

**Clinical Policy: Human Growth Hormone (Norditropin, Genotropin, Humatrope, Nutropin, NuSpin, Omnitrope, Saizen, Serostim, Sogroya, Zomacton, Zorbtive)**

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Line of Business: Arizona Medicaid (AzCH-CCP and Care1st)

[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®)
- Recombinant hGH (rhGH) formulations: somatropin (Genotropin®, Humatrope®, Norditropin®, Nutropin AQ®, Omnitrope®, Saizen®, Serostim®, Zomacton®, Zorbtive®)

**AHCCCS preferred drugs** in this class include- Norditropin (brand only) and Genotropin (brand only).

**AHCCCS non-preferred drugs** in this class include- Humatrope, Nutropin AQ NuSpin, Omnitrope, Saizen, Serostim, Sogroya, Zomacton and Zorbtive.

Drugs	Children								Adults		
	GHD	PWS	TS	NS	SHOX	CKD	SGA	ISS	GHD	HIV	SBS
Sogroya									X		
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		
NutropinAQ	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)**

**hGH Analogs:**

Sogroya is indicated for:

- Replacement of endogenous GH in adults with GHD

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#### **rhGH Formulations:**

Genotropin is indicated for:

- Pediatric Patients: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi syndrome, Small for Gestational Age, Turner syndrome, and Idiopathic Short Stature
- Adult Patients: Treatment of adults with either childhood-onset or adult-onset GHD

Humatrope is indicated for:

- Pediatric Patients: Treatment of children with short stature or growth failure associated with growth hormone (GH) deficiency, Turner syndrome, idiopathic short stature (ISS), short stature homeobox-containing gene (SHOX) deficiency, and failure to catch up in height after small for gestational age birth
- Adult Patients: Treatment of adults with either childhood-onset or adult-onset GHD

Norditropin FlexPro is indicated for:

- Pediatric Patients: Treatment of children with growth failure due to GHD, short stature associated with Noonan syndrome, short stature associated with Turner syndrome, and short stature born small for gestational age with no catch-up growth by age 2 to 4 years, Idiopathic Short Stature (ISS), and growth failure due to Prader-Willi Syndrome
- Adult Patients: Treatment of adults with either childhood-onset or adult-onset GHD

Nutropin AQ NuSpin is indicated for:

- Pediatric Patients: Treatment of children with growth failure due to GHD, ISS, Turner syndrome (TS), and chronic kidney disease (CKD) up to the time of renal transplantation
- Adult Patients: Treatment of adults with either childhood-onset or adult-onset GHD

Omnitrope is indicated for:

- Pediatric Patients: Treatment of children with growth failure due to GHD, Prader-Willi Syndrome, Small for Gestational Age, TS, and ISS
- Adult Patients: Treatment of adults with either childhood-onset or adult-onset GHD

Saizen is indicated for:

- Pediatric Patients: Treatment of children with growth failure due to GHD
- Adult Patients: Treatment of adults with either childhood-onset or adult-onset 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:

- Pediatric Patients: Treatment of pediatric patients who have growth failure due to inadequate secretion of normal endogenous GH, short stature associated with TS, ISS, SHOX

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deficiency, and short stature born small for gestational age (SGA) with no catch-up growth by 2 years to 4 years

- Adult Patients: For replacement of endogenous GH in adults with GH deficiency

Zorbtive is indicate for:

- For the treatment of Short Bowel Syndrome in patients receiving specialized nutritional support. Zorbtive therapy should be used in conjunction with optimal management of Short Bowel Syndrome.

#### 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 Arizona Complete Health-Complete Care Plan that somatropin (recombinant human growth hormone (rhGH)) is **medically necessary** when the following criteria are met:

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#### 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  $\leq$  1 month;
5. Serum GH concentration  $\leq$  5  $\mu$ g/L;
6. Member meets (a or b):
  - a. Imaging shows hypothalamic-pituitary abnormality;
  - b. Deficiency of  $\geq$  1 anterior pituitary hormone other than GH (e.g., ACTH, TSH, LH, FSH, prolactin);
7. The requested product is not prescribed concurrently with Increlex<sup>®</sup> (mecasermin);
8. If request is NOT for Norditropin or Genotropin but another somatropin formulation (a or b):
  - a. The requested product dose is  $<$  0.025 mg per injection;
  - b. Norditropin and Genotropin product excipients are contraindicated or member has experienced a clinically significant adverse effect to Norditropin and Genotropin;
9. 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. 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 (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;
7. Member meets (a, b, c, d, or e):
  - a. Two GH stimulation tests with peak serum levels  $\leq$  10  $\mu$ g/mL (e.g., stimulants: arginine, clonidine, glucagon);
  - b. Deficiency of  $\geq$  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);
8. Member meets (a or b):
  - a. SS: height  $>$  2 SD below the mean for age and gender (SD, height, date, and age in months within the last 90 days required);
  - b. GF: one of the following (i, ii, or iii):

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- 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);
9. The requested product is not prescribed concurrently with Increlex (mecasermin);
10. If request is NOT for Norditropin or Genotropin but another somatotropin formulation (a or b):
  - a. The requested product dose is  $< 0.025$  mg per injection;
  - b. Norditropin and Genotropin product excipients are contraindicated or member has experienced a clinically significant adverse effect to Norditropin and Genotropin;
11. 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. Request is for a somatotropin 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 (a or b):
  - a. SS: height  $> 2$  SD ( $> 1.5$  SD if TS) below the mean for age and gender (SD, height, date, and age in months within the last 90 days 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 Genotropin but another somatotropin formulation (a or b):
  - a. The requested product dose is  $< 0.025$  mg per injection;
  - b. Norditropin and Genotropin product excipients are contraindicated or member has experienced a clinically significant adverse effect to Norditropin and Genotropin;

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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: 12 months**

#### **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 (a, b, c, or d):
  - a. GFR < 60 mL/min per 1.73 m<sup>2</sup> for ≥ 3 months;
  - b. Dialysis dependent;
  - c. Diagnosis of nephropathic cystinosis;
  - d. History of kidney transplant ≥ 1 year ago;
7. Member meets (a or b):
  - a. SS: height >2 SD below the mean for age and gender (SD, height, date, and age within the last 90 days 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 Genotropin but another somatropin formulation (a or b):
  - a. The requested product dose is < 0.025 mg per injection;
  - b. Norditropin and Genotropin product excipients are contraindicated or member has experienced a clinically significant adverse effect to Norditropin and Genotropin;
10. 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. Request is for a somatropin formulation;



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3. Prescribed by or in consultation with a pediatric endocrinologist;
4. Age  $\geq 2$  years and  $< 18$  years;
5. If age  $> 10$  years, open epiphysis on x-ray;
6. Member meets (a and b):
  - a. Birth weight or length  $> 2$  SD below the mean for gestational age (SD, birth weight, length, and gestational age are required);
  - b. Current height  $> 2$  SD below the mean for age and sex measured within the last year at  $\geq 2$  years of age (SD, height, date, and age in months are required);
7. The requested product is not prescribed concurrently with Increlex (mecasermin);
8. If request is NOT for Norditropin or Genotropin but another somatotropin formulation (a or b):
  - a. The requested product dose is  $< 0.025$  mg per injection;
  - b. Norditropin and Genotropin product excipients are contraindicated or member has experienced a clinically significant adverse effect to Norditropin and Genotropin;
9. 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  $\geq 18$  years OR closed epiphysis on x-ray;
4. Member has NOT received somatotropin therapy for  $\geq 1$  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  $\leq 5$   $\mu\text{g/mL}$  (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  $\leq 5$   $\mu\text{g/ml}$  (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  $\geq 3$  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 for Sogroya, member has previous trial and failure, intolerance or contraindication to Norditropin and Genotropin;
8. If request is NOT for Norditropin or Genotropin but another somatotropin formulation (a or b):

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- a. The requested product dose is  $< 0.025$  mg per injection;
  - b. Norditropin and Genotropin product excipients are contraindicated or member has experienced a clinically significant adverse effect to Norditropin and Genotropin;
9. Dose does not exceed one of the following (a or b):
- a. For Sogroya: 8 mg once weekly;
  - b. For somatropin formulations: 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**

#### **G. 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  $\geq 18$  years;
5. Patient is dependent upon and receiving intravenous nutrition;
6. If request is NOT for Norditropin or Genotropin but another somatropin formulation (a or b):
  - a. The requested product dose is  $< 0.025$  mg per injection;
  - b. Norditropin and Genotropin product excipients are contraindicated or member has experienced a clinically significant adverse effect to Norditropin and Genotropin;
7. 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. Request is for a somatropin formulation;
3. Prescribed by or in consultation with a physician specializing in HIV management;
4. Age  $\geq 18$  years;
5. Unintentional weight loss of  $\geq 10\%$  in the last 12 months occurring while on antiretroviral therapy;
6. Failure of at least 2 pharmacologic therapies from two separate drug classes (*Appendix B*) unless contraindicated or clinically adverse effects are experienced;
7. If request is NOT for Norditropin or Genotropin but another somatropin formulation (a or b):
  - a. The requested product dose is  $< 0.025$  mg per injection;
  - b. Norditropin and Genotropin product excipients are contraindicated or member has experienced a clinically significant adverse effect to Norditropin and Genotropin;
8. Prescribed dose does not exceed 6 mg per day.

**Approval duration: 6 months**



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#### 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): AZ.CP.PMN.53 for Arizona 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  $\geq 2$  years, member's height has increased  $\geq 2$  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  $\geq 2$  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. Member is responding positively to therapy;
3. For IGF-1 test results and dosing (test conducted within the last 90 days) (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: 12 months**

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#### **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  $\geq 4$  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  $\geq 12$  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 AZ.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): AZ.CP.PMN.53 for Arizona 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 – AZ.CP.PMN.53 for Arizona Medicaid.
- 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).

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**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

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

*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.*

<b>Drug</b>	<b>Dosing Regimen</b>	<b>Dose Limit/Maximum Dose</b>
<b><i>Appetite stimulants</i></b>		
Megestrol (Megace®)	400 - 800 mg PO daily (10 – 20 ml/day)	800 mg/day
Dronabinol (Marinol®)	2.5 mg PO bid	20 mg/day
<b><i>Testosterone replacement products</i></b>		
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)
<b><i>Anabolic steroid</i></b>		
Oxandrolone (Oxandrin®)	2.5 – 20 mg PO /day	20 mg/day
Nandrolone decanoate	100 mg IM Q week	100 mg Q wk
<b><i>Nausea/vomiting treatments*</i></b>		
chlorpromazine	10 to 25 mg PO q4 to 6 hours prn	2,000 mg/day

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Drug	Dosing Regimen	Dose Limit/Maximum Dose
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
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 differ based on specific formulary used*

#### Appendix C: Contraindications/Boxed Warnings

- Somatropin contraindications:
  - 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
- Sogroya contraindications:
  - Acute critical illness
  - Active malignancy
  - Hypersensitivity to somapacitan-beco or excipients
  - Active proliferative or severe non-proliferative diabetic retinopathy
- 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.<sup>1</sup>
- 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<sup>2,3</sup> 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.<sup>4</sup>
- 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.<sup>5</sup>

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- 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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#### Appendix E: General Information

- Preferred products: Norditropin and Genotropin
- In childhood cancer survivors who were treated with radiation to the brain/head for their first neoplasm and who developed subsequent GHD and were treated with somatotropin, an increased risk of a second neoplasm has been reported. Intracranial tumors, in particular meningiomas, were the most common of these second neoplasms. In adults, it is unknown whether there is any relationship between somatotropin replacement therapy and CNS tumor recurrence.
- Short stature/growth failure prior to rhGH therapy is evidenced by one of the following:
  - Height > 3 SD below the mean
  - Height > 2 SD below the mean and (a or b)
    - a) Height velocity > 1 SD below the mean for chronological age over 1 year
    - b) Decrease in height SD > 0.5 over 1 year in children > 2 years of age
  - Height > 1.5 SD below midparental height
    - a) Boys: (father's height + mother's height + 13 cm)/2 or (Father's Height + Mother's Height + 5 inches)/2
    - b) Girls: (father's height + mother's height - 13 cm)/2 or Father's Height - 5 inches + Mother's Height) / 2
  - Height velocity > 2 SD below the mean over 1 year
  - Height velocity > 1.5 SD below the mean over 2 years

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- The 2009 American Association of Clinical Endocrinologists (AACE) guidelines for clinical practice for growth hormone use in growth hormone-deficient adults and transition patients state that “there is no evidence that one GH product is more advantageous over the other, apart from differences in pen devices, dose increments and decrements, and whether or not the product requires refrigeration; therefore, we do not recommend the use of one commercial GH preparation over another.”
- Examples of positive response to therapy for cachexia in HIV patients include a 2% increase in body weight and/or body cell mass (BCM). Once BCM is normalized, therapy may be stopped and the patient may be monitored for wasting to reoccur.
  - Body cell mass (BCM): The total mass of all the cellular elements in the body which constitute all the metabolically active tissue of the body. The preferred method for assessing BCM depletion is bioelectrical impedance analysis (BIA) which can be performed with portable equipment in the office setting.
- GF-1 and IGFBP-3 levels should be interpreted against reference ranges that are standardized for sex and age (or better, by stage of sexual development, such as Tanner Stage if available). The range varies with the assay used, and results should be interpreted against standards provided by the laboratory performing the test.
- Other than growth hormone (GH), pituitary hormones include the following:
  - ACTH: adrenocorticotrophic hormone
  - TSH: thyroid stimulating hormone
  - FSH: follicle stimulating hormone
  - LH: luteinizing hormone
  - PrL: Prolactin
  - Melanocyte-stimulating hormone (MSH)
  - Oxytocin
  - ADH: Antidiuretic hormone
- Growth Hormone Stimulation Test Agents
  - Glucagon
  - Clonidine
  - Insulin
  - Arginine (L-Arginine)
- Given the substantial number of healthy, normally growing children who test below accepted limits, inadequate response to two different provocative tests is required for diagnosis of GHD. While it is possible that combining tests might yield different results from tests performed on separate days, there is no evidence against performing both tests sequentially on the same day.
- Defined central nervous system pathology
  - Pituitary Hypoplasia
  - Craniofacial Developmental Defects
  - Empty Sella Syndrome
  - Septo-optic dysplasia
  - Pituitary Stalk Interruption Syndrome



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- a) Absent/hypoplastic anterior pituitary gland
- b) Thin or absent pituitary stalk
- c) Ectopic posterior pituitary

**V. Dosage and Administration**

Drug Name	Indication	Dosing Regimen	Maximum Dose
<b><i>Pediatric Indications (Subcutaneous administration; weekly doses should be divided)</i></b>			
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
<b><i>Adult Indications (Subcutaneous administration)</i></b>			
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	See dosing regimen

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Drug Name	Indication	Dosing Regimen	Maximum Dose
		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	0.5 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

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

## VI. Product Availability

Drug	Availability*
<b><i>hGH Analogs</i></b>	
Sogroya	MD pen: 5 mg/1.5 mL, 10 mg/1.5 mL
<b><i>rhGH Formulations</i></b>	
Genotropin lyophilized powder	MD dual-chamber syringe: 5 mg, 12 mg
Genotropin Miniquick	SD 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	MD pen cartridge: 6 mg, 12 mg, 24 mg MD vial: 5mg
Norditropin Flexpro	MD pen: 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 cartridge: 10 mg/2 mL, 20 mg/2 mL
Omnitrope	MD pen cartridge: 5 mg/1.5 mL, 10 mg/1.5 mL MD vial: 5.8 mg
Saizen	MD pen cartridge: 8.8 mg MD vial: 5 mg, 8.8 mg
Serostim	MD vial: 4 mg SD vial: 5 mg, 6 mg
Zomacton	MD vial: 5 mg, 10 mg
Zorbtive	MD vial: 8.8 mg

*SD*: single-dose, *MD*: multidose

## VII. References

### FDA Labels

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously approved policy AZ.CP.PHAR.55 Somatropin (Human Growth Hormones); retired AZ.CP.PHAR.55 Somatropin (Human Growth Hormones); no significant changes from previously approved policy; 1Q 2021 annual review: no significant changes; references reviewed and updated.	10.22.20	02.21
Added Care1st logo. Added verbiage to specify that criteria also applies to Care1st.	5.10.21	04.21
1Q 2022 annual review: 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.	01.07.22	02.22

#### **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

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