</tr>
<tr>
<td>Adults with either adult onset or childhood onset growth hormone deficiency</td>
<td>Either a non-weight based or a weight based dosing regimen may be followed, with doses adjusted based on treatment response and IGF-1 concentrations</td>
</tr>
<tr>
<td></td>
<td>Non-weight based dosing: A starting dose of approximately 0.2mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1-2 months by increments of approximately 0.1-0.2 mg/day</td>
</tr>
<tr>
<td></td>
<td>Weight based dosing: The recommended initial dose is not more than 0.04 mg/kg/week; the dose may be increased as tolerated to not more than 0.08 mg/kg/week at 4–8 week intervals.</td>
</tr>
</tbody>
</table>
GROWTH HORMONE THERAPY (cont.)

Resources: (cont.)

Humatrope Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>All indications</td>
<td>Administer subcutaneously</td>
</tr>
<tr>
<td>Children with short stature or growth failure associated with growth hormone (GH) deficiency</td>
<td>Weekly dosage given in divided doses 6 to 7 times per week: 0.18 to 0.30 mg/kg/week</td>
</tr>
<tr>
<td>Children with Turner Syndrome</td>
<td>Weekly dosage given in divided doses 6 to 7 times per week: Up to 0.375 mg/kg/week</td>
</tr>
<tr>
<td>Children with Idiopathic Short Stature</td>
<td>Weekly dosage given in divided doses 6 to 7 times per week: Up to 0.37 mg/kg/week</td>
</tr>
<tr>
<td>Children with SHOX deficiency</td>
<td>Weekly dosage given in divided doses 6 to 7 times per week: 0.35 mg/kg/week</td>
</tr>
<tr>
<td>Children with failure to catch up in height after small for gestational age birth</td>
<td>Weekly dosage given in divided doses 6 to 7 times per week: Up to 0.47 mg/kg/week</td>
</tr>
<tr>
<td>Adults with either childhood-onset or adult-onset GH deficiency</td>
<td>Either a non-weight based or a weight-based dosing regimen may be followed, with doses adjusted based on treatment response and IGF-I concentrations.</td>
</tr>
</tbody>
</table>

Non-weight based dosing: A starting dose of approximately 0.2 mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1-2 months by increments of approximately 0.1-0.2 mg/day.

Weight-based dosing: The recommended initial daily dose is not more than 0.006 mg/kg (6 μg/kg); the dose may be increased to a maximum of 0.0125 mg/kg (12.5 μg/kg) daily.
GROWTH HORMONE THERAPY (cont.)

Resources: (cont.)

Norditropin Package Insert:

FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>All indications</td>
<td>Administer subcutaneously and rotate injection sites to avoid lipoatrophy.</td>
</tr>
<tr>
<td>Children with growth failure due to growth hormone deficiency (GHD)</td>
<td>0.024 to 0.034 mg/kg/day, 6 to 7 times a week</td>
</tr>
<tr>
<td>Children with short stature associated with Noonan syndrome</td>
<td>Up to 0.066 mg/kg/day</td>
</tr>
<tr>
<td>Children with short stature associated with Turner Syndrome</td>
<td>Up to 0.067 mg/kg/day</td>
</tr>
<tr>
<td>Children of short stature born short for gestational age with no catch-up growth by 2 to 4 years</td>
<td>Up to 0.067 mg/kg/day</td>
</tr>
<tr>
<td>Adults with either adult onset or childhood onset growth hormone deficiency (GHD)</td>
<td>0.004 mg/kg/day to be increased as tolerated to not more than 0.016 mg/kg/day after approximately 6 weeks, or a starting dose of approximately 0.2 mg/day (range, 0.15 to 0.30 mg/day) increased gradually every 1 to 2 months by increments of approximately 0.1 to 0.2 mg/day</td>
</tr>
</tbody>
</table>
**GROWTH HORMONE THERAPY** (cont.)

**Resources:** (cont.)

Nutropin AQ Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>All indications</td>
<td>Administer subcutaneously and rotate injection sites to avoid lipoatrophy.</td>
</tr>
<tr>
<td>Children with growth failure due to growth hormone deficiency (GHD)</td>
<td>Up to 0.3 mg/kg/week divided into daily injections; in pubertal patients, a weekly dosage up to 0.7 mg/kg/week divided daily may be used</td>
</tr>
<tr>
<td>Children with Idiopathic Short Stature (ISS)</td>
<td>Up to 0.3 mg/kg/week divided into daily injections</td>
</tr>
<tr>
<td>Children with Turner Syndrome</td>
<td>Up to 0.375 mg/kg/week divided into equal doses 3 to 7 times per week</td>
</tr>
<tr>
<td>Children with chronic kidney disease (CKD) up to the time of renal transplantation</td>
<td>Up to 0.35 mg/kg/week divided into daily injections</td>
</tr>
<tr>
<td>Adults with either childhood-onset or adult-onset GHD</td>
<td>Either a non-weight based or weight-based dosing regimen may be followed, with doses adjusted based on treatment response and IGF-I concentrations</td>
</tr>
<tr>
<td></td>
<td><strong>Non-weight-based:</strong> A starting dose of approximately 0.2 mg/day (range 0.15 - 0.3 mg/day) increased gradually every 1 - 2 months by increments of approximately 0.1 - 0.2 mg/day.</td>
</tr>
<tr>
<td></td>
<td><strong>Weight-based:</strong> Initiate from not more than 0.006 mg/kg/day; the dose may be increased up to a maximum of 0.025 mg/kg/day in patients ≤ 35 years old or 0.0125 mg/kg/day in patients &gt; 35 years old.</td>
</tr>
</tbody>
</table>
GROWTH HORMONE THERAPY (cont.)

Resources: (cont.)

Omnitrope Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>All indications</td>
<td>Administer subcutaneously and rotate injection sites to avoid lipoatrophy.</td>
</tr>
<tr>
<td>Children with growth failure due to growth hormone deficiency (GHD)</td>
<td>0.16 to 0.24 mg/kg/week, divided into 6 to 7 daily injections</td>
</tr>
<tr>
<td>Children with Prader-Willi Syndrome</td>
<td>0.24 mg/kg/week, divided into 6 to 7 daily injections</td>
</tr>
<tr>
<td>Children Small for Gestational Age</td>
<td>Up to 0.48 mg/kg/week, divided into 6 to 7 daily injections</td>
</tr>
<tr>
<td>Children with Turner Syndrome</td>
<td>0.33 mg/kg/week, divided into 6 to 7 daily injections</td>
</tr>
<tr>
<td>Children with Idiopathic Short Stature</td>
<td>Up to 0.47 mg/kg/week, divided into 6 to 7 daily injections</td>
</tr>
<tr>
<td>Adults with either adult onset or childhood onset GHD</td>
<td>Not more than 0.04 mg/kg/week (divided into daily injections) to be increased as tolerated to not more than 0.08 mg/kg/week); to be increased gradually every 1 to 2 months</td>
</tr>
</tbody>
</table>

Saizen Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>All indications</td>
<td>Administer subcutaneously.</td>
</tr>
<tr>
<td>Children with growth failure due to growth hormone deficiency (GHD)</td>
<td>0.18 mg/kg/week, divided into equal doses given either on 3 alternate days, 6 times per week or daily</td>
</tr>
<tr>
<td>Adults with either adult-onset or childhood-onset GHD</td>
<td>Either a non-weight based or a weight based dosing regimen may be followed, with doses adjusted based on treatment response and IGF-1 concentrations</td>
</tr>
</tbody>
</table>

  Non-weight–based dosing: A starting dose of approximately 0.2 mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1 to 2 months by increments of approximately 0.1 to 0.2 mg/day

  Weight-based dosing: The recommended initial dose is not more than 0.005 mg/kg/day; the dose may be increased as tolerated to not more than 0.01 mg/kg/day after 4 weeks
**GROWTH HORMONE THERAPY** (cont.)

**Resources:** (cont.)

Serostim Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance</td>
<td>0.1 mg/kg subcutaneously (SC) daily (up to 6 mg) at bedtime for HIV patients with wasting or cachexia. Injection sites, which may be located on thigh, upper arm, abdomen or buttock, should be rotated to avoid local irritation.</td>
</tr>
</tbody>
</table>

Zomacton Package Insert:

FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children who have growth failure due to inadequate secretion of normal endogenous growth hormone</td>
<td>The recommended dose is up to 0.1 mg/kg administered subcutaneously three (3) times per week (up to 0.3 mg/kg/week).</td>
</tr>
</tbody>
</table>

Zorbtive Package Insert:

- FDA-approved indication and dosage:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short Bowel Syndrome in patients receiving specialized nutritional support.</td>
<td>Dose of approximately 0.1 mg/kg subcutaneously daily to a maximum of 8 mg daily. Administration for more than 4 weeks has not been adequately studied. Injections should be administered daily for 4 weeks.</td>
</tr>
</tbody>
</table>
GROWTH HORMONE THERAPY (cont.)

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ’s Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ’s Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe’é atah nílínígíí Blue Cross Blue Shield of Arizona haada yit’éego bíná’idílkidgo éí doodago Háida bíjá aniyeeélígíí t’aadoo le’e’é yína’idílkidgo beehaz’áanií hóló díí t’áá hazaadk’éhjí háháa a’dowolgo bee haz’á doob baqą́q ilínígóó. Ata’ halne’lígíí köjí bich’éjí hodilínighi 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於保險項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thể thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thợ dịch viên, xin gọi 877-475-4799.

Arabic: إن كان لديك أو أدى شخص ساعدك أسئلة بخصوص Blue Cross Blue Shield of Arizona غير ضرورية بلغت من دون أية تكلفة. للتحدث مع مترجم الصلب ب 877-475-4799.
GROWTH HORMONE THERAPY (cont.)

Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutuuanan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 홍역사와 얘기하기 위해서는 877-475-4799로 전화하십시오.

French: Si vous, ou quelqu'un que vous êtes en train d'aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d'obtenir de l'aide et l'information dans votre langue à aucun coût. Pour parler à un interprète,appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то у вас имеется право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizonaについてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかからません。通訳お電話される場合、877-475-4799までお電話ください。

Farsi: اگر شما با کمک شما به یا کمک می‌کنید، سوالات تو مورد اطلاعات به زبان خود را به طور رایگان درویت تا 877-475-4799 می‌توانید.


Serbo-Croatian: Ukoško Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคุณหรือลูกค้าของคุณมีปัญหาเกี่ยวกับ Blue Cross Blue Shield of Arizona คุณสามารถติดต่อกับเราผ่านอีเมล์หรือโทรศัพท์หมายเลขโทรศัพท์ โทร 877-475-4799