Clinical Policy: Somatropin (Human Growth Hormone)

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Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are recombinant human growth hormones (GH) requiring prior authorization: somatropin (Genotropin®, Humatrope®, Norditropin®, Nutropin AQ®, Omnitrope®, Saizen®, Serostim®, Zomacton®, Zorbtive®).

Drugs	Children								Adults		
	GHD	PWS	TS	NS	SHOX	CKD	SGA	ISS	GHD	HIV	SBS
Genotropin	GF	GF	GF				GF	GF	X		
Humatrope	SS/GF		SS/GF		SS/GF		SS/GF	SS/GF	X		
Norditropin	GF	GF	SS	SS			SS	SS	X		
Nutropin AQ	GF		GF			GF		GF	X		
Omnitrope	GF	GF	GF				GF	GF	X		
Saizen	GF								X		
Serostim										X	
Zomacton	GF		SS		SS		SS	SS	X		
Zorbtive											X

Abbreviations: CKD: chronic kidney disease, GF: growth failure, GHD: growth hormone deficiency, HIV: human immunodeficiency virus, ISS: idiopathic short stature, NS: Noonan syndrome, PWS: Prader-Willi syndrome, SBS: short bowel syndrome, SGA: small for gestational age, SHOX: short stature homeobox-containing gene, SS: short stature, TS: Turner syndrome

FDA Approved Indication(s)

Genotropin is indicated for treatment of:

- Children with GF due to GHD, PWS, SGA, TS, and ISS.
- Adults with either childhood-onset (CO) or adult-onset (AO) GHD.

Humatrope is indicated for treatment of:

- Children with SS or GF associated with GHD, TS, ISS, SHOX deficiency, and failure to catch up in height after SGA birth.
- Adults with either CO or AO GHD.

Norditropin FlexPro is indicated for the treatment of:
- Children with GF due to GHD, SS associated with NS, SS associated with TS, SS born SGA with no catch-up growth by age 2 to 4 years, ISS, and GF due to PWS.
- Adults with either CO or AO GHD.

Nutropin AQ is indicated for the treatment of:
- Children with GF due to GHD, ISS, TS, and CKD up to the time of renal transplantation.
- Adults with either CO or AO GHD.

Omnitrope is indicated for the treatment of:
- Children with GF due to GHD, PWS, SGA, TS, and ISS.
- Adults with either CO or AO GHD.

Saizen is indicated for:
- Children with GF due to GHD.
- Adults with either CO or AO GHD.

Serostim is indicated for treatment of:
- HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance.

Zomacton is indicated for:
- Treatment of pediatric patients who have GF due to inadequate secretion of normal endogenous GH, SS associated with TS, ISS, SS or GF in SHOX deficiency, and SS born SGA with no catch-up growth by 2 years to 4 years.
- Replacement of endogenous GH in adults with GHD.

Zorbtive is indicate for treatment of:
- SBS in adult patients receiving specialized nutritional support.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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It is the policy of health plans affiliated with Centene Corporation® that somatropin (recombinant human growth hormone (rhGH)) is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Growth Hormone Deficiency with Neonatal Hypoglycemia (off-label) (must meet all)**:**

1. Diagnosis of neonatal hypoglycemia due to GHD;
2. Prescribed by or in consultation with a pediatric endocrinologist;
3. Age ≤ 1 month;
4. Serum GH concentration ≤ 5 µg/L;
5. Member meets (a or b):
   a. Imaging shows hypothalamic-pituitary abnormality;
   b. Deficiency of ≥ 1 anterior pituitary hormone other than GH (e.g., ACTH, TSH, LH, FSH, prolactin);
6. The requested product is not prescribed concurrently with Increlex® (mecasermin);
7. If request is NOT for Zomacton, Zomacton product excipients are contraindicated or member has experienced a clinically significant adverse effect to Zomacton;
8. Dose does not exceed 0.30 mg/kg per week.

Approval duration: 12 months

B. Growth Hormone Deficiency with Short Stature/Growth Failure - Children *(open epiphyses)* (must meet all)**:**

1. Diagnosis of GHD;
2. Prescribed by or in consultation with a pediatric endocrinologist;
3. Age < 18 years;
4. If age > 10 years, open epiphysis on x-ray;
5. Member meets (a or b):
   a. Low insulin-like growth factor (IGF)-I serum level;
   b. Low insulin-like growth factor binding protein (IGFBP)-3 serum level;
6. Member meets (a, b, c, d, or e):
   a. Two GH stimulation tests with peak serum levels ≤ 10 µg/mL (e.g., stimulants: arginine, clonidine, glucagon);
   b. Deficiency of ≥ 3 pituitary hormones (i.e., ACTH, TSH, LH, FSH, prolactin);

c. Surgery or radiotherapy to the hypothalamic-pituitary region;
d. Imaging shows hypothalamic-pituitary abnormality;
e. GHD-specific mutation (e.g., POU1F1, PROP1, LHX3, LHX4, HESX1, OTX2, TBX19, SOX2, SOX3, GLI2, GHRHR, GH1);

7. Member meets (a or b):
   a. SS: height is > 2 SD below the mean for age and sex (SD, height, date, and age in months within the last 90 days are required);
   b. GF: one of the following (i, ii, or iii):
      i. Height deceleration across two growth chart percentiles representing > 1 SD below the mean for age and sex (SD and 2 heights, dates, and ages in months at least 6 months apart within the last year are required);
      ii. Growth velocity > 2 SD below the mean for age and sex over 1 year (SD and 2 heights, dates, and ages in months at least 1 year apart within the last year are required);
      iii. Growth velocity > 1.5 SD below the mean for age and sex sustained over 2 years (SD and 2 heights, dates, and ages in months at least 2 years apart within the last two years are required);
8. The requested product is not prescribed concurrently with Increlex (mecasermin);
9. If request is NOT for Zomacton, Zomacton product excipients are contraindicated or member has experienced a clinically significant adverse effect to Zomacton;
10. Dose does not exceed 0.30 mg/kg per week.

Approval duration: 12 months

C. Genetic Disorders with Short Stature/Growth Failure - Children (must meet all)**:**

1. Diagnosis of PWS, TS, NS, or SHOX deficiency confirmed by a genetic test;
2. Prescribed by or in consultation with a pediatric endocrinologist;
3. Age < 18 years;
4. If age > 10 years, open epiphysis on x-ray;
5. Member meets (a or b):
   a. SS: height is > 2 SD below the mean for age and sex (> 1.5 SD if TS) (SD, height, date, and age in months within the last 90 days are required);
   b. GF: one of the following (i, ii, or iii):
      i. Height deceleration across two growth chart percentiles representing > 1 SD below the mean for age and sex (SD and 2 heights, dates, and ages in months at least 6 months apart within the last year are required);
      ii. Growth velocity > 2 SD below the mean for age and sex over 1 year (SD and 2 heights, dates, and ages in months at least 1 year apart within the last year are required);
      iii. Growth velocity > 1.5 SD below the mean for age and sex sustained over 2 years (SD and 2 heights, dates, and ages in months at least 2 years apart within the last two years are required);
6. The requested product is not prescribed concurrently with Increlex (mecasermin);
7. If request is NOT for Zomacton, Zomacton product excipients are contraindicated or member has experienced a clinically significant adverse effect to Zomacton;
8. Request meets one of the following (a, b, or c):
   a. PWS: Dose does not exceed 0.24 mg/kg per week;

b. TS, NS: Dose does not exceed 0.5 mg/kg per week;
c. SHOX deficiency: Dose does not exceed 0.35 mg/kg per week.

Approval duration: 12 months

D. Chronic Kidney Disease with Growth Failure – Children (must meet all)**:**
1. Diagnosis of CKD;
2. Prescribed by or in consultation with a pediatric endocrinologist or nephrologist;
3. Age < 18 years;
4. If age > 10 years, open epiphysis on x-ray;
5. Member meets (a, b, c, or d):
   a. GFR < 60 mL/min per 1.73 m^2 for ≥ 3 months;
   b. Dialysis dependent;
   c. Diagnosis of nephropathic cystinosis;
   d. History of kidney transplant ≥ 1 year ago;
6. Member meets (a or b):
   a. SS: height is > 2 SD below the mean for age and sex (SD, height, date, and age in months within the last 90 days are required);
   b. GF: one of the following (i, ii, or iii):
      i. Height deceleration across two growth chart percentiles representing > 1 SD below the mean for age and sex (SD and 2 heights, dates, and ages in months at least 6 months apart within the last year are required);
      ii. Growth velocity > 2 SD below the mean for age and sex over 1 year (SD and 2 heights, dates, and ages in months at least 1 year apart within the last year are required);
      iii. Growth velocity > 1.5 SD below the mean for age and sex sustained over 2 years (SD and 2 heights, dates, and ages in months at least 2 years apart within the last two years are required);
7. The requested product is not prescribed concurrently with Increlex (mecasermin);
8. If request is NOT for Zomacton, Zomacton product excipients are contraindicated or member has experienced a clinically significant adverse effect to Zomacton;
9. Dose does not exceed 0.35 mg/kg per week.

Approval duration: 12 months

E. Born Small for Gestational Age with Short Stature/Growth Failure - Children (must meet all)**:**
1. Diagnosis of SGA:
2. Prescribed by or in consultation with a pediatric endocrinologist;
3. Age ≥ 2 years and < 18 years;
4. If age > 10 years, open epiphysis on x-ray;
5. Member meets (a and b):
   a. Birth weight or length > 2 SD below the mean for gestational age (SD, birth weight or length, and gestational age are required);
   b. Current height > 2 SD below the mean for age and sex measured within the last year at ≥ 2 years of age (SD, height, date, and age in months are required);
6. The requested product is not prescribed concurrently with Increlex (mecasermin);

7. If request is NOT for Zomacton, Zomacton product excipients are contraindicated or member has experienced a clinically significant adverse effect to Zomacton;
8. Dose does not exceed 0.48 mg/kg per week.

Approval duration: 12 months

F. Growth Hormone Deficiency – Adults and Transition Patients *(closed epiphyses)* (must meet all):

1. Diagnosis of GHD;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 18 years OR closed epiphysis on x-ray;
4. Member has NOT received somatropin therapy for ≥ 1 month prior to GH/IGF-I testing as outlined below;
5. Member meets (a, b, or c):
   a. Two fasting a.m. GH stimulation tests with peak serum levels ≤ 5 µg/mL (accepted stimulants: Macrilen™ [macimorelin] or combination of 2 stimulants such as arginine + glucagon);
   b. Both of the following (i and ii):
      i. One fasting a.m. GH stimulation test with peak serum level ≤ 5 µg/ml (accepted stimulants: Macrilen [macimorelin] or combination of 2 stimulants such as arginine + glucagon);
      ii. One low IGF-I serum level;
   c. One low IGF-I serum level and (i, ii, or iii):
      i. Imaging shows hypothalamic-pituitary abnormality;
      ii. Deficiency of ≥ 3 pituitary hormones (i.e., ACTH, TSH, LH, FSH, prolactin);
      iii. GHD-specific mutation (e.g., POU1F1, PROP1, LHX3, LHX4, HESX1, OTX2, TBX19, SOX2, SOX3, GLI2, GHRHR, GH1);
6. The requested product is not prescribed concurrently with Increlex (mecasermin);
7. If request is NOT for Zomacton, Zomacton product excipients are contraindicated or member has experienced a clinically significant adverse effect to Zomacton;
8. Dose does not exceed 0.4 mg/day (may adjust by up to 0.2 mg/day every 6 weeks to maintain normal IGF-1 serum levels; doses > 1.6 mg/day would be uncommon).

Approval duration: 6 months

G. Short Bowel Syndrome (must meet all):

1. Diagnosis of SBS;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Patient is dependent upon and receiving intravenous nutrition;
5. If request is NOT for Zomacton, Zomacton product excipients are contraindicated or member has experienced a clinically significant adverse effect to Zomacton;
6. Dose does not exceed 8 mg per day.

Approval duration: up to 4 weeks total

H. HIV-Associated Wasting or Cachexia (must meet all):

1. Diagnosis of HIV;
2. Prescribed by or in consultation with a physician specializing in HIV management;

3. Age ≥ 18 years;
4. Unintentional weight loss of ≥ 10% in the last 12 months occurring while on antiretroviral therapy;
5. Failure of at least 2 pharmacologic therapies from two separate drug classes *(Appendix B)* unless contraindicated or clinically adverse effects are experienced;
6. If request is NOT for Zomacton, Zomacton product excipients are contraindicated or member has experienced a clinically significant adverse effect to Zomacton;
7. Prescribed dose does not exceed 6 mg per day.

Approval duration: 6 months

I. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Pediatric Indications *(open epiphyses)* (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Age < 18 years OR open epiphysis on x-ray;
3. Member meets (a or b):
   a. For diagnosis of neonatal hypoglycemia, when member has received somatropin therapy for ≥ 2 years, member's height has increased ≥ 2 cm in the last year as documented by 2 height measurements taken no more than 1 year apart (dates and height measurements required);
   b. For all other pediatric diagnoses, member's height has increased ≥ 2 cm in the last year as documented by 2 height measurements taken no more than 1 year apart (dates and height measurements required);
4. If request is for a dose increase, request meets the one of the following (a, b, c, d, or e):
   a. GHD with or without neonatal hypoglycemia: New dose does not exceed 0.30 mg/kg per week;
   b. PWS: New dose does not exceed 0.24 mg/kg per week;
   c. TS, NS: New dose does not exceed 0.5 mg/kg per week;
   d. SHOX deficiency, CKD: New dose does not exceed 0.35 mg/kg per week;
   e. Born SGA: New dose does not exceed 0.48 mg/kg per week.

Approval duration: 12 months

B. Growth Hormone Deficiency - Adults and Transition Patients *(closed epiphyses)* (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. For IGF-1 test results and dosing (test conducted within the last 90 days) (a, b, or c):
   a. Low IGF-1 serum level: If request is for a dose increase, new dose does not exceed an incremental increase of more than 0.2 mg/day and a total dose of 1.6 mg/day;

b. Normal IGF-1 serum level: Requested dose is for the same or lower dose;
c. Elevated IGF-1 serum level: Requested dose has been titrated downward.

Approval duration: 12 months

C. Short Bowel Syndrome - Adults (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Member has not received the requested product for ≥ 4 weeks;
4. If request is for a dose increase, new dose does not exceed 8 mg per day.

Approval duration: up to 4 weeks total

D. HIV-Associated Wasting/Cachexia - Adults (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Member has not received ≥ 12 months of therapy;
4. If request is for a dose increase, new dose does not exceed 6 mg per day.

Approval duration: up to 12 months total

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized). Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.
B. Idiopathic short stature (ISS);
C. Constitutional delay of growth and puberty (i.e., constitutional growth delay; the member's growth rate is delayed compared to chronological age but appropriate for bone age as determined by x-ray);
D. Familial (genetic) short stature (i.e., height velocity and bone age, as determined by x-ray, are within the normal range and one or both parents are short);
E. Adult short stature or altered body habitus associated with antiviral therapy (other than HIV-associated wasting or cachexia);
F. Obesity treatment or enhancement of body mass/strength for non-medical reasons (e.g., athletic gains).

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CKD: chronic kidney disease
FDA: Food and Drug Administration
GFR: glomerular filtration rate
GH: growth hormone
GHD: growth hormone deficiency
HIV: human immunodeficiency virus
IGF-1: insulin-like growth factor-1
IGFBP-3: insulin-like growth factor binding protein-3
ISS: idiopathic short stature
NS: Noonan syndrome
PWS: Prader-Willi syndrome
rhGH: recombinant human growth hormone
SBS: short bowel syndrome
SD: standard deviation
SGA: small for gestational age
SHOX: short stature homeobox-containing gene
TS: Turner syndrome

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug	Dosing Regimen	Dose Limit/Maximum Dose
Appetite Stimulants		
Megestrol (Megace®)	400 - 800 mg PO daily (10 – 20 ml/day)	800 mg/day
Dronabinol (Marinol®)	2.5 mg PO bid	20 mg/day
Testosterone Replacement Products		
Testosterone enanthate or cypionate (Various brands)	50 - 400 mg IM Q2 – 4 wks	400 mg Q 2 wks
Androderm® (testosterone transdermal)	2.5 – 7.5 mg patch applied topically QD	7.5 mg/day
Androgel® (testosterone gel)	5 - 10 gm gel (delivers 50 – 100 mg testosterone) applied topically QD	10 gm/day gel (100 mg/day testosterone)
Testim® (testosterone gel)	5 - 10 gm gel (delivers 50 – 100 mg testosterone) applied topically QD	10 gm/day gel (100 mg/day testosterone)
Anabolic Steroids		
Oxandrolone (Oxandrin®)	2.5 – 20 mg PO /day	20 mg/day
Nandrolone decanoate	100 mg IM Q week	100 mg Q wk
Nausea/Vomiting Treatments*		
chlorpormazine	10 to 25 mg PO q4 to 6 hours prn	2,000 mg/day
perphenazine	8 to 16 mg/day PO in divided doses	64 mg/day
prochlorperazine	5 to 10 mg PO TID or QID	40 mg/day
promethazine	12.5 to 25 mg PO q4 to 6 hours prn	50 mg/dose; 100 mg/day

Drug	Dosing Regimen	Dose Limit/Maximum Dose
trimethobenzamide	300 mg PO TID or QID prn	1,200 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Preferred status may be formulary-specific.*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Acute critical illness
  - Children with PWS who are severely obese or have severe respiratory impairment (reports of sudden death)
  - Active malignancy
  - Product hypersensitivity
  - Active proliferative or severe non-proliferative diabetic retinopathy
  - Children with closed epiphyses
- Boxed warning(s): none reported

Appendix D: Short Stature and Growth Failure

- For SS, the policy follows the World Health Organization (WHO) definition of > 2 SD below the mean for age and sex.[1]
- For GF, the policy follows
  - Haymond et al (2013) and Rogol et al (2014) for height deceleration across two major percentiles representing a change of > 1 SD corrected for age and sex[2,3] and
  - the Growth Hormone Research Society (2000) for height velocity in the absence of SS that would prompt further investigation, namely, a height velocity > 2 SD below the mean over 1 year or > 1.5 SD below the mean sustained over 2 years for age and sex.[4]
- The Centers for Disease Control and Prevention (CDC) recommend WHO growth charts for infants and children age 0 to < 2 years and CDC growth charts for children age 2 years to < 20 years in the U.S.[5]
  - Based on CDC recommended growth chart data, SD approximations of major height percentiles falling below the mean are listed below:
    - 2nd percentile: 2 SD below the mean
    - 5th percentile: 1.5 SD below the mean
    - 15th percentile: 1 SD below the mean
    - 30th percentile: 0.5 SD below the mean
    - 50th percentile: 0 SD mean
  - CDC recommended growth charts, data tables, and related information that may be helpful in assessing length, height and growth are available at the following link: https://www.cdc.gov/growthcharts/index.htm.

1. WHO Child Growth Standards: Length/Height-for-Age, Weight-for-Age, Weight-for-Length, Weight-for-Height and Body Mass Index-for-Age: Methods and Development. Geneva, Switzerland: World Health Organization; 2006. As cited in CDC. Division of Nutrition, Physical Activity, and Obesity. Growth Chart Training: Using the WHO Growth Charts. Page last reviewed April 15, 2015. Available at https://www.cdc.gov/nccdphp/dnpao/growthcharts/who/using/assessing_growth.htm. Accessed May 1, 2020.

2. Haymond M, Kappelgaard AM, Czernichow P, et al. Early recognition of growth abnormalities permitting early intervention. Acta Pædiatrica ISSN 0803-5253. April 2013. DOI:10.1111/apa.12266.
3. Rogol AD, Hayden GF. Etiologies ad early diagnosis of short stature and growth failure in children and adolescents. J Pediatr. 2014 May;164(5 Suppl):S1-14.e6. doi: 10.1016/j.jpeds.2014.02.027.
4. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. JCEM. 2000; 85(11): 3990-3993.
5. Centers for Disease Control and Prevention, National Center for Health Statistics. CDC growth charts: United States. http://www.cdc.gov/growthcharts/. Accessed April 22, 2020.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Pediatric Indications (Subcutaneous administration; weekly doses should be divided)			
Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Saizen, Zomacton	GHD	G, O: 0.16 to 0.24 mg/kg/week H, Z: 0.18 to 0.30 mg/kg/week N: 0.17 to 0.24 mg/kg/week Nu: to 0.30 mg/kg/week S: 0.18 mg/kg/week	See dosing regimens
Genotropin, Norditropin, Omnitrope	PWS	G, N, O: 0.24 mg/kg/week	0.24 mg/kg/week
Genotropin, Humatrope, Norditropin, Omnitrope, Zomacton	SGA	G, O: to 0.48 mg/kg/week H, N, Z: to 0.47 mg/kg/week	0.48 mg/kg/week
Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Zomacton	TS	G, O: 0.33 mg/kg/week H, Nu, Z: to 0.375 mg/kg/week N: to 0.47 mg/kg/week	See dosing regimens
Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Zomacton	ISS	G, O, No: to 0.47 mg/kg/week H, Z: to 0.37 mg/kg/week Nu: to 0.30 mg/kg/week	See dosing regimens
Humatrope, Zomacton	SHOX	H, Z: 0.35 mg/kg/week	0.35 mg/kg/week
Norditropin	NS	0.46 mg/kg/week	0.46 mg/kg/week
Nutropin	CKD	0.35 mg/kg/week	0.35 mg/kg/week
Adult Indications (Subcutaneous administration)			
Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Saizen, Zomacton	GHD	0.4 mg/day - may adjust by increments up to 0.2 mg/day every 6 weeks to maintain normal IGF-1 serum levels.* _____ **Dosing regimen from Endocrine Society guidelines (Fleseriu, et al., 2016).* Adult GHD dosing should be substantially lower than that prescribed for children. Adult doses beyond 1.6 mg/day would be uncommon.	See dosing regimen

Drug Name	Indication	Dosing Regimen	Maximum Dose
Serostim	HIV-associated wasting	0.1 mg/kg QOD or QD to 6 mg QD	6 mg/day up to 24 weeks
Zorbtive	SBS	0.1 mg/kg QD to 8 mg QD	8 mg/day up to 4 weeks

Abbreviations: G: genotropin, H: humatrope, N: norditropin, Nu: nutropin, O: omnitrope, S: saizen, Z: zomacton

VI. Product Availability

Drug	Availability
Genotropin lyophilized powder	Dual-chamber syringe: 5 mg, 12 mg
Genotropin Miniquick ***(without preservative)***	Pen cartridge: 0.2 mg, 0.4 mg, 0.6 mg, 0.8 mg, 1.0 mg, 1.2 mg, 1.4 mg, 1.6 mg. 1.8 mg, and 2.0 mg
Humatrope	Pen cartridge: 6 mg, 12 mg, 24 mg Vial: 5mg
Norditropin Flexpro	Pen: 5 mg/1.5 mL, 10 mg/1.5 mL, 15 mg/1.5 mL, 30 mg/3 mL
Nutropin AQ	NuSpin: 5 mg/2 mL, 10 mg/2 mL, 20 mg/2 mL
Omnitrope	Pen cartridge: 5 mg/1.5 mL, 10 mg/1.5 mL Vial: 5.8 mg
Saizen	Pen cartridge: 8.8 mg Vial: 5 mg, 8.8 mg
Serostim	Vial: 4 mg, 5 mg, 6 mg
Zomacton	Vial: 5 mg, 10 mg
Zorbtive	Vial: 8.8 mg

VII. References

FDA Labels

1. Genotropin Prescribing Information. NY, NY: Pfizer, Inc.; April 2019. Available at www.genotropin.com. Accessed October 29, 2019.
2. Humatrope Prescribing Information. Indianapolis, IN: Eli Lilly; December 2016. Available at: www.humatrope.com. Accessed October 29, 2019.
3. Norditropin Prescribing Information. Plainsboro, NJ: Novo Nordisk; February 2018. Available at: www.norditropin.com. Accessed October 29, 2019.
4. Nutropin AQ. Prescribing Information. South San Francisco, CA: Genentech; December 2016. Available at: www.nutropin.com. Accessed October 29, 2019.
5. Omnitrope Prescribing Information. Princeton, NJ: Sandoz; June 2019. Available at: www.omnitrope.com. Accessed October 29, 2019.
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7. Serostim Prescribing Information. Rockland, MA: EMD Serono Inc.; May 2018. Available at: https://serostim.com/. Accessed October 29, 2019.
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9. Zomacton Prescribing information. Parsippany, NJ: Ferring Pharmaceuticals Inc., July 2018. Available at: www.zomacton.com. Accessed October 29, 2019.

Compendia

10. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically.
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Somatropin Therapy - Children

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Committee review with recommendations 12/15, required specialist review. Updates: I.A: updated definitions of short stature and growth failure; changed age for treatment to open epiphyses instead of 18 year,	01.16	02.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
I.B change bone age for girls to 15 and for boys 17 as these are the ages that 99% of growth has been completed.		
Added table of contents and minor edit for clarity, no criteria changes	03.16	
Incorporated expert recommendations to clinical criteria: Listed genetic syndromes included in other causes of growth failure Expanded confirmation of Noonan syndrome to include geneticist diagnosis Clarified age requirement to 2 years for failure to manifest catch-up growth in children born small for gestational age Removed redundancies in criteria related to absence of short stature in pediatric patients Added maximum dosing criteria for growth hormone agents used for pediatric diagnoses as well as for Serostim and Zorbtive	04.16	
Policy converted to new template. Products are made interchangeable with preference for Norditropin; Zomacton is added. Neonatal hypoglycemia criteria is added. "Endogenous" is removed from childhood GHD. Childhood dosing is based on highest dose across Pis for a given indication. Neonatal hypoglycemia is based on GHD childhood dosing. Adult dosing is based on Pis for SBS and HIV; adult dosing is not included for GHD given the potential variability in required amounts. Dosing is titrated via height and IGF-1 levels in children and IGF-1 levels in adults. Adult age requirement is required for HIV and SBS only; open epiphyses are required for all childhood diagnoses other than neonatal hypoglycemia. Required GH stimulation tests, and IGF-1 and IGFBP-3 levels are edited as follows: for childhood GHD: two GH stim tests and either a low IGF-1 or IGFBP-3 level, or just a low Igf-1 level if additional risk factors; for adults, two GH stim tests, or one GH stim test and one IGF-1 level, or one IGF-1 level with additional risk factors. Contraindications common to all indications are listed in App B. Contraindications specific to an indication are placed within the applicable criteria. Short stature/growth failure is moved to App B and is removed as a requirement from SGA. Adult GHD approval period is lengthened from 3 to 12 months to give time for dose titration before re-auth. CKD diagnosis – option "c" (a combination of a and b without a duration requirement) is added. Removed requirement for normalized IGF-1 levels on continued approval for childhood GHD. Specialist reviewed.	05.16	06.16
Added criteria for adult and transition PWS to initial and continuation criteria per the GH Research Society PWS 2013 consensus statement.	09.16	09.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Re-auth: removed reasons to discontinue. Removed preexisting papilledema and concomitant administration of GH and Increlex from Appendix B.	05.17	06.17
2Q 2018 annual review: added HIM; removed requirements regarding contraindications; removed requirements for ruling out alternative of diagnoses; neonatal hypoglycemia: removed brain MRI and random GH measurement requirement; GHD, small for gestational age: removed requirements for open epiphyses, evidence of growth failure via appendix C, defined central nervous system pathology documented by MRI or CT; Prader-Willi syndrome: removed requirements for closed epiphyses, rGH will be titrated to maintain normal range IGF-1 level for age and sex matched controls, ruling out of contraindications, untreated severe sleep apnea, and active psychosis; CKD: removed requirements for open epiphyses, evidence of growth failure per appendix C, dx of CKD via Structural or functional abnormalities of the kidney for ≥ 3 months, GFR < 60 mL/min per 1.73 m^2 for ≥ 3 months, occurrence of both together of any duration, member does not have a functioning renal allograft; SBS: removed requirements for member's SBS therapeutic plan requires specialized nutritional support; changed approval duration from 3 months to 4 weeks; HIV-related wasting or cachexia: removed requirement for ruling out alternate causes of cachexia, unexplained loss of > 10% body weight from baseline, treatment with therapies other than rhGH have been suboptimal; added requirements for trial of appetite stimulants or anti-nausea tx as well as trial of testosterone and anabolic steroid in males; continued tx: removed documentation of adherence to therapy; removed examples of positive response criteria if not mandatory and objective; for Adult GHD: corrected peak GH level ≤ 5 µg/mL to ≤ 5 µg/L; aligned labs required for diagnosis with 2009 AACE guidelines; for Child/adolescent GHD: corrected peak GH level ≤ 10 µg/L to 10; GH use in children: added requirement for documentation of baseline height for initial approval.	02.20.18	05.18
No significant changes: added 4 newly FDA-approved pediatric indications for Zomacton; no change to usage criteria as the policy already addressed use of Zomacton for these 4 indications.	09.26.18	
2Q 2019 annual review: added requirement for initial approval for use in children that member's bone age is ≤ 15 years if girl or ≤ 17 years if boy, consistent with existing requirement for continued therapy; references reviewed and updated.	02.06.19	05.19
1Q 2020 annual review: pediatric endocrinologist, open epiphyses, diagnostic criteria, auxology, and dosing added to all pediatric indications; post transplantation off-label use added to CKD; closed epiphyses added to adult GHD if younger than 18 years; dosing added to all adult indications; intravenous nutrition requirement add to SBS with	11.19.19	02.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
gastroenterologist consultation; HIV-associated wasting - specialist added, GH treatment limited to one year per pivotal trial, failed trials edited to require two from two different therapeutic classes (Appendix B); references reviewed and updated.		
HIM line of business removed from policy, HIM.PA.SP39 policy created.	12.05.19	
Revised preferred product from Norditropin to Zomacton per April SDC and prior clinical guidance; removed alternative pathway bypassing redirection for dose requests < 0.025 mg/injection.	04.22.20	
Auxology updates: correction for age and sex, GH Research Society GF options, and Appendix D added.	06.02.20	08.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise

professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.