Clinical Policy: Human Growth Hormone (Somapacitan, Somatrogon, Somatropin, Lonapegsomatropin-tcgd)

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Line of Business: Commercial - Health Net of Oregon

Coding Implications
Revision Log

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

Description

The following human growth hormone (hGH) formulations require prior authorization:

- hGH analogs: somapacitan-beco (Sogroya®), somatrogon-ghla (Ngenla™)
- Recombinant hGH (rhGH) formulations: somatropin (Genotropin®, Humatrope®, Norditropin®, Nutropin AQ® NuSpin®, Omnitrope®, Saizen®, Serostim®, Zomacton®, Zorbtive®), longpegsomatropin-tcgd (Skytrofa)®

Drugs	Children								Adults		
	GHD	PWS	TS	NS	SHOX	CKD	SGA	ISS	GHD	HIV	SBS
Sogroya	GF								X		
Genotropin	GF	GF	GF				GF	GF	X		
Humatrope	GF		SS		SS/GF		SS	SS/GF	X		
Ngenla	GF										
Norditropin	GF	GF	SS	SS			SS	SS	X		
NutropinAQ	GF		GF			GF		GF	X		
Omnitrope	GF	GF	GF				GF	GF	X		
Saizen	GF								X		
Serostim										X	
Skytrofa	GF										
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)

hGH Analogs:

Sogroya is indicated for:

- Treatment of pediatric patients aged 2.5 years and older who have GF due to inadequate secretion of endogenous GH
- Replacement of endogenous GH in adults with GHD

Ngenla is indicated for:

- Treatment of pediatric patients aged 3 years and older who have GF due to inadequate secretion of endogenous GH

rhGH Formulations:
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:
- Pediatric patients: GF due to inadequate secretion of endogenous GH; SS associated with TS; ISS, high standard deviation score (SDS) <- 2.25, and associated with growth rates unlikely to permit attainment of adult height in the normal range; SS or GF in SHOX deficiency; SS born small for SGA with no catch-up growth by 2 years to 4 years of age.
- Replacement of endogenous GH in adults with 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.
- Replacement of endogenous GH in adults with 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 the treatment of:
- HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance.

Skytrofa is indicated for treatment of:
- Pediatric patients 1 year and older who weigh at least 11.5 kg and have GF due to inadequate secretion of endogenous GH.

Zomacton is indicated for:
- Treatment of pediatric patients who have GF due to inadequate secretion of 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 indicated 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.

It is the policy of Health Net of Oregon that Skytrofa, Sogroya, Ngenla and somatropin are **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. Request is for a somatropin formulation;
3. Prescribed by or in consultation with a pediatric endocrinologist;
4. Age ≤ 1 month;
5. Serum GH concentration ≤ 5 µg/L;
6. Member meets one of the following (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);
7. The requested product is not prescribed concurrently with Increlex® (mecasermin);
8. If request is NOT for Norditropin or Humatrope, one of the following (a, b, or c):
   a. Member must use Norditropin* and Humatrope*;
   b. If both Norditropin and Humatrope are not available (e.g., due to drug shortages) member must use Omnitrope* vial, unless contraindicated or clinically significant adverse effects are experienced;
   c. Norditropin, Humatrope, and Omnitrope are all contraindicated or clinically significant adverse effects are experienced;

   **Prior authorization may be required for Norditropin, Humatrope, and Omnitrope*
9. Dose does not exceed 0.30 mg/kg per week.

Approval duration: 6 months or to member's renewal period whichever is longer

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 request is for Skytrofa, age ≥ 1 years and weight ≥ 11.5 kg;
5. If request is for Sogroya, age ≥ 2.5 years;
6. If request is for Ngenla, age ≥ 3 years;
7. If age > 10 years, open epiphysis on x-ray;
8. Member meets one of the following (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;
9. Member meets one of the following (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. Prior 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);

10. Member meets one of the following (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);
11. The requested product is not prescribed concurrently with Increlex (mecasermin);
12. If request is NOT for Norditropin or Humatrope, one of the following (a, b, or c):
    a. Member must use Norditropin* and Humatrope*;
    b. If both Norditropin and Humatrope are not available (e.g., due to drug shortages) member must use Omnitrope* vial, unless contraindicated or clinically significant adverse effects are experienced;
    c. Norditropin, Humatrope, and Omnitrope are all contraindicated or clinically significant adverse effects are experienced;

    **Prior authorization may be required for Norditropin, Humatrope, and Omnitrope*
13. Dose does not exceed one of the following (a, b, c, or d):
    a. For Ngenla: 0.66 mg/kg per week;
    b. For Skytrofa: 0.24 mg/kg per week;
    c. For Sogroya: 0.16 mg/kg per week;
    d. For somatropin agents: 0.30 mg/kg per week.

Approval duration: 6 months or to member's renewal period whichever is longer

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. Request is for a somatropin formulation;
3. Prescribed by or in consultation with a pediatric endocrinologist;
4. Age < 18 years;
5. If age > 10 years, open epiphysis on x-ray;
6. Member meets one of the following (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);

7. The requested product is not prescribed concurrently with Increlex (mecasermin);
8. If request is NOT for Norditropin or Humatrope, one of the following (a, b, or c):
   a. Member must use Norditropin* and Humatrope*;
   b. If both Norditropin and Humatrope are not available (e.g., due to drug shortages) member must use Omnitrope* vial, unless contraindicated or clinically significant adverse effects are experienced;
   c. Norditropin, Humatrope, and Omnitrope are all contraindicated or clinically significant adverse effects are experienced;

   **Prior authorization may be required for Norditropin, Humatrope, and Omnitrope*
9. 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: 6 months or to member's renewal period whichever is longer

D. Chronic Kidney Disease with Growth Failure – Children (must meet all)**:**
1. Diagnosis of CKD;
2. Request is for a somatropin formulation;
3. Prescribed by or in consultation with a pediatric endocrinologist or nephrologist;
4. Age < 18 years;
5. If age > 10 years, open epiphysis on x-ray;
6. Member meets one of the following (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;
7. Member meets one of the following (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 Norditropin or Humatrope, one of the following (a, b, or c):
   a. Member must use Norditropin* and Humatrope*;
   b. If both Norditropin and Humatrope are not available (e.g., due to drug shortages) member must use Omnitrope* vial, unless contraindicated or clinically significant adverse effects are experienced;
   c. Norditropin, Humatrope, and Omnitrope are all contraindicated or clinically significant adverse effects are experienced;

   **Prior authorization may be required for Norditropin, Humatrope, and Omnitrope*
10. Dose does not exceed 0.35 mg/kg per week.

Approval duration: 6 months or to member's renewal period whichever is longer

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

1. Diagnosis of GHD;
2. Request is for a somatropin or somapacitan formulation;
3. Prescribed by or in consultation with an endocrinologist;
4. Age ≥ 18 years OR closed epiphysis on x-ray;
5. Member has NOT received somatropin therapy for ≥ 1 month prior to GH/IGF-I testing as outlined below;
6. Member meets one of the following (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);
7. The requested product is not prescribed concurrently with Increlex (mecasermin);
8. If request is NOT for Norditropin or Humatrope, one of the following (a, b, or c):
   a. Member must use Norditropin* and Humatrope*;
   b. If both Norditropin and Humatrope are not available (e.g., due to drug shortages) member must use Omnitrope* vial, unless contraindicated or clinically significant adverse effects are experienced;
   c. Norditropin, Humatrope, and Omnitrope are all contraindicated or clinically significant adverse effects are experienced;

   **Prior authorization may be required for Norditropin, Humatrope, and Omnitrope*
9. Dose does not exceed one of the following (a or b):

a. For Sogroya: 8 mg once weekly;
b. For somatropin agents: 0.4 mg/day (may adjust by up to 0.2 mg/day every 4 weeks to maintain normal IGF-1 serum levels; doses > 1.6 mg/day would be uncommon).

Approval duration: 6 months or to member's renewal period whichever is longer

F. Short Bowel Syndrome (must meet all):
1. Diagnosis of SBS;
2. Request is for a somatropin formulation;
3. Prescribed by or in consultation with a gastroenterologist;
4. Age ≥ 18 years;
5. Patient is dependent upon and receiving intravenous nutrition;
6. If request is NOT for Norditropin or Humatrope, one of the following (a, b, or c):
   a. Member must use Norditropin* and Humatrope*;
   b. If both Norditropin and Humatrope are not available (e.g., due to drug shortages) member must use Omnitrope* vial, unless contraindicated or clinically significant adverse effects are experienced;
   c. Norditropin, Humatrope, and Omnitrope are all contraindicated or clinically significant adverse effects are experienced;

   * *Prior authorization may be required for Norditropin, Humatrope, and Omnitrope*
7. Dose does not exceed 8 mg per day.

Approval duration: up to 4 weeks total

G. HIV-Associated Wasting or Cachexia (must meet all):
1. Diagnosis of HIV;
2. Request is for a somatropin formulation;
3. Prescribed by or in consultation with a physician specializing in HIV management;
4. Age ≥ 18 years;
5. Member meets one of the following (a, b, or c):
   a. Unintentional weight loss of ≥ 10% in the last 12 months occurring while on antiretroviral therapy;
   b. Weight < 90% of the lower limit of ideal body weight;
   c. Body mass index (BMI) ≤ 20 kg/m^2;
6. Failure of at least 2 pharmacologic therapies from two separate drug classes *(Appendix B)* unless contraindicated or clinically adverse effects are experienced;
7. Member is currently on antiretroviral therapy;
8. If request is NOT for Norditropin or Humatrope, one of the following (a, b, or c):
   a. Member must use Norditropin* and Humatrope*;
   b. If both Norditropin and Humatrope are not available (e.g., due to drug shortages) member must use Omnitrope* vial, unless contraindicated or clinically significant adverse effects are experienced;
   c. Norditropin, Humatrope, and Omnitrope are all contraindicated or clinically significant adverse effects are experienced;

   Prior authorization may be required for Norditropin, Humatrope, and Omnitrope
9. Dose does not exceed 6 mg per day.

Approval duration: 6 months or to member's renewal period whichever is longer (up to 12 months total)

H. Other diagnoses/indications (must meet 1 and 2)**:**
1. If request is NOT for Norditropin or Humatrope, one of the following (a, b, or c):
   a. Member must use Norditropin* and Humatrope*;
   b. If both Norditropin and Humatrope are not available (e.g., due to drug shortages) member must use Omnitrope* vial, unless contraindicated or clinically significant adverse effects are experienced;
   c. Norditropin, Humatrope, and Omnitrope are all contraindicated or clinically significant adverse effects are experienced;

   **PA may be required for Norditropin, Humatrope, and Omnitrope*
2. Member meets one of the following (a or b):
   a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):
      i. For drugs on the formulary, the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
      ii. For drugs NOT on the formulary, the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2a above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial.

II. Continued Therapy

A. All Pediatric Indications *(open epiphyses)* (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Age < 18 years OR open epiphysis on x-ray;
3. Member meets one of the following (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 one of the following (a, b, c, d, or e):
   a. GHD, one of the following (i, ii, iii, or iv):
      i. For Ngenla (without neonatal hypoglycemia): New dose does not exceed 0.66 mg/kg per week;
      ii. For Skytrofa (without neonatal hypoglycemia): New dose does not exceed 0.24 mg/kg per week;

iii. For Sogroya (without neonatal hypoglycemia): New dose does not exceed 0.16 mg/kg per week;
iv. For somatropin agents (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;

Approval duration: 6 months or to member's renewal period whichever is longer

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. For IGF-1 test results and dosing (test conducted within the last 90 days), one of the following (a, b, or c):
   a. Low IGF-1 serum level (i or ii):
      i. For Sogroya: 8 mg once weekly;
      ii. For somatropin formulations: 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: 6 months or to member's renewal period whichever is longer

C. Short Bowel Syndrome - Adults (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

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: 6 months or to member's renewal period whichever is longer (up to 12 months total)

E. Other diagnoses/indications (must meet 1 and 2)**:**

1. If request is NOT for Norditropin or Humatrope, one of the following (a, b, or c):
   a. Member must use Norditropin* and Humatrope*;
   b. If both Norditropin and Humatrope are not available (e.g., due to drug shortages) member must use Omnitrope* vial, unless contraindicated or clinically significant adverse effects are experienced;
   c. Norditropin, Humatrope, and Omnitrope are all contraindicated or clinically significant adverse effects are experienced;

   **Prior authorization may be required for Norditropin, Humatrope, and Omnitrope*
2. Member meets one of the following (a or b):
   a. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (i or ii):
      i. For drugs on the, the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
      ii. For drugs NOT on the formulary, the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2a above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial.

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 policy – CP.CPA.09 for commercial, or evidence of coverage documents;

B. Small for gestational age (SGA) (NOT A COVERED BENEFIT)

C. Idiopathic Short Stature (ISS) (NOT A COVERED BENEFIT)

D. 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);

E. 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);

F. Adult short stature or altered body habitus associated with antiviral therapy (other than HIV-associated wasting or cachexia);

G. Obesity treatment or enhancement of body mass/strength for non-medical reasons (e.g., athletic gains).

IV. Appendices/General Information

Appendix A: Abbreviation

AO: adult-onset
CKD: chronic kidney disease
CO: childhood-onset
FDA: Food and Drug Administration
GF: growth failure
GFR: glomerular filtration rate
GH: growth hormone
GHD: growth hormone deficiency
hGH: human growth hormone
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
SS: short stature
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®, Syndros®)	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 patch)	2.5 – 7.5 mg patch applied topically QD	7.5 mg/day
testosterone transdermal gel (Androgel®, Testim®)	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
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

- Contraindications:
  - Acute critical illness
  - Children with PWS who are severely obese, have history of upper airway obstruction, sleep apnea, or have severe respiratory impairment due to risk of sudden death
  - Active malignancy
  - Hypersensitivity to product or any of the excipients
  - 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.

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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.
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V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Pediatric Indications (Subcutaneous administration; weekly doses should be divided [except Skytrofa, Sogroya and Ngenla])			
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
Skytrofa	GHD	0.24 mg/kg/week	0.24 mg/kg/week
Sogroya	GHD	0.16 mg/kg once weekly	0.16 mg/kg/week
Ngenla	GHD	0.66 mg/kg once weekly	0.66 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).*	See dosing regimen

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Adult GHD dosing should be substantially lower than that prescribed for children. Adult doses beyond 1.6 mg/day would be uncommon.	
Serostim	HIV-associated wasting	0.1 mg/kg QOD or QD to 6 mg QD	6 mg/day up to 24 weeks
Sogroya	GHD	1.5 mg once weekly – increase by increments of 0.5-1.5 mg every 2-4 weeks based on clinical response and serum IGF-1 concentrations	8 mg/week
Zorbtive	SBS	0.1 mg/kg QD to 8 mg QD	8 mg/day up to 4 weeks

VI. Product Availability

Drug	Availability*
Genotropin lyophilized powder	MD dual-chamber syringes: 5 mg, 12 mg
Genotropin Miniquick	SD pen cartridges: 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	MD pen cartridges: 6 mg, 12 mg, 24 mg MD vial: 5mg
Ngenla	MD pens: 24 mg/1.2 mL, 60 mg/1.2 mL
Norditropin Flexpro	MD pens: 5 mg/1.5 mL, 10 mg/1.5 mL, 15 mg/1.5 mL, 30 mg/3 mL
Nutropin AQ	MD: NuSpin: 5 mg/2 mL, 10 mg/2 mL, 20 mg/2 mL MD pen cartridges: 10 mg/2 mL, 20 mg/2 mL
Omnitrope	MD pen cartridges: 5 mg/1.5 mL, 10 mg/1.5 mL MD vial: 5.8 mg
Saizen	MD pen cartridges: 8.8 mg MD vials: 5 mg, 8.8 mg
Serostim	MD vial: 4 mg SD vials: 5 mg, 6 mg
Skytrofa	SD prefilled cartridges: 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg, 13.3 mg
Sogroya	MD pens: 5 mg/1.5 mL, 10 mg/1.5 mL, 15 mg/1.5 mL
Zomacton	MD vials: 5 mg, 10 mg
Zorbtive	MD vial: 8.8 mg

SD: single-dose, MD: multidose

VII. References

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Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2941	Injection, somatropin, 1 mg
C9399	Unclassified drugs or biologics
J3590	Unclassified biologics

Reviews, Revisions, and Approvals	Date	Plan Approval Date
Policy created; adapted from previously approved policy OR.CP.PCH.39 Human Growth Hormone (Somapacitan, Somatropin). Modified Norditropin and Humatrope redirection to state member must use per template language; for adult GHD continuation of therapy added requirement that member is responding positively to therapy; RT4 Sogroya added new 5 mg/1.5 mL formulation; references reviewed and updated.	12.20.21	01.06.22
1Q 2023 annual review: FDA indication updated for Humatrope; for ISS, increased max dose to 0.5 mg/kg/week per PI; for HIV-associated wasting or cachexia added criteria member is currently	12.14.22	01.05.23

Reviews, Revisions, and Approvals	Date	Plan Approval Date
on antiretroviral therapy; references reviewed and updated.		
Per February SDC and prior clinical guidance, added additional stepwise redirection to Omnitrope vial if Norditropin and Humatrope are not available (e.g., due to drug shortages); Template changes applied to other diagnoses/indications and continued therapy section.	03.15.23	04.06.23
1Q 2024 annual review: added Sogroya pediatric extension for GF due to GHD and new 15 mg/1.5 mL strength, for pediatric GHD criteria set; added Sogroya specific age limit and dosing, and updated Appendix C with Sogroya pediatric contraindications; added Ngenla to policy; for HIV-associated wasting or cachexia, added options for member to meet criteria if weight < 90% of the lower limit of ideal body weight or BMI ≤ 20 kg/m2; added HCPCS/CPT code [C9399, J3590]; template changes applied to other diagnoses/indications and continued therapy section; references reviewed and updated.	12.27.23	02.20.24
Added Skytrofa to policy.	07.15.24	09.17.24
1Q 2025 annual review: no significant changes; references reviewed and updated.	01.15.25	02.11.25

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.

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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.

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