



UnitedHealthcare Pharmacy  
Clinical Pharmacy Programs

Program Number	2021 P 2016-11
Program	Prior Authorization/Medical Necessity
Medication	<p><u>Human Growth Hormone</u>: Somatropin (Genotropin<sup>®*</sup>, Humatrope<sup>®*</sup>, Norditropin<sup>®*</sup>, NordiFlex<sup>®*</sup>, Nutropin<sup>®</sup>, Nutropin AQ<sup>®</sup>, Nutropin AQ<sup>®</sup> NuSpin<sup>™</sup>, Omnitrope<sup>®*</sup>, Saizen<sup>®*</sup>, Zomacton<sup>®</sup>, Zorbtive<sup>®*</sup>, and Serostim<sup>®</sup>)</p> <p><u>Growth Stimulating Products</u>: Mecasermin (Increlex<sup>®</sup>)</p> <p>*Product is excluded for lines of business with therapeutic equivalent exclusions</p>
P&T Approval Date	2/2014, 8/2014, 5/2015, 8/2015, 6/2016, 12/2016, 11/2017, 11/2018, 12/2019, 4/2020, 7/2021
Effective Date	10/1/2021; Oxford only: 10/1/2021

**1. Background:**

Somatropin is indicated for the treatment of growth hormone deficiency, short stature associated with Turner syndrome or Noonan syndrome, short-stature homeobox (SHOX) gene deficiency, growth failure due to Prader-Willi syndrome, short stature in children born small for gestational age, growth failure in children with chronic renal insufficiency up to the time of transplant, short bowel syndrome in patients receiving specialized nutritional support, and HIV-associated wasting. Somatropin is also indicated for replacement of endogenous growth hormone in adults with confirmed growth hormone deficiency.

Mecasermin is indicated for the treatment of growth failure in children with severe primary insulin-like growth factor-1 (IGF-1) deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone.

**Coverage Information**

Since short stature in the absence of defined pathology is not a sickness or injury, growth hormone is not a covered health service for these indications. The standard UnitedHealthcare Pharmacy Rider explicitly excludes coverage of growth hormone for short stature caused by heredity and not by a diagnosed medical condition.

Coverage for somatropin (Genotropin\*, Humatrope\*, Norditropin\*, NordiFlex\*, Nutropin, Nutropin AQ, Nutropin AQ NuSpin, Omnitrope\*, Saizen\*, and Zomacton) and mecasermin (Increlex) will be provided for members who meet the following criteria:

## 2. Coverage Criteria:

### A. **Pediatric Growth Hormone Deficiency (GHD)**

*Note: Includes children who have undergone brain radiation. If patient is a Transition Phase Adolescent or Adult who had childhood onset GH deficiency, utilize criteria for Transition Phase Adolescent or Adult GH Deficiency.*

#### 1. **Initial Therapy**

a. **Somatropin** will be approved based on **one** of the following criteria:

(1) **One** of the following:

(a) **All** of the following:

- i. Infant is < 4 months of age
- ii. Infant has growth deficiency
- iii. Prescribed by an endocrinologist

**-OR-**

(b) **Both** of the following:

- i. History of neonatal hypoglycemia associated with pituitary disease
- ii. Prescribed by an endocrinologist

**-OR-**

(c) **Both** of the following:

- i. Diagnosis of panhypopituitarism
- ii. Prescribed by an endocrinologist

**-OR-**

(2) **All** of the following:

(a) Diagnosis of pediatric GH deficiency as confirmed by **one** of the following:

- i. Projected height (as determined by extrapolating pre-treatment growth trajectory along current channel to 18-20 year mark) is > 2.0 standard deviations [SD] below

midparental height utilizing age and gender growth charts related to height

**-OR-**

ii. Height is  $> 2.25$  SD below population mean (below the 1.2 percentile for age and gender) utilizing age and gender growth charts related to height

**-OR-**

iii. Growth velocity is  $> 2$  SD below mean for age and gender

**-OR-**

iv. Delayed skeletal maturation of  $> 2$  SD below mean for age and gender (e.g., delayed  $> 2$  years compared with chronological age)

**-AND-**

(b) **One** of the following:

i. Patient is male and **one** of the following:

- Tanner stage less than IV
- Bone age  $< 16$  years measured in the past 12 months

**-OR-**

ii. Patient is female and **one** of the following:

- Tanner stage less than IV
- Bone age  $< 14$  years measured in the past 12 months

**-AND-**

(c) Submission of medical records (e.g., chart notes, laboratory values) documenting **one** of the following:

i. **Both** of the following:

- Patient has undergone **two** of the following provocative GH stimulation tests:

- Arginine

- Clonidine
- Glucagon
- Insulin
- Levodopa
- Growth hormone releasing hormone

-AND-

- **Both** GH response values are < 10 mcg/L

-OR-

ii. **Both** of the following:

- Patient is < 1 year of age

-AND-

- **One** of the following is below the age and gender adjusted normal range as provided by the physician's lab:
  - Insulin-like Growth Factor 1 (IGF-1/Somatomedin-C)
  - Insulin Growth Factor Binding Protein-3 (IGFBP-3)

-AND-

(d) **One** of the following:

- i. Request does not exceed a maximum supply limit of 0.3 mg/kg/week

-OR-

ii. **Both** of the following:

- Tanner Stage 3 or greater
- Request does not exceed a maximum supply limit of 0.7 mg/kg/week

-AND-

(e) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**Note: Documentation of previous height, current height and goal expected adult height will be required for renewal.**

**2. Reauthorization**

**a. Somatropin** will be approved based on **all** of the following criteria:

(1) Height increase of at least 2 cm/year over the previous year documented by **both** of the following:

- (a) Previous height and date obtained
- (b) Current height and date obtained

**-AND-**

(2) **Both** of the following:

- (a) Expected adult height not attained
- (b) Documentation of expected adult height goal (e.g. genetic potential)

**-AND-**

(3) Calculated height (growth) velocity over the past 12 months

**-AND-**

(4) Documentation of **one** of the following

i. Patient is male and **one** of the following:

- Tanner stage less than IV
- Bone age < 16 years measured in the past 12 months

**-OR-**

ii. Patient is female and **one** of the following:

- Tanner stage less than IV
- Bone age < 14 years measured in the past 12 months

**-AND-**

(5) **One** of the following:

(a) Request does not exceed a maximum supply limit of 0.3 mg/kg/week

**-OR-**

(b) **Both** of the following:

i. Tanner Stage 3 or greater

ii. Request does not exceed a maximum supply limit of 0.7 mg/kg/week

**-AND-**

(6) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

## **B. Prader-Willi Syndrome**

### **1. Initial Therapy**

a. **Somatropin** will be approved based on **both** the following criterion:

(1) Diagnosis of Prader-Willi Syndrome

**-AND-**

(2) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

### **2. Reauthorization**

a. **Somatropin** will be approved based on **one** of the following criteria:

(1) **Both** of the following:

(a) Evidence of positive response to therapy (e.g. increase in total lean body mass, decrease in fat mass)

**-AND-**

(b) Prescribed by an endocrinologist

-OR-

(2) **All** of the following:

- (a) Height increase of at least 2 cm/year over the previous year of treatment as documented by **both** of the following:
  - i. Previous height and date obtained
  - ii. Current height and date obtained

-AND-

(b) **Both** of the following:

- i. Expected adult height not attained
- ii. Documentation of expected adult height goal

-AND-

(c) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**C. Growth Failure in Children Small for Gestational Age (SGA)**

**1. Initial Therapy**

**a. Somatropin** will be approved based on **all** of the following criteria:

(1) Diagnosis of SGA based on demonstration of catch up growth failure in the first 24 months of life using a birth to 36 month growth chart as confirmed by the following criterion:

(a) Documentation that **one** of the following is below the 3<sup>rd</sup> percentile for gestational age ( $\geq 2$  SD below population mean):

- i. Birth weight
- ii. Birth length

-AND-

(b) Patient has demonstrated failure of catch up growth in the first 24 months of life

-AND-

- (2) Documentation that height remains  $\leq 3^{\text{rd}}$  percentile ( $\geq 2$  SD below population mean)

-AND-

- (3) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**Note: Documentation of previous height, current height and goal expected adult height will be required for renewal.**

## 2. Reauthorization

- a. **Somatropin** will be approved based on **all** of the following criteria:

- (1) Height increase of at least 2 cm/year over the previous year documented by **both** of the following:
- (a) Previous height and date obtained
  - (b) Current height and date obtained

-AND-

- (2) Documentation of **both** of the following:
- (a) Expected adult height not attained
  - (b) Expected adult height goal

-AND-

- (3) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

## D. Turner Syndrome or Noonan Syndrome

### 1. Initial Therapy

- a. **Somatropin** will be approved based on **all** of the following criteria:

- (1) Diagnosis of pediatric growth failure associated with **one** of the following:



(a) **Both** of the following:

i. Turner Syndrome (Gonadal Dysgenesis)

**-AND-**

ii. Patient is female and **one** of the following:

- Tanner stage less than IV
- Bone age < 14 years measured in the past 12 months

**-OR-**

(b) **Both** of the following:

i. Noonan Syndrome

**-AND-**

ii. Documentation of **one** of the following:

▪ Patient is male and one of the following:

- Tanner stage less than IV
- Bone age < 16 years measured in the past 12 months

**-OR-**

▪ Patient is female and **one** of the following:

- Tanner stage less than IV
- Bone age < 14 years measured in the past 12 months

**-AND-**

(2) Height is below the 5<sup>th</sup> percentile on growth charts for age and gender

**-AND-**

(3) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**Note: Documentation of previous height, current height and goal expected adult height will be required for renewal.**

## 2. Reauthorization

a. **Somatropin** will be approved based on **all** of the following criteria:

- (1) Height increase of at least 2 cm/year over the previous year documented by **both** of the following:
  - (a) Previous height and date obtained
  - (b) Current height and date obtained

-AND-

- (2) Documentation of **both** of the following:
  - (a) Expected adult height not attained
  - (b) Expected adult height goal

-AND-

- (3) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

## E. Short-Stature Homeobox (SHOX) Gene Deficiency

### 1. Initial Therapy

a. **Somatropin** will be approved based on **all** of the following criteria:

- (1) Diagnosis of pediatric growth failure with short-stature homeobox (SHOX) gene deficiency as confirmed by genetic testing

-AND-

- (2) **One** of the following:
  - (a) Patient is male and **one** of the following:

- i. Tanner stage less than IV
- ii. Bone age < 16 years measured in the past 12 months

-OR-

- (b) Patient is female and **one** of the following:

- i. Tanner stage less than IV
- ii. Bone age < 14 years measured in the past 12 months

-AND-

(3) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**Note: Documentation of previous height, current height and goal expected adult height will be required for renewal.**

**2. Reauthorization**

**a. Somatropin** will be approved based on **all** of the following criteria:

(1) Height increase of at least 2 cm/year over the previous year documented by **both** of the following:

- (a) Previous height and date obtained
- (b) Current height and date obtained

-AND-

(2) Documentation of **both** of the following:

- (a) Expected adult height not attained
- (b) Expected adult height goal

-AND-

(3) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**F. Growth Failure associated with Chronic Renal Insufficiency**

**1. Initial Therapy**

**a. Somatropin** will be approved based on **all** of the following criteria:

(1) Diagnosis of pediatric growth failure associated with chronic renal insufficiency

-AND-

(2) Documentation of **one** of the following:

(a) Patient is male and **one** of the following:

- i. Tanner stage less than IV
- ii. Bone age < 16 years measured in the past 12 months

**-OR-**

(b) Patient is female and **one** of the following:

- i. Tanner stage less than IV
- ii. Bone age < 14 years measured in the past 12 months

**-AND-**

(3) Prescribed by **one** of the following:

- (a) Endocrinologist
- (b) Nephrologist

**Authorization will be issued for 12 months.**

**Note: Documentation of previous height, current height and goal expected adult height will be required for renewal.**

## **2. Reauthorization**

**a. Somatropin** will be approved based on **all** of the following criteria:

(1) Height increase of at least 2 cm/year over the previous year documented by **both** of the following:

- (a) Previous height and date obtained
- (b) Current height and date obtained

**-AND-**

(2) Documentation of **both** of the following:

- (a) Expected adult height not attained
- (b) Expected adult height goal

**-AND-**

(3) Prescribed by **one** of the following:

- (a) Endocrinologist
- (b) Nephrologist

**Authorization will be issued for 12 months.**

**G. Adult Growth Hormone Deficiency**

**1. Initial Therapy**

**a. Somatropin** will be approved based on **all** of the following criteria:

(1) Diagnosis of adult GH deficiency as a result of **one** of the following:

(a) Clinical records supporting a diagnosis of childhood-onset GHD

**-OR-**

(b) **Both** of the following:

i. Adult-onset GHD

**-AND-**

ii. Clinical records documenting that hormone deficiency is a result of hypothalamic-pituitary disease from organic or known causes (e.g., damage from surgery, cranial irradiation, head trauma, or subarachnoid hemorrhage)

**-AND-**

(2) Submission of medical records (e.g., chart notes, laboratory values) documenting **one** of the following:

(a) **Both** of the following:

i. Patient has undergone **one** of the following GH stimulation tests to confirm adult GH deficiency:

- Insulin tolerance test (ITT)
- Arginine & GHRH (GHRH+ARG)
- Glucagon
- Arginine (ARG)
- Macrilen (macimorelin)

**-AND-**

ii. **One** of the following peak GH values:

- ITT  $\leq 5$   $\mu\text{g/L}$
- GHRH+ARG ( $\leq 11$   $\mu\text{g/L}$  if body mass index [BMI]  $< 25$   $\text{kg/m}^2$ ;  $\leq 8$   $\mu\text{g/L}$  if BMI  $\geq 25$  and  $< 30$   $\text{kg/m}^2$ ;  $\leq 4$   $\mu\text{g/L}$  if BMI  $\geq 30$   $\text{kg/m}^2$ )
- Glucagon  $\leq 3$   $\mu\text{g/L}$
- ARG  $\leq 0.4$   $\mu\text{g/L}$
- Macimorelin  $< 2.8$   $\text{ng/mL}$  30, 45, 60 and 90 minutes following macimorelin administration

**-OR-**

(b) **Both** of the following:

- i. Submission of medical records (e.g., chart notes, laboratory values) documenting deficiency of **three** of the following anterior pituitary hormones:
  - Prolactin
  - ACTH
  - TSH
  - FSH/LH

**-AND-**

- ii. IGF-1/Somatomedin-C level is below the age and gender adjusted normal range as provided by the physician's lab

**-AND-**

(3) **One** of the following:

(a) Diagnosis of panhypopituitarism

**-OR-**

(b) Other diagnosis **and** not used in combination with the following:

- i. Aromatase inhibitors [e.g., Arimidex (anastrozole), Femara (letrozole)]
- ii. Androgens [e.g., Delatestryl (testoseterone enanthate), Depo-Testosterone (testosterone cypionate)]

**-AND-**

- (4) Request does not exceed a maximum supply limit of 0.3 mg/kg/week

-AND-

- (5) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

## 2. Reauthorization

- a. **Somatropin** will be approved based on the following criterion:

- (1) Documentation of IGF-1/Somatomedin C level within the past 12 months

-AND-

- (2) **One** of the following:

- (a) Diagnosis of panhypopituitarism

-OR-

- (b) Other diagnosis **and** not used in combination with the following:

- Aromatase inhibitors [e.g., Arimidex (anastrozole), Femara (letrozole)]
- Androgens [e.g., Delatestryl (testoseterone enanthate), Depo-Testosterone (testosterone cypionate)]

-AND-

- (3) Request does not exceed a maximum supply limit of 0.3 mg/kg/week)

-AND-

- (4) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

## H. Transition Phase Adolescent Patients

1. **Initial Therapy**

a. **Somatropin** will be approved based on **all** of the following criteria:

(1) Request does not exceed a maximum supply limit of 0.3 mg/kg/week)

-AND-

(2) Documentation of **one** of the following:

- (a) Attained expected adult height
- (b) Closed epiphyses on bone radiograph

-AND-

(3) Submission of medical records (e.g., chart notes, laboratory values) documenting **one** of the following:

(a) **Both** of the following:

i. Documentation of high risk of GH deficiency due to GH deficiency in childhood from **one** of the following:

- Embryopathic/congenital defects
- Genetic mutations
- Irreversible structural hypothalamic-pituitary disease
- Panhypopituitarism
- Deficiency of **three** of the following anterior pituitary hormones:

- ACTH
- TSH
- Prolactin
- FSH/LH

-AND-

ii. **One** of the following:

- IGF-1/Somatomedin-C level is below the age and gender adjusted normal range as provided by the physician's lab

-OR-



○ **All** of the following:

- Patient does not have a low IGF-1/Somatomedin C level

**-AND-**

- Discontinued GH therapy for at least 1 month

**-AND-**

- Patient has undergone a **one** of the following GH stimulation tests after discontinuation of therapy for at least 1 month:

- ITT
- GHRH+ARG
- ARG
- Glucagon

**-AND-**

- **One** of the following peak GH values:

- ITT  $\leq 5$   $\mu\text{g/L}$
- GHRH+ARG ( $\leq 11$   $\mu\text{g/L}$  if body mass index [BMI]  $< 25$   $\text{kg/m}^2$ ;  $\leq 8$   $\mu\text{g/L}$  if BMI  $\geq 25$  and  $< 30$   $\text{kg/m}^2$ ;  $\leq 4$   $\mu\text{g/L}$  if BMI  $\geq 30$   $\text{kg/m}^2$ )
- Glucagon  $\leq 3$   $\mu\text{g/L}$
- ARG  $\leq 0.4$   $\mu\text{g/L}$

**-OR-**

(b) **All** of the following:

- i. At low risk of severe GH deficiency (eg, due to isolated and/or idiopathic GH deficiency)

**-AND-**

- ii. Discontinued GH therapy for at least 1 month

**-AND-**

- iii. **Both** of the following:

- Patient has undergone **one** of the following GH stimulation tests after discontinuation of therapy for at least 1 month:

- ITT
- GHRH+ARG
- ARG
- Glucagon

-AND-

- **One** of the following peak GH values:

- ITT  $\leq 5$   $\mu\text{g/L}$
- GHRH+ARG ( $\leq 11$   $\mu\text{g/L}$  if body mass index [BMI]  $< 25$   $\text{kg/m}^2$ ;  $\leq 8$   $\mu\text{g/L}$  if BMI  $\geq 25$  and  $< 30$   $\text{kg/m}^2$ ;  $\leq 4$   $\mu\text{g/L}$  if BMI  $\geq 30$   $\text{kg/m}^2$ )
- Glucagon  $\leq 3$   $\mu\text{g/L}$
- ARG  $\leq 0.4$   $\mu\text{g/L}$

-AND-

(4) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

## 2. Reauthorization

a. **Somatropin** will be approved based on the following criterion:

(1) Documentation of positive response to therapy (e.g., increase in total lean body mass, exercise capacity or IGF-1 and IGFBP-3 levels)

-AND-

(2) Request does not exceed a maximum supply limit of 0.3 mg/kg/week)

-AND-

(3) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

### **I. Human Immunodeficiency Virus (HIV)-Associated Cachexia (Serostim**

**only)**

**1. Initial Therapy**

a. Serostim will be approved based on **all** of the following criteria:

(1) Diagnosis of HIV-associated wasting syndrome or cachexia

**-AND-**

(2) Documentation of **one** of the following:

(a) Unintentional weight loss of > 10% over the last 12 months

(b) Unintentional weight loss of > 7.5% over the last 6 months

(c) Loss of 5% body cell mass (BCM) within 6 months

(d) Body mass index (BMI) < 20 kg/m<sup>2</sup>

(e) **One** of the following:

i. **All** of the following

- Patient is male
- BCM < 35% of total body weight
- BMI < 27 kg/m<sup>2</sup>

**-OR-**

ii. **All** of the following:

- Patient is female
- BCM < 23% of total body weight
- BMI < 27 kg/m<sup>2</sup>

**-AND-**

(3) A nutritional evaluation has been completed since onset of wasting first occurred

**-AND-**

(4) Patient has not had weight loss as a result of other underlying treatable conditions (e.g., depression, mycobacterium avium complex, chronic infectious diarrhea, or malignancy with the exception of Kaposi's sarcoma limited to skin or mucous membranes)

**-AND-**

- (5) Patient's anti-retroviral therapy has been optimized to decrease the viral load

**Authorization will be issued for 3 months.**

**2. Reauthorization**

- a. **Serostim** will be approved based on **both** of the following criteria:

- (1) Evidence of positive response to therapy (i.e.,  $\geq 2\%$  increase in body weight and/or BCM)

**-AND-**

- (2) **One** of the following targets or goals has not been achieved:

- (a) Weight
- (b) BCM
- (c) BMI

**Authorization will be issued for 6 months.**

**J. Short Bowel Syndrome (Zorbtive only)**

1. **Zorbtive** will be approved based on **all** of the following criteria:

- a. Diagnosis of Short Bowel Syndrome

**-AND-**

- b. Patient is currently receiving specialized nutritional support (e.g., intravenous parenteral nutrition, fluid, and micronutrient supplements)

**-AND-**

- c. Patient has not previously received 4 weeks of treatment with Zorbtive

**Authorization will be issued for 4 weeks.**

**Note: Treatment with Zorbtive will not be authorized beyond 4 weeks. Administration for more than 4 weeks has not been adequately studied.**

**K. Idiopathic Short Stature (for the state of Maryland and California)**

**only)**

**1. Initial Therapy**

**a. Somatropin** will be approved based on **all** of the following criteria:

(1) Diagnosis of idiopathic short stature

**-AND-**

(2) Other causes associated with short stature (e.g., growth-hormone deficiency, chronic renal insufficiency, etc.) have been excluded

**-AND-**

(3) Documentation of height  $\leq$  -2.25 SD score (SDS) below the corresponding mean height for age and gender

**-AND-**

(4) Documentation of growth velocity that is less than 25<sup>th</sup> percentile for bone age

**-AND-**

(5) Documentation of **one** of the following:

(a) Patient is male and **one** of the following:

- i. Tanner stage less than IV
- ii. Bone age < 16 years measured in the past 12 months

**-OR-**

(b) Patient is female and **one** of the following:

- i. Tanner stage less than IV
- ii. Bone age < 14 years measured in the past 12 months

**-AND-**

(6) **One** of the following:

(a) Request does not exceed a maximum supply limit of 0.3 mg/kg/week

-OR-

(b) **Both** of the following:

- i. Tanner Stage 3 or greater
- ii. Request does not exceed a maximum supply limit of 0.7 mg/kg/week

-AND-

(7) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**Note: Documentation of previous height, current height and goal expected adult height will be required for renewal.**

## 2. Reauthorization

a. **Somatropin** will be approved based on **all** of the following criteria:

(1) Height increase at least 2 cm/year over the previous year of treatment as documented by **both** of the following:

- (a) Previous height and date obtained
- (b) Current height and date obtained

-AND-

(2) Documentation of **both** of the following:

- (a) Expected adult height not attained
- (b) Expected adult height goal

-AND-

(3) **One** of the following:

- (a) Request does not exceed a maximum supply limit of 0.3 mg/kg/week

-OR-

(b) **Both** of the following:

- i. Tanner Stage 3 or greater
- ii. Request does not exceed a maximum supply limit of 0.7 mg/kg/week

-AND-

- (4) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**L. Severe Primary IGF-1 Deficiency / Growth Hormone Gene Deletion (Increlex only)**

**1. Initial Therapy**

- a. **Increlex** will be approved based on **one** of the following criteria:

- (1) Documentation of **all** of the following:

- (a) Diagnosis of severe primary IGF-1 deficiency

-AND-

- (b) Height standard deviation score  $\leq -3.0$

-AND-

- (c) Basal IGF-1 standard deviation score  $\leq -3.0$

-AND-

- (d) Normal or elevated growth hormone levels

-AND-

- (e) Documentation of open epiphyses on last bone radiograph

-AND-

- (f) The patient will not be treated with concurrent growth hormone therapy

-AND-

- (g) Prescribed by an endocrinologist

-OR-

b. **All** of the following:

(1) Diagnosis of growth hormone gene deletion and has developed neutralizing antibodies to growth hormone

-AND-

(2) Documentation of open epiphyses on last bone radiograph

-AND-

(3) The patient will not be treated with concurrent growth hormone therapy

-AND-

(4) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**Note: Documentation of previous height, current height and goal expected adult height will be required for renewal.**

## 2. **Reauthorization**

a. **Increlex** will be approved based on **all** of the following criteria:

(1) Height increase of at least 2 cm/year over the previous year of treatment as documented by **both** of the following:

- (a) Previous height and date obtained
- (b) Current height and date obtained

-AND-

(2) Documentation of **both** of the following:

- (a) Expected adult height not obtained
- (b) Expected adult height goal

-AND-

(3) Patient is not treated with concurrent growth hormone therapy

-AND-



(4) Prescribed by an endocrinologist

**Authorization will be issued for 12 months.**

**\*Educational Statement:** Documentation of previous height, current height and goal expected adult height will be required for renewal.

### Essential versus Nonessential Use

The Patient Protection and Affordable Care Act (PPACA) of 2010 includes a mandate that prohibits annual dollar maximum limits for “essential” benefits. A strict definition of “essential” was not provided in PPACA or in federal health care regulations published as of the date this program was revised. UnitedHealthcare defines an “essential” use of growth hormone as therapy to treat a deficiency as part of chronic disease management. Other uses such as replacement therapy in a disorder where a deficiency is not noted are considered “nonessential.”

This information applies to groups with benefit caps in place for growth hormone therapy. If the diagnosis is considered an essential use of the medication, the cap will not apply. For these cases, an override for the cap amount will be entered at the same time the authorization (if criteria met) is entered for the medication. If the diagnosis is a nonessential use of the medication, then only the authorization for the medication will be entered.

<b>Diagnosis</b>	
Pediatric growth hormone deficiency	Essential
Growth failure in children small for gestational age	Nonessential
Growth failure due to chronic renal insufficiency	Nonessential
Growth failure due to Turner Syndrome	Nonessential
Growth failure due to Noonan Syndrome	Nonessential
Growth failure due to short-stature homeobox (SHOX) gene deficiency	Nonessential
Prader-Willi Syndrome	Nonessential
Adult growth hormone deficiency	Essential
Transition phase adolescent patients	Essential
HIV-associated wasting syndrome/cachexia	Essential
Short bowel syndrome	Essential
Severe primary IGF-1 deficiency	Essential
Idiopathic short stature (not currently covered per criteria)	Nonessential

### 3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

- Genotropin, Humatrope, Norditropin, NordiFlex, Omnitrope, Saizen and Zomacton are excluded for lines of business with therapeutic equivalent exclusions.

#### 4. References:

1. AACE Growth Hormone Task Force. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use in Adults and Children – 2003 Update. *Endocr Pract.* 2003;9(1):64-76.
2. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use in Growth Hormone-Deficient Adults and Transition Patients—2009 Update. *Endocr Pract.* 2009;15(Suppl 2):1-29.
3. Clayton PE, Cuneo RC, Juul A, et al. Consensus statement on the management of the GH-treated adolescent in the transition to adult care. *Eur J Endocrinol.* 2005;152:165-170.
4. Clayton PE, Cianfarani P, Czernichow G, et al. Management of the child born small for gestational age through to adulthood: a consensus statement of the International Societies of Pediatric Endocrinology and the Growth Hormone Research Society. *J Clin Endocrinol Metab.* 2007 Mar;92(3):804-10.
5. Consensus guidelines for the diagnosis and treatment of adults with growth hormone deficiency: summary statement of the growth hormone research society workshop on adult growth hormone deficiency. *J Clin Endocrinol Metab.* 1998;83:379-81.
6. Consensus Guidelines for the Diagnosis and Treatment of Growth Hormone (GH) Deficiency in Childhood and Adolescence: Summary Statement of the GH Research Society. *J Clin Endocrinol Metab.* 2000;85(11):3990-3.
7. Genotropin [package insert]. New York, NY: Pharmacia & Upjohn Company; December 2012.
8. Deal CL, Tony M, Höybye C, et al. Growth hormone research society workshop summary: consensus guidelines for recombinant human growth hormone therapy in prader-willi syndrome. *J Clin Endocrinol Metab.* 2013 Jun;98(6):E1072-87.
9. HIV Clinical Resource. General nutrition, weight lost and wasting syndrome. Available at <http://www.hivguidelines.org/clinical-guidelines/adults/general-nutrition-weight-loss-and-wasting-syndrome/>. Accessed June 29, 2012.
10. Ho KKY. Consensus guidelines for the diagnosis and treatment of adults with GH deficiency II: a statement of the GH Research Society in association with the European Society for Pediatric Endocrinology, Lawson Wilkins Society, European Society of Endocrinology, Japan Endocrine Society, and Endocrine Society of Australia. *Eur J Endocrinol.* 2007;157(6):695-700.
11. Humatrope [package insert]. Indianapolis, IN: Eli Lilly and Company; October 2019.
12. Increlex [package insert]. Brisbane, CA: Tercia, Inc.; January 2019.
13. Mauras N, Attie KM, Reiter EO, et al. High dose recombinant human growth hormone (GH) treatment of GH-deficient patients in puberty increases near-final height: a randomized, multicenter trial. Genentech, Inc., Cooperative Study Group. *J Clin Endocrinol Metab.* 2000 Oct;85(10):3653-60.
14. Mauras N, Pescovitz OH, Allada V, et al. Limited efficacy of growth hormone (GH) during transition of GH-deficient patients from adolescence to adulthood: a phase III

- multicenter, double-blind, randomized two-year trial. *J Clin Endocrinol Metab.* 2005;90:3946-55.
15. Mauras N. Treatment of Growth Hormone Deficiency in the Transition of Adolescence to Adulthood. *Growth and Growth Hormone: Current Applications and Clinical Updates.* Vindico Medical Education 2008.
  16. Molitch ME, Clemmons DR, Malozowski S, et al. Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2011 Jun;96(6):1587-609.
  17. National Institute for Health and Clinical Excellence (2010) [Human growth hormone (somatropin) for the treatment of growth failure in children]. [TA188]. London: National Institute for Health and Clinical Excellence.
  18. Norditropin Flexpro [package insert]. Princeton, NJ: Novo Nordisk Pharmaceuticals, Inc.; February 2018.
  19. Nutropin [package insert]. South San Francisco, CA: Genentech, Inc.; December 2016.
  20. Nutropin AQ, Nutropin AQ NuSpin [package insert]. South San Francisco, CA: Genentech, Inc.; April 2012.
  21. Nwosu BU and Lee MM. Evaluation of short and tall stature in children. *Am Fam Physician.* 2008 Sep 1;78(5):597-604.
  22. Omnitrope [package insert]. Princeton, NJ: Sandoz, Inc.; December 2016.
  23. Owens G, Balfour D, Biller B, et al. Clinical Presentation and Diagnosis: Growth Hormone Deficiency in Adults. *Am J Manag Care.* 2004;10(13 Suupl):S424-30.
  24. Polsky B, Kotler D, Steinhart C. HIV-associated wasting in the HAART era: guidelines for assessment, diagnosis and treatment. *AIDS Patient Care STDS.* 2001;15(8):411-23.
  25. Saizen [package insert]. Rockland, MA: EMD Serono, Inc.; May 2017.
  26. Serostim [package insert]. Rockland, MA: EMD Serono, Inc.; May 2017.
  27. Wilson TA, Rose SR, Cohen P, et al. Update of guidelines for the use of growth hormone in children: the Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. *J Pediatr.* 2003 Oct;143(4):415-21.
  28. Zorbtive [package Insert]. Rockland, MA: EMD Serono, Inc.; January 2012.
  29. Zomacton [package insert]. Horsham, PA: Teva Select Brands; September 2016.
  30. Macrilen [package insert]. Frankfurt, Germany: Aeterna Zentaris; December 2017.
  31. Yuen, K., Biller, B., Radovick, S., Carmichael, J. D., Jasim, S., Pantalone, K. M., & Hoffman, A. R. (2019). AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY GUIDELINES FOR MANAGEMENT OF GROWTH HORMONE DEFICIENCY IN ADULTS AND PATIENTS TRANSITIONING FROM PEDIATRIC TO ADULT CARE. *Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*, 25(11), 1191–1232.

Program	Prior Authorization/Medical Necessity - Human Growth Hormone and Growth Stimulating Products
<b>Change Control</b>	
2/2014	Developed new medical necessity criteria through revised criteria to include dosing, specialist prescriber and no combination therapy for adult GHD.

8/2014	Clarified medical record requirement language.
5/2015	Added dosing charts for ped & adult GHD. Removed Tev-tropin.
8/2015	Added Zomacton. Removed dosing charts and added requirement for SL dosing maximum to pediatric GHD, adult GHD, transitional, and ISS Updated formatting.
6/2016	Added Tanner Stage 3 to pediatric GHD as a requirement for dosing up to a maximum of 0.7 mg/kg/week. Added bone age and growth velocity to pediatric GHD and ISS. Clarified expected adult height.
12/2016	Revised medical record requirement language and clarified criteria for diagnosis of pediatric GH deficiency.
11/2017	Annual Review. Updated references.
11/2018	Annual review. Added macrilen (macimorelin) as an option for the diagnosis of adult growth hormone deficiency and updated references.
12/2019	Annual review. Updated bone age requirement, supply limits, and references.
4/2020	Added requirement for state of California.
7/2021	Annual review. No change to clinical criteria. Updated references.