



# MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

## Pharmacy Medical Policy Growth Hormone and Insulin-like Growth Factor

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### Policy Number: 257

BCBSA Reference Number: 5.01.06

### Related Policies

None

### Policy

#### Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

**Note:** All requests for outpatient retail pharmacy for indications listed and not listed on the medical policy guidelines may be submitted to BCBSMA Clinical Pharmacy Operations by completing the Prior Authorization Form on the last page of this document. Physicians may also call BCBSMA Pharmacy Operations department at (800)366-7778 to request a prior authorization/formulary exception verbally. Physicians may also submit requests for retail pharmacy exceptions via the web using Express PA which can be found on the BCBSMA provider portal or directly on the web at <https://provider.express-path.com>. Patients must have pharmacy benefits under their subscriber certificates.

Please refer to the chart below for the formulary and step status of the medications affected by this policy.

Standard Formulary	
Drug	Formulary Status
Egrifta™ (tesamorelin)	PA required
Genotropin®*^ (somatropin)	Not covered*
Genotropin Miniquick®*^ (somatropin)	Not covered*
Humatrope®*^ (somatropin)	PA required
Increlex®*^ (mecasermin)	PA required
Norditropin®*^ (somatropin)	Not covered*
Nutropin®*^ (somatropin)	PA required
Nutropin AQ®*^ (somatropin)	PA required
Nutropin® Depot*^ (somatropin)	PA required
Omnitrope®*^ (somatropin)	Not covered*

<b>Saizen<sup>®*</sup></b> (somatropin)	Not covered*
<b>Serostim<sup>®*</sup></b> (somatropin)	PA required
<b>Skytrofa<sup>™*</sup></b> (lonapegsomatropin-tcgd)	PA required
<b>Tev-Tropin<sup>®*</sup></b> (somatropin)	Not covered*
<b>Zomacton<sup>®</sup></b> (somatropin)	Not covered*
<b>Zorbitive<sup>®*</sup></b> (somatropin)	PA required

\*^ - This Drug is part of Medications covered only under the pharmacy benefit program.

\*Coverage of these medications will only be approved if the patient meets the pharmacy medical policy criteria below AND has tried and failed treatment with two covered formulary alternatives.

## GROWTH HORMONE

### For Humatrope<sup>®</sup>, Nutropin<sup>®</sup> and Nutropin AQ<sup>®</sup>:

Recombinant human growth hormone (GH) therapy may be considered medically necessary for the following patients:

- Children with proven growth hormone deficiency
- Children with growth failure due to Prader-Willi syndrome, who do not have the following contraindications: history of upper airway obstruction or sleep apnea or severe respiratory impairment
- Children with height below the 3rd percentile for chronologic age with chronic renal insufficiency
- Patients with Turner syndrome
- Patients with short stature due to Noonan syndrome
- Children with short stature due to SHOX (short stature homeobox-containing gene) deficiency
- Promotion of wound healing in burn patients
- Prevention of growth delay in children with severe burns
- Patients with AIDS wasting
- Patients with short bowel syndrome receiving specialized nutritional support in conjunction with optimal management of short bowel syndrome
- Adults with proven growth hormone deficiency.

The following indications approved by the Food and Drug Administration are considered not medically necessary:

- Pediatric patients born small for gestational age who fail to show catch-up growth by age 2 years
- Children with height standard deviation score of -2.25 or below without documented growth hormone deficiency.

## LONG-ACTING GROWTH HORMONE

### For Skytrofa<sup>™</sup>:

Long-acting recombinant human growth hormone (GH) therapy may be considered medically necessary when **all** the following criteria are met:

- Age is greater than or equal to 1 years of age, AND
- The child's weight is at least 11.5 kg (25.3 Lbs.), AND
- Confirmed open epiphyses, AND
- Confirmed diagnosis with proven growth failure due to inadequate secretion of endogenous growth hormone (GH)
- Trial of Formulary endogenous growth hormone (GH) product of **Humatrope<sup>®</sup> or Nutropin<sup>®</sup> or Nutropin AQ<sup>®</sup>**.

Recombinant human growth hormone is considered investigational for all other applications including, but not limited to the following:

- Treatment of altered body habitus (eg, buffalo hump) associated with antiviral therapy in HIV- infected patients

- Constitutional delay (lower than expected height percentiles compared with target height percentiles and delayed skeletal maturation when growth velocities and rates of bone age advancement are normal)
- Treatment of children with “genetic potential” (ie, lower than expected height percentiles based on parents’ height)
- In conjunction with gonadotropin-releasing hormone analogues as a treatment of precocious puberty
- Growth hormone therapy in older adults without proven deficiency
- Treatment of cystic fibrosis
- Anabolic therapy (except for AIDS) provided to counteract acute or chronic catabolic illness (eg, surgery outcomes, trauma, cancer, chronic hemodialysis, chronic infectious disease) producing catabolic (protein wasting) changes in both adult and pediatric patients
- Anabolic therapy to enhance body mass or strength for professional, recreational, or social reasons
- Glucocorticoid-induced growth failure
- Short stature due to Down syndrome
- Treatment of obesity
- Treatment of idiopathic dilated cardiomyopathy
- Treatment of juvenile idiopathic or juvenile chronic arthritis.

We may cover GH therapy for patients with HIV wasting syndrome in patients who meet all of the following:<sup>3, 11, 22</sup>

- Documented AIDS.
- Weight loss of at least 10% from baseline weight or BMI < 20 kg/m<sup>2</sup>.
- Wasting syndrome rather than malnutrition, mental illness, endocrine disease, or other causes for weight loss.
- Concomitant anti-viral therapy for the duration of treatment.<sup>16</sup>

We may cover GH therapy for promotion of wound healing in burn patients.

**Note:** GH therapy for burn patients should be limited to those patients with 3rd-degree burns.<sup>22</sup>

We may cover GH therapy for prevention of growth delay in children with severe burns.

**Note:** Children with severe burns have been successfully treated with 0.05 to 0.2mg/kg rhGH per day during acute hospitalization and for up to 1 year after burn.<sup>22</sup>

We may cover Somatropin (Zorbtive™/Serostim®) in the treatment of Short Bowel Syndrome for adult patients for 4 weeks when **ALL** of the following criteria are met:

- Patient is ≥ 18 years of age
- Currently receiving specialized nutritional support such as dietary adjustments, enteral feedings, parenteral nutrition, or micronutrient supplementation.

We may cover Egrifta™ (tesamorelin) for the reduction of excess abdominal fat due to lipodystrophy due to antiretroviral therapy in HIV-infected patients.

For adults, proven GHD is defined as:

- a. An abnormal response to TWO provocative stimulation tests, such as L-dopa, clonidine, glucagons, arginine, growth hormone–releasing hormone (GH-RH), or insulin. The insulin tolerance test is considered the best predictor of GHD; however, this test is contraindicated in patients with seizures or coronary artery disease. A provocation test using arginine and GH-RH is also acceptable and is considered more stringent than tests using arginine alone or levodopa alone. Although an abnormal GH response has been traditionally defined as less than 10 ng/mL, different tests have different potencies, and the cutoff is likely to be lower when using monoclonal-based GH assays and recombinant human GH reference preparations. Twenty-four-hour continuous measurements of GH, serum levels of insulin-like growth factor-I (IGF-I), or serum of levels insulin-like growth factor–binding protein are considered inadequate to document GHD.

- b. An abnormal response to ONE provocative stimulation test in patients with defined central nervous system pathology, history of irradiation, multiple pituitary hormone deficiency, or a genetic defect
- c. Low IGF-I concentration in patients with complete hypopituitarism.

**For Genotropin® (somatropin), Genotropin Miniquick® (somatropin), Norditropin® (somatropin), Omnitrope® (somatropin), Saizen® (somatropin), Tev-Tropin® (somatropin), and Zomacton® (somatropin):**

We may cover GH therapy as listed in the criteria above **AND** when the member has had previous treatment failure with or contraindication to the formulary products: Humatrope and Nutropin/AQ®.

**INSULIN-LIKE GROWTH FACTOR:**

We may cover mecasermin (rDNA origin), Icrelex® for the treatment of growth failure in children with severe primary insulin-like growth factor-1 (IGF-1) deficiency (primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH when **ALL** of the following criteria are met<sup>23</sup>:

- Height standard deviation score less than or equal to -3 for age and sex.
- Basal IGF-1 standard deviation score less than or equal to -3 for age and sex.
- Normal or elevated growth hormone (defined as stimulated serum GH peak level of greater than 10 ng/ml or basal (unstimulated) serum GH level greater than 5ng/ml).

**Guidelines for continuation of therapy**

**For Humatrope® (somatropin), Nutropin® (somatropin), and Nutropin AQ® (somatropin):**

We may cover continuation of GH when **ALL** the following are met:

- Open epiphyses (as determined within the last year by radiographic evidence)
- **NO** evidence of tumor activity or active neoplasm
- Growth velocity > 2cm/yr
- Absence of significant side effects
- Compliance with therapy
- **NOT** being used in combination with another somatropin agent (such as Serostim, Zorbtive or any other GH).

**For Genotropin® (somatropin), Genotropin Miniquick® (somatropin), Norditropin® (somatropin), Omnitrope® (somatropin), Saizen® (somatropin), and Tev-Tropin® (somatropin):**

We may cover GH therapy as listed in the criteria above **AND** when the member has had previous treatment failure with or contraindication to the formulary products: Humatrope and Nutropin/AQ®.

**Non-covered diagnoses**

We do not cover GH therapy for other conditions not listed above, including:

- Short children who are not GH deficient<sup>22</sup>
- Growth hormone insensitivity (Laron Syndrome)<sup>5</sup>
- Children with constitutional growth delay<sup>22</sup>
- Children with growth failure caused by glucocorticoids<sup>22</sup>
- Children who are not growth hormone deficient but have short stature associated with chronic disease<sup>11</sup>
- Children with functioning renal transplants
- Children with chromosomal and genetic disorders<sup>11</sup> (except Turner's and Prader Willi Syndromes)<sup>11</sup> or familial short stature<sup>11</sup>
- Russell Silver syndrome<sup>21</sup>
- Anabolic therapy to enhance body mass or strength for professional, recreational or social reasons<sup>22</sup>
- Anabolic therapy, except for AIDS, provided to counteract acute or chronic catabolic illness (e.g., surgery outcomes, trauma, cancer, chronic hemodialysis) producing catabolic (protein wasting) changes in both adult and pediatric patients<sup>22</sup>
- Altered body habitus or lipodystrophy such as buffalo hump associated with antiviral therapy in HIV-infected patients<sup>22</sup>

- In conjunction with GnRH (gonadotropin releasing hormone) analogs as a treatment of precocious puberty<sup>22</sup>
- Treatment of obesity<sup>22</sup>
- Treatment of cystic fibrosis<sup>22</sup>
- Treatment of idiopathic dilated cardiomyopathy<sup>22</sup>
- Treatment of juvenile idiopathic arthritis.<sup>22</sup>

We do not cover GH therapy for congestive heart failure (CHF), because the precise mechanism of GH action has not been established and its long-term effectiveness is not known.<sup>10</sup>

We do not cover GH therapy for adults with age-related GH deficiency (AR-GHD), who have no organic causes or childhood origin of growth hormone deficiency. It has not been proven in the medical literature to improve the disability and quality of life of patients with AR-GHD.<sup>17</sup>

We do not cover Insulin-like Growth Factor for secondary forms of IGF-1 deficiency to include (but not limited to):<sup>23</sup>

- GH Deficiency
- Malnutrition
- Hypothyroidism
- Chronic treatment with pharmacologic doses of anti-inflammatory steroids.

### Other Information

Blue Cross Blue Shield of Massachusetts (BCBSMA\*) members (other than Medex®; Blue MedicareRx, Medicare Advantage plans that include prescription drug coverage) will be required to fill their prescriptions for the above medications at one of the providers in our retail specialty pharmacy network, see link below:

[Link to Specialty Pharmacy List](#)

### Individual Consideration

All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual's unique clinical circumstances may be considered in light of current scientific literature. Physicians may send relevant clinical information for individual patients for consideration to:

Blue Cross Blue Shield of Massachusetts  
 Pharmacy Operations Department  
 25 Technology Place  
 Hingham, MA 02043  
 Tel: 1-800-366-7778  
 Fax: 1-800-583-6289

### Prior Authorization Information

#### Outpatient

For services described in this policy, see below for products where prior authorization **IS REQUIRED** if the procedure is performed **outpatient**.

	<b>Outpatient</b>
<b>Commercial Managed Care (HMO and POS)</b>	Prior authorization is <b>required</b> .
<b>Commercial PPO</b>	Prior authorization is <b>required</b> .

### CPT Codes / HCPCS Codes / ICD Codes

*Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.*

*Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.*

*The following codes are included below for informational purposes only; this is not an all-inclusive list.*

**The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:**

### HCPCS Codes

<b>HCPCS codes:</b>	<b>Code Description</b>
J2940	Injection, somatrem, 1 mg (Protropin)
J2941	Injection, somatropin, 1 mg (Humatrope, Genotropin Nutropin, Biotropin, Genotropin, Genotropin Miniquick, Norditropin, Nutropin, Nutropin AQ, Saizen, Saizen Somatropin RDNA Origin, Serostim, Serostim RDNA Origin, Zorbtive)

**The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT codes above if medical necessity criteria are met:**

### ICD-10 Diagnosis Codes

<b>ICD-10-CM Diagnosis codes:</b>	<b>Code Description</b>
B20	Human immunodeficiency virus [HIV] disease
E23.0	Hypopituitarism
E23.1	Drug-induced hypopituitarism
E89.3	Postprocedural hypopituitarism
K91.2	Postsurgical malabsorption, not elsewhere classified
N18.1	Chronic kidney disease, stage 1
N18.2	Chronic kidney disease, stage 2 (mild)
N18.30	Chronic kidney disease, stage 3 unspecified
N18.31	Chronic kidney disease, stage 3a
N18.32	Chronic kidney disease, stage 3b
N18.4	Chronic kidney disease, stage 4 (severe)
N18.5	Chronic kidney disease, stage 5
N18.6	End stage renal disease
N18.9	Chronic kidney disease, unspecified
N29	Other disorders of kidney and ureter in diseases classified elsewhere
P05.9	Newborn affected by slow intrauterine growth, unspecified
Q87.11	Prader-Willi syndrome
Q87.19	Other congenital malformation syndromes predominantly associated with short stature
Q96.0	Karyotype 45, X
Q96.1	Karyotype 46, X iso (Xq)
Q96.2	Karyotype 46, X with abnormal sex chromosome, except iso (Xq)
Q96.3	Mosaicism, 45, X/46, XX or XY
Q96.4	Mosaicism, 45, X/other cell line(s) with abnormal sex chromosome
Q96.8	Other variants of Turner's syndrome
Q96.9	Turner's syndrome, unspecified

R64	Cachexia
T20.30xA	Burn of third degree of head, face, and neck, unspecified site, initial encounter
T20.30xD	Burn of third degree of head, face, and neck, unspecified site, subsequent encounter
T20.30xS	Burn of third degree of head, face, and neck, unspecified site, sequela
T20.311A	Burn of third degree of right ear [any part, except ear drum], initial encounter
T20.311D	Burn of third degree of right ear [any part, except ear drum], subsequent encounter
T20.311S	Burn of third degree of right ear [any part, except ear drum], sequela
T20.312A	Burn of third degree of left ear [any part, except ear drum], initial encounter
T20.312D	Burn of third degree of left ear [any part, except ear drum], subsequent encounter
T20.312S	Burn of third degree of left ear [any part, except ear drum], sequela
T20.319A	Burn of third degree of unspecified ear [any part, except ear drum], initial encounter
T20.319D	Burn of third degree of unspecified ear [any part, except ear drum], subsequent encounter
T20.319S	Burn of third degree of unspecified ear [any part, except ear drum], sequela
T20.32xA	Burn of third degree of lip(s), initial encounter
T20.32xD	Burn of third degree of lip(s), subsequent encounter
T20.32xS	Burn of third degree of lip(s), sequela
T20.33xA	Burn of third degree of chin, initial encounter
T20.33xD	Burn of third degree of chin, subsequent encounter
T20.33xS	Burn of third degree of chin, sequela
T20.34xA	Burn of third degree of nose (septum), initial encounter
T20.34xD	Burn of third degree of nose (septum), subsequent encounter
T20.34xS	Burn of third degree of nose (septum), sequela
T20.35xA	Burn of third degree of scalp [any part], initial encounter
T20.35xD	Burn of third degree of scalp [any part], subsequent encounter
T20.35xS	Burn of third degree of scalp [any part], sequela
T20.36xA	Burn of third degree of forehead and cheek, initial encounter
T20.36xD	Burn of third degree of forehead and cheek, subsequent encounter
T20.36xS	Burn of third degree of forehead and cheek, sequela
T20.37xA	Burn of third degree of neck, initial encounter
T20.37xD	Burn of third degree of neck, subsequent encounter
T20.37xS	Burn of third degree of neck, sequela
T20.39xA	Burn of third degree of multiple sites of head, face, and neck, initial encounter
T20.39xD	Burn of third degree of multiple sites of head, face, and neck, subsequent encounter
T20.39xS	Burn of third degree of multiple sites of head, face, and neck, sequela
T21.30xA	Burn of third degree of trunk, unspecified site, initial encounter
T21.30xD	Burn of third degree of trunk, unspecified site, subsequent encounter
T21.30xS	Burn of third degree of trunk, unspecified site, sequela
T21.31xA	Burn of third degree of chest wall, initial encounter
T21.31xD	Burn of third degree of chest wall, subsequent encounter
T21.31xS	Burn of third degree of chest wall, sequela
T21.32xA	Burn of third degree of abdominal wall, initial encounter
T21.32xD	Burn of third degree of abdominal wall, subsequent encounter
T21.32xS	Burn of third degree of abdominal wall, sequela
T21.33xA	Burn of third degree of upper back, initial encounter
T21.33xD	Burn of third degree of upper back, subsequent encounter
T21.33xS	Burn of third degree of upper back, sequela
T21.34xA	Burn of third degree of lower back, initial encounter
T21.34xD	Burn of third degree of lower back, subsequent encounter
T21.34xS	Burn of third degree of lower back, sequela
T21.35xA	Burn of third degree of buttock, initial encounter

T21.35xD	Burn of third degree of buttock, subsequent encounter
T21.35xS	Burn of third degree of buttock, sequela
T21.36xA	Burn of third degree of male genital region, initial encounter
T21.36xD	Burn of third degree of male genital region, subsequent encounter
T21.36xS	Burn of third degree of male genital region, sequela
T21.37xA	Burn of third degree of female genital region, initial encounter
T21.37xD	Burn of third degree of female genital region, subsequent encounter
T21.37xS	Burn of third degree of female genital region, sequela
T21.39xA	Burn of third degree of other site of trunk, initial encounter
T21.39xD	Burn of third degree of other site of trunk, subsequent encounter
T21.39xS	Burn of third degree of other site of trunk, sequela
T22.30xA	Burn of third degree of shoulder and upper limb, except wrist and hand, unspecified site, initial encounter
T22.30xD	Burn of third degree of shoulder and upper limb, except wrist and hand, unspecified site, subsequent encounter
T22.30xS	Burn of third degree of shoulder and upper limb, except wrist and hand, unspecified site, sequela
T22.311A	Burn of third degree of right forearm, initial encounter
T22.311D	Burn of third degree of right forearm, subsequent encounter
T22.311S	Burn of third degree of right forearm, sequela
T22.312A	Burn of third degree of left forearm, initial encounter
T22.312D	Burn of third degree of left forearm, subsequent encounter
T22.312S	Burn of third degree of left forearm, sequela
T22.319A	Burn of third degree of unspecified forearm, initial encounter
T22.319D	Burn of third degree of unspecified forearm, subsequent encounter
T22.319S	Burn of third degree of unspecified forearm, sequela
T22.321A	Burn of third degree of right elbow, initial encounter
T22.321D	Burn of third degree of right elbow, subsequent encounter
T22.321S	Burn of third degree of right elbow, sequela
T22.322A	Burn of third degree of left elbow, initial encounter
T22.322D	Burn of third degree of left elbow, subsequent encounter
T22.322S	Burn of third degree of left elbow, sequela
T22.329A	Burn of third degree of unspecified elbow, initial encounter
T22.329D	Burn of third degree of unspecified elbow, subsequent encounter
T22.329S	Burn of third degree of unspecified elbow, sequela
T22.331A	Burn of third degree of right upper arm, initial encounter
T22.331D	Burn of third degree of right upper arm, subsequent encounter
T22.331S	Burn of third degree of right upper arm, sequela
T22.332A	Burn of third degree of left upper arm, initial encounter
T22.332D	Burn of third degree of left upper arm, subsequent encounter
T22.332S	Burn of third degree of left upper arm, sequela
T22.339A	Burn of third degree of unspecified upper arm, initial encounter
T22.339D	Burn of third degree of unspecified upper arm, subsequent encounter
T22.339S	Burn of third degree of unspecified upper arm, sequela
T22.341A	Burn of third degree of right axilla, initial encounter
T22.341D	Burn of third degree of right axilla, subsequent encounter
T22.341S	Burn of third degree of right axilla, sequela
T22.342A	Burn of third degree of left axilla, initial encounter
T22.342D	Burn of third degree of left axilla, subsequent encounter
T22.342S	Burn of third degree of left axilla, sequela
T22.349A	Burn of third degree of unspecified axilla, initial encounter



T22.349D	Burn of third degree of unspecified axilla, subsequent encounter
T22.349S	Burn of third degree of unspecified axilla, sequela
T22.351A	Burn of third degree of right shoulder, initial encounter
T22.351D	Burn of third degree of right shoulder, subsequent encounter
T22.351S	Burn of third degree of right shoulder, sequela
T22.352A	Burn of third degree of left shoulder, initial encounter
T22.352D	Burn of third degree of left shoulder, subsequent encounter
T22.352S	Burn of third degree of left shoulder, sequela
T22.359A	Burn of third degree of unspecified shoulder, initial encounter
T22.359D	Burn of third degree of unspecified shoulder, subsequent encounter
T22.359S	Burn of third degree of unspecified shoulder, sequela
T22.361A	Burn of third degree of right scapular region, initial encounter
T22.361D	Burn of third degree of right scapular region, subsequent encounter
T22.361S	Burn of third degree of right scapular region, sequela
T22.362A	Burn of third degree of left scapular region, initial encounter
T22.362D	Burn of third degree of left scapular region, subsequent encounter
T22.362S	Burn of third degree of left scapular region, sequela
T22.369A	Burn of third degree of unspecified scapular region, initial encounter
T22.369D	Burn of third degree of unspecified scapular region, subsequent encounter
T22.369S	Burn of third degree of unspecified scapular region, sequela
T22.391A	Burn of third degree of multiple sites of right shoulder and upper limb, except wrist and hand, initial encounter
T22.391D	Burn of third degree of multiple sites of right shoulder and upper limb, except wrist and hand, subsequent encounter
T22.391S	Burn of third degree of multiple sites of right shoulder and upper limb, except wrist and hand, sequela
T22.392A	Burn of third degree of multiple sites of left shoulder and upper limb, except wrist and hand, initial encounter
T22.392D	Burn of third degree of multiple sites of left shoulder and upper limb, except wrist and hand, subsequent encounter
T22.392S	Burn of third degree of multiple sites of left shoulder and upper limb, except wrist and hand, sequela
T22.399A	Burn of third degree of multiple sites of unspecified shoulder and upper limb, except wrist and hand, initial encounter
T22.399D	Burn of third degree of multiple sites of unspecified shoulder and upper limb, except wrist and hand, subsequent encounter
T22.399S	Burn of third degree of multiple sites of unspecified shoulder and upper limb, except wrist and hand, sequela
T23.301A	Burn of third degree of right hand, unspecified site, initial encounter
T23.301D	Burn of third degree of right hand, unspecified site, subsequent encounter
T23.301S	Burn of third degree of right hand, unspecified site, sequela
T23.302A	Burn of third degree of left hand, unspecified site, initial encounter
T23.302D	Burn of third degree of left hand, unspecified site, subsequent encounter
T23.302S	Burn of third degree of left hand, unspecified site, sequela
T23.309A	Burn of third degree of unspecified hand, unspecified site, initial encounter
T23.309D	Burn of third degree of unspecified hand, unspecified site, subsequent encounter
T23.309S	Burn of third degree of unspecified hand, unspecified site, sequela
T23.311A	Burn of third degree of right thumb (nail), initial encounter
T23.311D	Burn of third degree of right thumb (nail), subsequent encounter
T23.311S	Burn of third degree of right thumb (nail), sequela
T23.312A	Burn of third degree of left thumb (nail), initial encounter
T23.312D	Burn of third degree of left thumb (nail), subsequent encounter

T23.312S	Burn of third degree of left thumb (nail), sequela
T23.319A	Burn of third degree of unspecified thumb (nail), initial encounter
T23.319D	Burn of third degree of unspecified thumb (nail), subsequent encounter
T23.319S	Burn of third degree of unspecified thumb (nail), sequela
T23.321A	Burn of third degree of single right finger (nail) except thumb, initial encounter
T23.321D	Burn of third degree of single right finger (nail) except thumb, subsequent encounter
T23.321S	Burn of third degree of single right finger (nail) except thumb, sequela
T23.322A	Burn of third degree of single left finger (nail) except thumb, initial encounter
T23.322D	Burn of third degree of single left finger (nail) except thumb, subsequent encounter
T23.322S	Burn of third degree of single left finger (nail) except thumb, sequela
T23.329A	Burn of third degree of unspecified single finger (nail) except thumb, initial encounter
T23.329D	Burn of third degree of unspecified single finger (nail) except thumb, subsequent encounter
T23.329S	Burn of third degree of unspecified single finger (nail) except thumb, sequela
T23.331A	Burn of third degree of multiple right fingers (nail), not including thumb, initial encounter
T23.331D	Burn of third degree of multiple right fingers (nail), not including thumb, subsequent encounter
T23.331S	Burn of third degree of multiple right fingers (nail), not including thumb, sequela
T23.332A	Burn of third degree of multiple left fingers (nail), not including thumb, initial encounter
T23.332D	Burn of third degree of multiple left fingers (nail), not including thumb, subsequent encounter
T23.332S	Burn of third degree of multiple left fingers (nail), not including thumb, sequela
T23.339A	Burn of third degree of unspecified multiple fingers (nail), not including thumb, initial encounter
T23.339D	Burn of third degree of unspecified multiple fingers (nail), not including thumb, subsequent encounter
T23.339S	Burn of third degree of unspecified multiple fingers (nail), not including thumb, sequela
T23.341A	Burn of third degree of multiple right fingers (nail), including thumb, initial encounter
T23.341D	Burn of third degree of multiple right fingers (nail), including thumb, subsequent encounter
T23.341S	Burn of third degree of multiple right fingers (nail), including thumb, sequela
T23.342A	Burn of third degree of multiple left fingers (nail), including thumb, initial encounter
T23.342D	Burn of third degree of multiple left fingers (nail), including thumb, subsequent encounter
T23.342S	Burn of third degree of multiple left fingers (nail), including thumb, sequela
T23.349A	Burn of third degree of unspecified multiple fingers (nail), including thumb, initial encounter
T23.349D	Burn of third degree of unspecified multiple fingers (nail), including thumb, subsequent encounter
T23.349S	Burn of third degree of unspecified multiple fingers (nail), including thumb, sequela
T23.351A	Burn of third degree of right palm, initial encounter
T23.351D	Burn of third degree of right palm, subsequent encounter
T23.351S	Burn of third degree of right palm, sequela
T23.352A	Burn of third degree of left palm, initial encounter
T23.352D	Burn of third degree of left palm, subsequent encounter
T23.352S	Burn of third degree of left palm, sequela
T23.359A	Burn of third degree of unspecified palm, initial encounter
T23.359D	Burn of third degree of unspecified palm, subsequent encounter
T23.359S	Burn of third degree of unspecified palm, sequela
T23.361A	Burn of third degree of back of right hand, initial encounter
T23.361D	Burn of third degree of back of right hand, subsequent encounter
T23.361S	Burn of third degree of back of right hand, sequela

T23.362A	Burn of third degree of back of left hand, initial encounter
T23.362D	Burn of third degree of back of left hand, subsequent encounter
T23.362S	Burn of third degree of back of left hand, sequela
T23.369A	Burn of third degree of back of unspecified hand, initial encounter
T23.369D	Burn of third degree of back of unspecified hand, subsequent encounter
T23.369S	Burn of third degree of back of unspecified hand, sequela
T23.371A	Burn of third degree of right wrist, initial encounter
T23.371D	Burn of third degree of right wrist, subsequent encounter
T23.371S	Burn of third degree of right wrist, sequela
T23.372A	Burn of third degree of left wrist, initial encounter
T23.372D	Burn of third degree of left wrist, subsequent encounter
T23.372S	Burn of third degree of left wrist, sequela
T23.379A	Burn of third degree of unspecified wrist, initial encounter
T23.379D	Burn of third degree of unspecified wrist, subsequent encounter
T23.379S	Burn of third degree of unspecified wrist, sequela
T23.391A	Burn of third degree of multiple sites of right wrist and hand, initial encounter
T23.391D	Burn of third degree of multiple sites of right wrist and hand, subsequent encounter
T23.391S	Burn of third degree of multiple sites of right wrist and hand, sequela
T23.392A	Burn of third degree of multiple sites of left wrist and hand, initial encounter
T23.392D	Burn of third degree of multiple sites of left wrist and hand, subsequent encounter
T23.392S	Burn of third degree of multiple sites of left wrist and hand, sequela
T23.399A	Burn of third degree of multiple sites of unspecified wrist and hand, initial encounter
T23.399D	Burn of third degree of multiple sites of unspecified wrist and hand, subsequent encounter
T23.399S	Burn of third degree of multiple sites of unspecified wrist and hand, sequela
T24.301A	Burn of third degree of unspecified site of right lower limb, except ankle and foot, initial encounter
T24.301D	Burn of third degree of unspecified site of right lower limb, except ankle and foot, subsequent encounter
T24.301S	Burn of third degree of unspecified site of right lower limb, except ankle and foot, sequela
T24.302A	Burn of third degree of unspecified site of left lower limb, except ankle and foot, initial encounter
T24.302D	Burn of third degree of unspecified site of left lower limb, except ankle and foot, subsequent encounter
T24.302S	Burn of third degree of unspecified site of left lower limb, except ankle and foot, sequela
T24.309A	Burn of third degree of unspecified site of unspecified lower limb, except ankle and foot, initial encounter
T24.309D	Burn of third degree of unspecified site of unspecified lower limb, except ankle and foot, subsequent encounter
T24.309S	Burn of third degree of unspecified site of unspecified lower limb, except ankle and foot, sequela
T24.311A	Burn of third degree of right thigh, initial encounter
T24.311D	Burn of third degree of right thigh, subsequent encounter
T24.311S	Burn of third degree of right thigh, sequela
T24.312A	Burn of third degree of left thigh, initial encounter
T24.312D	Burn of third degree of left thigh, subsequent encounter
T24.312S	Burn of third degree of left thigh, sequela
T24.319A	Burn of third degree of unspecified thigh, initial encounter
T24.319D	Burn of third degree of unspecified thigh, subsequent encounter
T24.319S	Burn of third degree of unspecified thigh, sequela
T24.321A	Burn of third degree of right knee, initial encounter

T24.321D	Burn of third degree of right knee, subsequent encounter
T24.321S	Burn of third degree of right knee, sequela
T24.322A	Burn of third degree of left knee, initial encounter
T24.322D	Burn of third degree of left knee, subsequent encounter
T24.322S	Burn of third degree of left knee, sequela
T24.329A	Burn of third degree of unspecified knee, initial encounter
T24.329D	Burn of third degree of unspecified knee, subsequent encounter
T24.329S	Burn of third degree of unspecified knee, sequela
T24.331A	Burn of third degree of right lower leg, initial encounter
T24.331D	Burn of third degree of right lower leg, subsequent encounter
T24.331S	Burn of third degree of right lower leg, sequela
T24.332A	Burn of third degree of left lower leg, initial encounter
T24.332D	Burn of third degree of left lower leg, subsequent encounter
T24.332S	Burn of third degree of left lower leg, sequela
T24.339A	Burn of third degree of unspecified lower leg, initial encounter
T24.339D	Burn of third degree of unspecified lower leg, subsequent encounter
T24.339S	Burn of third degree of unspecified lower leg, sequela
T24.391A	Burn of third degree of multiple sites of right lower limb, except ankle and foot, initial encounter
T24.391D	Burn of third degree of multiple sites of right lower limb, except ankle and foot, subsequent encounter
T24.391S	Burn of third degree of multiple sites of right lower limb, except ankle and foot, sequela
T24.392A	Burn of third degree of multiple sites of left lower limb, except ankle and foot, initial encounter
T24.392D	Burn of third degree of multiple sites of left lower limb, except ankle and foot, subsequent encounter
T24.392S	Burn of third degree of multiple sites of left lower limb, except ankle and foot, sequela
T24.399A	Burn of third degree of multiple sites of unspecified lower limb, except ankle and foot, initial encounter
T24.399D	Burn of third degree of multiple sites of unspecified lower limb, except ankle and foot, subsequent encounter
T24.399S	Burn of third degree of multiple sites of unspecified lower limb, except ankle and foot, sequela
T25.311A	Burn of third degree of right ankle, initial encounter
T25.311D	Burn of third degree of right ankle, subsequent encounter
T25.311S	Burn of third degree of right ankle, sequela
T25.312A	Burn of third degree of left ankle, initial encounter
T25.312D	Burn of third degree of left ankle, subsequent encounter
T25.312S	Burn of third degree of left ankle, sequela
T25.319A	Burn of third degree of unspecified ankle, initial encounter
T25.319D	Burn of third degree of unspecified ankle, subsequent encounter
T25.319S	Burn of third degree of unspecified ankle, sequela
T25.321A	Burn of third degree of right foot, initial encounter
T25.321D	Burn of third degree of right foot, subsequent encounter
T25.321S	Burn of third degree of right foot, sequela
T25.322A	Burn of third degree of left foot, initial encounter
T25.322D	Burn of third degree of left foot, subsequent encounter
T25.322S	Burn of third degree of left foot, sequela
T25.329A	Burn of third degree of unspecified foot, initial encounter
T25.329D	Burn of third degree of unspecified foot, subsequent encounter
T25.329S	Burn of third degree of unspecified foot, sequela
T25.331A	Burn of third degree of right toe(s) (nail), initial encounter

T25.331D	Burn of third degree of right toe(s) (nail), subsequent encounter
T25.331S	Burn of third degree of right toe(s) (nail), sequela
T25.332A	Burn of third degree of left toe(s) (nail), initial encounter
T25.332D	Burn of third degree of left toe(s) (nail), subsequent encounter
T25.332S	Burn of third degree of left toe(s) (nail), sequela
T25.339A	Burn of third degree of unspecified toe(s) (nail), initial encounter
T25.339D	Burn of third degree of unspecified toe(s) (nail), subsequent encounter
T25.339S	Burn of third degree of unspecified toe(s) (nail), sequela
T25.391A	Burn of third degree of multiple sites of right ankle and foot, initial encounter
T25.391D	Burn of third degree of multiple sites of right ankle and foot, subsequent encounter
T25.391S	Burn of third degree of multiple sites of right ankle and foot, sequela
T25.392A	Burn of third degree of multiple sites of left ankle and foot, initial encounter
T25.392D	Burn of third degree of multiple sites of left ankle and foot, subsequent encounter
T25.392S	Burn of third degree of multiple sites of left ankle and foot, sequela
T25.399A	Burn of third degree of multiple sites of unspecified ankle and foot, initial encounter
T25.399D	Burn of third degree of multiple sites of unspecified ankle and foot, subsequent encounter
T25.399S	Burn of third degree of multiple sites of unspecified ankle and foot, sequela
T30.0	Burn of unspecified body region, unspecified degree
Z21	Asymptomatic human immunodeficiency virus [HIV] infection status

## Policy History

Date	Action
2/2022	Updated policy to include Skytrofa™ to the policy.
12/2021	BCBSA National medical policy review. No changes to policy statements. New references added.
12/2020	BCBSA National medical policy review. No changes to policy statements. New references added.
10/2020	Clarified coding information
10/2019	Clarified coding information.
1/2019	Clarified coding information.
8/2018	Clarified coding information.
5/2018	Clarify criteria with Association language.
10/2017	Updated to change Walgreens Specialty Name.
7/2017	Updated to add AllCare to Pharmacy Specialty list.
6/2017	Updated address for Pharmacy Operations.
4/2017	Clarified criteria for Omnitrope®.
1/2016	New references added from BCBSA National medical policy.
10/2015	Updated to included revised language for Pharmacy only medications.
7/2015	Added Zomacton® To the policy.
12/2014	New references added from BCBSA National medical policy.
7/2014	Updated to include ICD-10 and to add Coverage for Egrifta™.
2/2014	Removal of Curascript from specialty pharmacy section.
1/2014	Updated ExpressPAth Language and removed Blue Value.
4/2012	Updated 4/2012 to update specialty pharmacy contact information.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
1/2012	Updated to include medical necessity criteria requirement to have treatment failure or contraindication to formulary products.
5/2011	Reviewed - Medical Policy Group - Pediatrics and Endocrinology. No changes to policy statements.
5/2011	Updated to include new FDA approved medication Egrifta™.

5/2010	Reviewed - Medical Policy Group - Pediatrics and Endocrinology. No changes to policy statements.
2/2010	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.
2/2010	Updated to reflect formulary changes and update Specialty Pharmacy information for Walgreens Specialty Pharmacy.
10/2009	Updated to reflect UM requirements and to remove Medicare Part D criteria from policy.
5/2009	Reviewed - Medical Policy Group - Pediatrics and Endocrinology. No changes to policy statements.
2/2009	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.
5/2008	Reviewed - Medical Policy Group - Pediatrics and Endocrinology. No changes to policy statements.
2/2008	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.
5/2007	Reviewed - Medical Policy Group - Pediatrics and Endocrinology. No changes to policy statements.
2/2007	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.
10/1989	New policy, effective 10/1989, describing covered and non-covered indications.

## References

1. Lo JC, Mulligan K, Tai VW, et al. "Buffalo hump" in men with HIV-1 infection. *Lancet*. Mar 21 1998; 351(9106): 867-70. PMID 9525364
2. Strasburger CJ, Vanuga P, Payer J, et al. MOD-4023, a long-acting carboxy-terminal peptide-modified human growth hormone: results of a Phase 2 study in growth hormone-deficient adults. *Eur J Endocrinol*. Mar 2017; 176(3): 283-294. PMID 27932411
3. Luo X, Hou L, Liang L, et al. Long-acting PEGylated recombinant human growth hormone (Jintrolong) for children with growth hormone deficiency: phase II and phase III multicenter, randomized studies. *Eur J Endocrinol*. Aug 2017; 177(2): 195-205. PMID 28566441
4. Hoybye C, Pfeiffer AF, Ferone D, et al. A phase 2 trial of long-acting TransCon growth hormone in adult GH deficiency. *Endocr Connect*. Apr 2017; 6(3): 129-138. PMID 28196799
5. Blethen SL, Allen DB, Graves D, et al. Safety of recombinant deoxyribonucleic acid-derived growth hormone: The National Cooperative Growth Study experience. *J Clin Endocrinol Metab*. May 1996; 81(5): 1704-10. PMID 8626820
6. Critical evaluation of the safety of recombinant human growth hormone administration: statement from the Growth Hormone Research Society. *J Clin Endocrinol Metab*. May 2001; 86(5): 1868-70. PMID 11344173
7. Hoybye C, Beck-Peccoz P, Murray RD, et al. Safety and effectiveness of replacement with biosimilar growth hormone in adults with growth hormone deficiency: results from an international, post-marketing surveillance study (PATRO Adults). *Pituitary*. Aug 2021; 24(4): 622-629. PMID 33742320
8. Beck-Peccoz P, Hoybye C, Murray RD, et al. Malignancy risk in adults with growth hormone deficiency undergoing long-term treatment with biosimilar somatotropin (Omnitrope (R) ): data from the PATRO Adults study. *Ther Adv Endocrinol Metab*. 2020; 11: 2042018820943377. PMID 32973992
9. Thomas-Teinturier C, Oliver-Petit I, Pacquement H, et al. Influence of growth hormone therapy on the occurrence of a second neoplasm in survivors of childhood cancer. *Eur J Endocrinol*. Oct 2020; 183(4): 471-480. PMID 32738133
10. Swerdlow AJ, Cooke R, Beckers D, et al. Cancer Risks in Patients Treated With Growth Hormone in Childhood: The SAGhE European Cohort Study. *J Clin Endocrinol Metab*. May 01 2017; 102(5): 1661-1672. PMID 28187225
11. Carel JC, Ecosse E, Landier F, et al. Long-term mortality after recombinant growth hormone treatment for isolated growth hormone deficiency or childhood short stature: preliminary report of the French SAGhE study. *J Clin Endocrinol Metab*. Feb 2012; 97(2): 416-25. PMID 22238382
12. Poidvin A, Touze E, Ecosse E, et al. Growth hormone treatment for childhood short stature and risk of stroke in early adulthood. *Neurology*. Aug 26 2014; 83(9): 780-6. PMID 25122206

13. Tidblad A, Bottai M, Kieler H, et al. Association of Childhood Growth Hormone Treatment With Long-term Cardiovascular Morbidity. *JAMA Pediatr.* Feb 01 2021; 175(2): e205199. PMID 33346824
14. Pfizer. Highlights of Prescribing Information: Genotropin (somatropin [rDNA origin] for injection). 2019; <http://labeling.pfizer.com/ShowLabeling.aspx?id=577>. Accessed August 15, 2021.
15. Eli Lilly. Highlights of Prescribing Information: Humatrope (somatropin [rDNA ORIGIN] for injection, for Subcutaneous Use). 2019; <http://pi.lilly.com/us/humatrope-pi.pdf>. Accessed August 15, 2021.
16. Root AW, Kemp SF, Rundle AC, et al. Effect of long-term recombinant growth hormone therapy in children--the National Cooperative Growth Study, USA, 1985-1994. *J Pediatr Endocrinol Metab.* 1998; 11(3): 403-12. PMID 11517956
17. Reiter EO, Price DA, Wilton P, et al. Effect of growth hormone (GH) treatment on the near-final height of 1258 patients with idiopathic GH deficiency: analysis of a large international database. *J Clin Endocrinol Metab.* Jun 2006; 91(6): 2047-54. PMID 16537676
18. Beauregard C, Utz AL, Schaub AE, et al. Growth hormone decreases visceral fat and improves cardiovascular risk markers in women with hypopituitarism: a randomized, placebo-controlled study. *J Clin Endocrinol Metab.* Jun 2008; 93(6): 2063-71. PMID 18381581
19. Widdowson WM, Gibney J. The effect of growth hormone replacement on exercise capacity in patients with GH deficiency: a metaanalysis. *J Clin Endocrinol Metab.* Nov 2008; 93(11): 4413-7. PMID 18697875
20. Widdowson WM, Gibney J. The effect of growth hormone (GH) replacement on muscle strength in patients with GH-deficiency: a meta-analysis. *Clin Endocrinol (Oxf).* Jun 2010; 72(6): 787-92. PMID 19769614
21. Xue P, Wang Y, Yang J, et al. Effects of growth hormone replacement therapy on bone mineral density in growth hormone deficient adults: a meta-analysis. *Int J Endocrinol.* 2013; 2013: 216107. PMID 23690770
22. Barake M, Klibanski A, Tritos NA. Effects of recombinant human growth hormone therapy on bone mineral density in adults with growth hormone deficiency: a meta-analysis. *J Clin Endocrinol Metab.* Mar 2014; 99(3): 852-60. PMID 24423364
23. Hoffman AR, Kuntze JE, Baptista J, et al. Growth hormone (GH) replacement therapy in adult-onset gh deficiency: effects on body composition in men and women in a double-blind, randomized, placebo-controlled trial. *J Clin Endocrinol Metab.* May 2004; 89(5): 2048-56. PMID 15126520
24. Maison P, Chanson P. Cardiac effects of growth hormone in adults with growth hormone deficiency: a meta-analysis. *Circulation.* Nov 25 2003; 108(21): 2648-52. PMID 14623813
25. Sesmilo G, Biller BM, Llevadot J, et al. Effects of growth hormone administration on inflammatory and other cardiovascular risk markers in men with growth hormone deficiency. A randomized, controlled clinical trial. *Ann Intern Med.* Jul 18 2000; 133(2): 111-22. PMID 10896637
26. Gotherstrom G, Svensson J, Koranyi J, et al. A prospective study of 5 years of GH replacement therapy in GH-deficient adults: sustained effects on body composition, bone mass, and metabolic indices. *J Clin Endocrinol Metab.* Oct 2001; 86(10): 4657-65. PMID 11600522
27. Ishii H, Shimatsu A, Nishinaga H, et al. Assessment of quality of life on 4-year growth hormone therapy in Japanese patients with adult growth hormone deficiency: A post-marketing, multicenter, observational study. *Growth Horm IGF Res.* Oct 2017; 36: 36-43. PMID 28923784
28. Frixou M, Vlek D, Lucas-Herald AK, et al. The use of growth hormone therapy in adults with Prader-Willi syndrome: A systematic review. *Clin Endocrinol (Oxf).* Apr 2021; 94(4): 645-655. PMID 33296095
29. Luo Y, Zheng Z, Yang Y, et al. Effects of growth hormone on cognitive, motor, and behavioral development in Prader-Willi syndrome children: a meta-analysis of randomized controlled trials. *Endocrine.* Feb 2021; 71(2): 321-330. PMID 33222122
30. Passone CGB, Franco RR, Ito SS, et al. Growth hormone treatment in Prader-Willi syndrome patients: systematic review and meta-analysis. *BMJ Paediatr Open.* 2020; 4(1): e000630. PMID 32411831
31. Kuppens RJ, Bakker NE, Siemensma EP, et al. Beneficial Effects of GH in Young Adults With Prader-Willi Syndrome: A 2-Year Crossover Trial. *J Clin Endocrinol Metab.* Nov 2016; 101(11): 4110-4116. PMID 27552545
32. Craig ME, Cowell CT, Larsson P, et al. Growth hormone treatment and adverse events in Prader-Willi syndrome: data from KIGS (the Pfizer International Growth Database). *Clin Endocrinol (Oxf).* Aug 2006; 65(2): 178-85. PMID 16886957

33. Van Vliet G, Deal CL, Crock PA, et al. Sudden death in growth hormone-treated children with Prader-Willi syndrome. *J Pediatr.* Jan 2004; 144(1): 129-31. PMID 14722532
34. Grugni G, Livieri C, Corrias A, et al. Death during GH therapy in children with Prader-Willi syndrome: description of two new cases. *J Endocrinol Invest.* Jun 2005; 28(6): 554-7. PMID 16117198
35. Wu Y, Cheng W, Yang XD, et al. Growth hormone improves growth in pediatric renal transplant recipients--a systemic review and meta-analysis of randomized controlled trials. *Pediatr Nephrol.* Jan 2013; 28(1): 129-33. PMID 22660958
36. Hodson EM, Willis NS, Craig JC. Growth hormone for children with chronic kidney disease. *Cochrane Database Syst Rev.* Feb 15 2012; (2): CD003264. PMID 22336787
37. Hokken-Koelega AC, Stijnen T, de Muinck Keizer-Schrama SM, et al. Placebo-controlled, double-blind, cross-over trial of growth hormone treatment in prepubertal children with chronic renal failure. *Lancet.* Sep 07 1991; 338(8767): 585-90. PMID 1715501
38. Hokken-Koelega A, Mulder P, De Jong R, et al. Long-term effects of growth hormone treatment on growth and puberty in patients with chronic renal insufficiency. *Pediatr Nephrol.* Jul 2000; 14(7): 701-6. PMID 10912546
39. Li P, Cheng F, Xiu L. Height outcome of the recombinant human growth hormone treatment in Turner syndrome: a meta-analysis. *Endocr Connect.* Apr 2018; 7(4): 573-583. PMID 29581156
40. Baxter L, Bryant J, Cave CB, et al. Recombinant growth hormone for children and adolescents with Turner syndrome. *Cochrane Database Syst Rev.* Jan 24 2007; (1): CD003887. PMID 17253498
41. Juloski J, Dumancic J, Scepan I, et al. Growth hormone positive effects on craniofacial complex in Turner syndrome. *Arch Oral Biol.* Nov 2016; 71: 10-15. PMID 27372203
42. Giacomozzi C, Deodati A, Shaikh MG, et al. The impact of growth hormone therapy on adult height in noonan syndrome: a systematic review. *Horm Res Paediatr.* 2015; 83(3): 167-76. PMID 25721697
43. MacFarlane CE, Brown DC, Johnston LB, et al. Growth hormone therapy and growth in children with Noonan's syndrome: results of 3 years' follow-up. *J Clin Endocrinol Metab.* May 2001; 86(5): 1953-6. PMID 11344190
44. Takeda A, Cooper K, Bird A, et al. Recombinant human growth hormone for the treatment of growth disorders in children: a systematic review and economic evaluation. *Health Technol Assess.* Sep 2010; 14(42): 1-209, iii-iv. PMID 20849734
45. Blum WF, Crowe BJ, Quigley CA, et al. Growth hormone is effective in treatment of short stature associated with short stature homeobox-containing gene deficiency: Two-year results of a randomized, controlled, multicenter trial. *J Clin Endocrinol Metab.* Jan 2007; 92(1): 219-28. PMID 17047016
46. Benabbad I, Rosilio M, Child CJ, et al. Safety Outcomes and Near-Adult Height Gain of Growth Hormone-Treated Children with SHOX Deficiency: Data from an Observational Study and a Clinical Trial. *Horm Res Paediatr.* 2017; 87(1): 42-50. PMID 28002818
47. Child CJ, Zimmermann AG, Chrousos GP, et al. Safety Outcomes During Pediatric GH Therapy: Final Results From the Prospective GeNeSIS Observational Program. *J Clin Endocrinol Metab.* Feb 01 2019; 104(2): 379-389. PMID 30219920
48. Breederveld RS, Tuinebreijer WE. Recombinant human growth hormone for treating burns and donor sites. *Cochrane Database Syst Rev.* Dec 12 2012; 12: CD008990. PMID 23235668
49. Knox J, Demling R, Wilmore D, et al. Increased survival after major thermal injury: the effect of growth hormone therapy in adults. *J Trauma.* Sep 1995; 39(3): 526-30; discussion 530-2. PMID 7473919
50. Singh KP, Prasad R, Chari PS, et al. Effect of growth hormone therapy in burn patients on conservative treatment. *Burns.* Dec 1998; 24(8): 733-8. PMID 9915674
51. Losada F, Garcia-Luna PP, Gomez-Cia T, et al. Effects of human recombinant growth hormone on donor-site healing in burned adults. *World J Surg.* Jan 2002; 26(1): 2-8. PMID 11898025
52. Hart DW, Herndon DN, Klein G, et al. Attenuation of posttraumatic muscle catabolism and osteopenia by long-term growth hormone therapy. *Ann Surg.* Jun 2001; 233(6): 827-34. PMID 11371741
53. Aili Low JF, Barrow RE, Mittendorfer B, et al. The effect of short-term growth hormone treatment on growth and energy expenditure in burned children. *Burns.* Aug 2001; 27(5): 447-52. PMID 11451596
54. Moyle GJ, Schoelles K, Fahrback K, et al. Efficacy of selected treatments of HIV wasting: a systematic review and meta-analysis. *J Acquir Immune Defic Syndr.* Dec 01 2004; 37 Suppl 5: S262-76. PMID 15722869



55. Evans WJ, Kotler DP, Staszewski S, et al. Effect of recombinant human growth hormone on exercise capacity in patients with HIV-associated wasting on HAART. *AIDS Read*. Jun 2005; 15(6): 301-3, 306-8, 310, 314. PMID 15962453
56. Wales PW, Nasr A, de Silva N, et al. Human growth hormone and glutamine for patients with short bowel syndrome. *Cochrane Database Syst Rev*. Jun 16 2010; (6): CD006321. PMID 20556765
57. Scolapio JS. Effect of growth hormone, glutamine, and diet on body composition in short bowel syndrome: a randomized, controlled study. *JPEN J Parenter Enteral Nutr*. Nov-Dec 1999; 23(6): 309-12; discussion 312-3. PMID 10574477
58. Seguy D, Vahedi K, Kapel N, et al. Low-dose growth hormone in adult home parenteral nutrition-dependent short bowel syndrome patients: a positive study. *Gastroenterology*. Feb 2003; 124(2): 293-302. PMID 12557135
59. Szkudlarek J, Jeppesen PB, Mortensen PB. Effect of high dose growth hormone with glutamine and no change in diet on intestinal absorption in short bowel patients: a randomised, double blind, crossover, placebo controlled study. *Gut*. Aug 2000; 47(2): 199-205. PMID 10896910
60. Maiorana A, Cianfarani S. Impact of growth hormone therapy on adult height of children born small for gestational age. *Pediatrics*. Sep 2009; 124(3): e519-31. PMID 19706577
61. Lindboe JB, Langkilde A, Eugen-Olsen J, et al. Low-dose growth hormone therapy reduces inflammation in HIV-infected patients: a randomized placebo-controlled study. *Infect Dis (Lond)*. Nov-Dec 2016; 48(11-12): 829-37. PMID 27417288
62. Wanke C, Gerrior J, Kantaros J, et al. Recombinant human growth hormone improves the fat redistribution syndrome (lipodystrophy) in patients with HIV. *AIDS*. Oct 22 1999; 13(15): 2099-103. PMID 10546863
63. Bryant J, Baxter L, Cave CB, et al. Recombinant growth hormone for idiopathic short stature in children and adolescents. *Cochrane Database Syst Rev*. Jul 18 2007; (3): CD004440. PMID 17636758
64. Deodati A, Cianfarani S. Impact of growth hormone therapy on adult height of children with idiopathic short stature: systematic review. *BMJ*. Mar 11 2011; 342: c7157. PMID 21398350
65. Paltoglou G, Dimitropoulos I, Kourlaba G, et al. The effect of treatment with recombinant human growth hormone (rhGH) on linear growth and adult height in children with idiopathic short stature (ISS): a systematic review and meta-analysis. *J Pediatr Endocrinol Metab*. Dec 16 2020; 33(12): 1577-1588. PMID 33035189
66. Idiopathic short stature: results of a one-year controlled study of human growth hormone treatment. Genentech Collaborative Study Group. *J Pediatr*. Nov 1989; 115(5 Pt 1): 713-9. PMID 2681637
67. Ackland FM, Jones J, Buckler JM, et al. Growth hormone treatment in non-growth hormone-deficient children: effects of stopping treatment. *Acta Paediatr Scand Suppl*. 1990; 366: 32-7. PMID 2206005
68. Cowell CT. Effects of growth hormone in short, slowly growing children without growth hormone deficiency. Australasian Paediatric Endocrine Group. *Acta Paediatr Scand Suppl*. 1990; 366: 29-30; discussion 31. PMID 2206004
69. Leschek EW, Rose SR, Yanovski JA, et al. Effect of growth hormone treatment on adult height in peripubertal children with idiopathic short stature: a randomized, double-blind, placebo-controlled trial. *J Clin Endocrinol Metab*. Jul 2004; 89(7): 3140-8. PMID 15240584
70. McCaughey ES, Mulligan J, Voss LD, et al. Growth and metabolic consequences of growth hormone treatment in prepubertal short normal children. *Arch Dis Child*. Sep 1994; 71(3): 201-6. PMID 7979491
71. Barton JS, Gardineri HM, Cullen S, et al. The growth and cardiovascular effects of high dose growth hormone therapy in idiopathic short stature. *Clin Endocrinol (Oxf)*. Jun 1995; 42(6): 619-26. PMID 7634503
72. Soliman AT, Abdul Khadir MM. Growth parameters and predictors of growth in short children with and without growth hormone (GH) deficiency treated with human GH: a randomized controlled study. *J Trop Pediatr*. Oct 1996; 42(5): 281-6. PMID 8936959
73. Kamp GA, Waelkens JJ, de Muinck Keizer-Schrama SM, et al. High dose growth hormone treatment induces acceleration of skeletal maturation and an earlier onset of puberty in children with idiopathic short stature. *Arch Dis Child*. Sep 2002; 87(3): 215-20. PMID 12193430
74. Volta C, Bernasconi S, Tondi P, et al. Combined treatment with growth hormone and luteinizing hormone releasing hormone-analogue (LHRHa) of pubertal children with familial short stature. *J Endocrinol Invest*. Nov 1993; 16(10): 763-7. PMID 8144848

75. McCaughey ES, Mulligan J, Voss LD, et al. Randomised trial of growth hormone in short normal girls. *Lancet*. Mar 28 1998; 351(9107): 940-4. PMID 9734940
76. Albertsson-Wikland K, Aronson AS, Gustafsson J, et al. Dose-dependent effect of growth hormone on final height in children with short stature without growth hormone deficiency. *J Clin Endocrinol Metab*. Nov 2008; 93(11): 4342-50. PMID 18728172
77. Hindmarsh PC, Brook CG. Effect of growth hormone on short normal children. *Br Med J (Clin Res Ed)*. Sep 05 1987; 295(6598): 573-7. PMID 3117236
78. Wit JM, Rietveld DH, Drop SL, et al. A controlled trial of methionyl growth hormone therapy in prepubertal children with short stature, subnormal growth rate and normal growth hormone response to secretagogues. Dutch Growth Hormone Working Group. *Acta Paediatr Scand*. May 1989; 78(3): 426-35. PMID 2662700
79. Volta C, Ghizzoni L, Muto G, et al. Effectiveness of growth-promoting therapies. Comparison among growth hormone, clonidine, and levodopa. *Am J Dis Child*. Feb 1991; 145(2): 168-71. PMID 1994682
80. Lanes R. Effects of two years of growth hormone treatment in short, slowly growing non-growth hormone deficient children. *J Pediatr Endocrinol Metab*. Jul-Sep 1995; 8(3): 167-71. PMID 8521190
81. Tao S, Li G, Wang Q, et al. Efficacy and Safety of Human Growth Hormone in Idiopathic Short Stature. *Indian J Pediatr*. Jul 2015; 82(7): 625-8. PMID 25893526
82. Zadik Z, Mira U, Landau H. Final height after growth hormone therapy in peripubertal boys with a subnormal integrated concentration of growth hormone. *Horm Res*. 1992; 37(4-5): 150-5. PMID 1490656
83. Wit JM, Boersma B, de Muinck Keizer-Schrama SM, et al. Long-term results of growth hormone therapy in children with short stature, subnormal growth rate and normal growth hormone response to secretagogues. Dutch Growth Hormone Working Group. *Clin Endocrinol (Oxf)*. Apr 1995; 42(4): 365-72. PMID 7750190
84. Hindmarsh PC, Brook CG. Final height of short normal children treated with growth hormone. *Lancet*. Jul 06 1996; 348(9019): 13-6. PMID 8691923
85. Buchlis JG, Irizarry L, Crotzer BC, et al. Comparison of final heights of growth hormone-treated vs. untreated children with idiopathic growth failure. *J Clin Endocrinol Metab*. Apr 1998; 83(4): 1075-9. PMID 9543120
86. Lopez-Siguero JP, Garcia-Garcia E, Carralero I, et al. Adult height in children with idiopathic short stature treated with growth hormone. *J Pediatr Endocrinol Metab*. Nov-Dec 2000; 13(9): 1595-602. PMID 11154155
87. Coutant R, Rouleau S, Despert F, et al. Growth and adult height in GH-treated children with nonacquired GH deficiency and idiopathic short stature: the influence of pituitary magnetic resonance imaging findings. *J Clin Endocrinol Metab*. Oct 2001; 86(10): 4649-54. PMID 11600520
88. Wit JM, Rekers-Mombarg LT. Final height gain by GH therapy in children with idiopathic short stature is dose dependent. *J Clin Endocrinol Metab*. Feb 2002; 87(2): 604-11. PMID 11836292
89. van Gool SA, Kamp GA, Odink RJ, et al. High-dose GH treatment limited to the prepubertal period in young children with idiopathic short stature does not increase adult height. *Eur J Endocrinol*. Apr 2010; 162(4): 653-60. PMID 20110402
90. Lopez-Siguero JP, Martinez-Aedo MJ, Moreno-Molina JA. Final height after growth hormone therapy in children with idiopathic short stature and a subnormal growth rate. *Acta Paediatr*. 1996;85:113-57.
91. Shemesh-Iron M, Lazar L, Lebenthal Y, et al. Growth hormone therapy and short stature-related distress: A randomized placebo-controlled trial. *Clin Endocrinol (Oxf)*. May 2019; 90(5): 690-701. PMID 30721549
92. Ross JL, Sandberg DE, Rose SR, et al. Psychological adaptation in children with idiopathic short stature treated with growth hormone or placebo. *J Clin Endocrinol Metab*. Oct 2004; 89(10): 4873-8. PMID 15472178
93. Theunissen NC, Kamp GA, Koopman HM, et al. Quality of life and self-esteem in children treated for idiopathic short stature. *J Pediatr*. May 2002; 140(5): 507-15. PMID 12032514
94. Downie AB, Mulligan J, McCaughey ES, et al. Psychological response to growth hormone treatment in short normal children. *Arch Dis Child*. Jul 1996; 75(1): 32-5. PMID 8813867
95. Liu S, Liu Q, Cheng X, et al. Effects and safety of combination therapy with gonadotropin-releasing hormone analogue and growth hormone in girls with idiopathic central precocious puberty: a meta-analysis. *J Endocrinol Invest*. Oct 2016; 39(10): 1167-78. PMID 27225286

96. Tuvemo T, Gustafsson J, Proos LA. Growth hormone treatment during suppression of early puberty in adopted girls. Swedish Growth Hormone Advisory Group. *Acta Paediatr.* Sep 1999; 88(9): 928-32. PMID 10519330
97. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Recombinant Human Growth Hormone (GH) Therapy in Adults with Age-Related GH Deficiency. TEC Assessment. 2001;Tab 11. PMID
98. Thaker V, Haagensen AL, Carter B, et al. Recombinant growth hormone therapy for cystic fibrosis in children and young adults. *Cochrane Database Syst Rev.* Jun 05 2013; (6): CD008901. PMID 23737090
99. Thaker V, Carter B, Putman M. Recombinant growth hormone therapy for cystic fibrosis in children and young adults. *Cochrane Database Syst Rev.* Dec 17 2018; 12: CD008901. PMID 30557452
100. Phung OJ, Coleman CI, Baker EL, et al. Recombinant human growth hormone in the treatment of patients with cystic fibrosis. *Pediatrics.* Nov 2010; 126(5): e1211-26. PMID 20921071
101. Stalvey MS, Anbar RD, Konstan MW, et al. A multi-center controlled trial of growth hormone treatment in children with cystic fibrosis. *Pediatr Pulmonol.* Mar 2012; 47(3): 252-63. PMID 21905270
102. Raman S, Grimberg A, Waguespack SG, et al. Risk of Neoplasia in Pediatric Patients Receiving Growth Hormone Therapy--A Report From the Pediatric Endocrine Society Drug and Therapeutics Committee. *J Clin Endocrinol Metab.* Jun 2015; 100(6): 2192-203. PMID 25839904
103. Grimberg A, Allen DB. Growth hormone treatment for growth hormone deficiency and idiopathic short stature: new guidelines shaped by the presence and absence of evidence. *Curr Opin Pediatr.* Aug 2017; 29(4): 466-471. PMID 28525404
104. Grimberg A, DiVall SA, Polychronakos C, et al. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency. *Horm Res Paediatr.* 2016; 86(6): 361-397. PMID 27884013
105. Gravholt CH, Andersen NH, Conway GS, et al. Clinical practice guidelines for the care of girls and women with Turner syndrome: proceedings from the 2016 Cincinnati International Turner Syndrome Meeting. *Eur J Endocrinol.* Sep 2017; 177(3): G1-G70. PMID 28705803
106. Fleseriu M, Hashim IA, Karavitaki N, et al. Hormonal Replacement in Hypopituitarism in Adults: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* Nov 2016; 101(11): 3888-3921. PMID 27736313
107. Sklar CA, Antal Z, Chemaitilly W, et al. Hypothalamic-Pituitary and Growth Disorders in Survivors of Childhood Cancer: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* Aug 01 2018; 103(8): 2761-2784. PMID 29982476
108. National Institute for Health and Care Excellence (NICE). Human growth hormone (somatropin) for growth failure in children [TA188]. 2010; <https://www.nice.org.uk/guidance/ta188>. Accessed August 16, 2021.
109. Yuen KCJ, Biller BMK, Radovick S, et al. 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. *Endocr Pract.* Nov 2019; 25(11): 1191-1232. PMID 31760824
110. Cohen P, Rogol AD, Deal CL, et al. Consensus statement on the diagnosis and treatment of children with idiopathic short stature: a summary of the Growth Hormone Research Society, the Lawson Wilkins Pediatric Endocrine Society, and the European Society for Paediatric Endocrinology Workshop. *J Clin Endocrinol Metab.* Nov 2008; 93(11): 4210-7. PMID 18782877
111. Deal CL, Tony M, Hoybye C, et al. GrowthHormone Research Society workshop summary: consensus guidelines for recombinant human growth hormone therapy in Prader-Willi syndrome. *J Clin Endocrinol Metab.* Jun 2013; 98(6): E1072-87. PMID 23543664
112. Allen DB, Backeljauw P, Bidlingmaier M, et al. GH safety workshop position paper: a critical appraisal of recombinant human GH therapy in children and adults. *Eur J Endocrinol.* Feb 2016; 174(2): P1-9. PMID 26563978
113. Collett-Solberg PF, Ambler G, Backeljauw PF, et al. Diagnosis, Genetics, and Therapy of Short Stature in Children: A Growth Hormone Research Society International Perspective. *Horm Res Paediatr.* 2019; 92(1): 1-14. PMID 31514194

114. Kaplowitz P, Bloch C, Sills IN, et al. Evaluation and Referral of Children With Signs of Early Puberty. *Pediatrics*. Jan 2016; 137(1). PMID 26668298

## Endnotes

1. Revised 1/96 to include the Guidelines for the use of growth hormone in children of short stature, A report by the Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society, as published in the *Journal of Pediatrics*, December 1995; 127:857-67.
2. 2000 Consensus Guidelines for the Diagnosis and Treatment of GH deficiency in childhood and adolescence: Summary statement of the GH research society; *Journal of Clinical Endocrinology and Metabolism*, vol.85, No.11.
3. See Recombinant Human Growth hormone in Patients with HIV-Associated Wasting. A randomized, placebo-controlled trial. By Schambelan et al., and the Serostim Study Group, *Annals Internal Medicine* 1996;125:873-882.
4. Criteria provided by Massachusetts General Hospital Department of Pediatric Endocrinology, September 1996.
5. The American Academy of Pediatrics Committee on Drugs and Committee on Bioethics, *Considerations Related to the Use of Recombinant Human Growth Hormone in Children*, *Pediatrics* vol. 99 No. 1 January 1997.
6. The American Medical Association's October 15, 1996 DATTA (Diagnostic and Therapeutic Technology Assessment) entitled *Use of Recombinant Growth Hormone in Children with Short Stature*, Glade MJ.
7. *Growth Hormone Deficiency in Adults: A Review*, by Torstein et al, *Am J Medical Sciences*, 1996;311(4):253-168. Authors state that in adults, neither IGF-I nor IGFBP-III are reliable parameters. The review discusses effects of GH deficiency on various organ systems.
8. *Growth hormone deficiency in adults: Characteristics and response to GH replacement*, by Lieberman and Hoffman, *J Pediatrics* 1996;128:S58-60.
9. *Australian multicenter trial of GH treatment in GH-deficient adults*, by Cuneo, et al, *J Clin Endocrinol Metab* 83:107-116, 1998.
10. See *A preliminary study of growth hormone in the treatment of dilated cardiomyopathy*, Serafino Fazio, et al. *NEJM* 1996;334:809-14.
11. See the 2003 American Association of Clinical Endocrinologists Clinical Practice Guidelines for Growth Hormone Use in Adults and Children, at their web site, <http://www.aace.com>
12. See the December 1997 American Medical Association Diagnostic & Therapeutic Technology Assessment: Use of Recombinant Human Growth hormone (rhGH) in Children with Short Stature and Turner Syndrome..
13. See the December 1997 American Medical Association Diagnostic & Therapeutic Technology Assessment: Use of Recombinant Human Growth hormone (rhGH) in Children with Short Stature and Noonan Syndrome.
14. See HIV Wasting Syndrome: Balog et al, *Annals of Pharmacotherapy* 1998, April, volume 32, pp. 446-458.
15. Based on recommendations from Richard Siegel, MD, New England Medical Center, *Electric Blue Review*, February 2000
16. Based on recommendations from the Clinical Pharmacy Unit, May 2000.
17. American Academy of Pediatrics, volume 99, number 1, January 1997. *Considerations Related to the use of Recombinant Human Growth Hormone in Children*.
18. Based on the 11/01 TEC (Technology Evaluation Center) assessment including review of the medical literature from 1995 through October 2001.
19. American Family Physician May 2000, volume 61, number 9. *Growth hormone in children and adolescents of short stature*.
20. See *Pediatrics* 2003; 111:1253-1261. International Small for Gestational Age Advisory Board Consensus Development Conference Statement: Management of short children born small for gestational age, April 24-October1, 2001.
21. Recommendations from the 2/02 Medical Policy Group meeting.
22. Based on Blue Cross Blue Shield Association National policy 5.01.06, issued 5/15/02.

23. See the 2003 American Association of Clinical Endocrinologists Clinical Practice Guidelines for Growth Hormone Use in Adults and Children, at their website, <http://www.aace.com>.
24. Based upon FDA approved indications for Insulin-like Growth Factor.

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