

## **Clinical Policy: Somatropin (Human Growth Hormone)**

Reference Number: CP.PHAR.55

Effective Date: 03.11

Last Review Date: 05.19

Line of Business: HIM, 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 requiring prior authorization: somatropin (Genotropin<sup>®</sup>, Genotropin Miniquick<sup>®</sup>, Humatrope<sup>®</sup>, Humatrope Combo Pack<sup>®</sup>, Norditropin FlexPro<sup>®</sup>, Nutropin AQ<sup>®</sup> NuSpin<sup>®</sup>, Omnitrope<sup>®</sup>, Saizen<sup>®</sup>, Serostim<sup>®</sup>, Zomacton<sup>™</sup>, Zorbtive<sup>™</sup>).

### **FDA Approved Indication(s)**

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

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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 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 (SBS) in patients receiving specialized nutritional support. Zorbtive therapy should be used in conjunction with optimal management of SBS.

#### **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 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 Use in Children (must meet all):**

1. Diagnosis of one of the following (a, b, c, d, e, f, or g):
  - a. GHD as evidenced by low or low normal insulin-like growth factor (IGF)-I or insulin-like growth factor binding protein (IGFBP)-3 level and one of the following (i, ii, iii, or iv):
    - i. Two GH stimulation tests with peak levels  $\leq 10$   $\mu\text{g/L}$ ;
    - ii. Evidence of  $\geq 3$  pituitary hormone deficiencies (*see Appendix D*);
    - iii. History of surgery or irradiation in the hypothalamic-pituitary region;
    - iv. Defined central nervous system pathology;
  - b. SHOX deficiency with Shoxdna Dx® genetic test that detects mutations and deletions in the SHOX gene;
  - c. Growth failure secondary to chronic kidney disease in pre-transplantation;
  - d. Prader-Willi syndrome, Turner syndrome, Noonan syndrome;
  - e. Neonatal hypoglycemia;
  - f. Central nervous system tumor treated with radiation;
  - g. Small for gestational age as defined by both of the following (i and ii):

- i. Birth weight or length > 2 standard deviations (SD) below the mean for gestational age;
  - ii. Failure to manifest catch-up growth to reach normal height range by age 2;
2. Prescribed by or in consultation with an endocrinologist;
3. Age  $\leq$  18 years;
4. For Prader-Willi syndrome, Turner syndrome, Noonan syndrome, and SHOX deficiency: confirmation of diagnosis by genetic testing;
5. Documentation of baseline height at the time of request;
6. Member's bone age is  $\leq$  15 years if girl or  $\leq$  17 years if boy;
7. If request is for an rhGH product other than Norditropin, the Norditropin formulations are inappropriate (e.g., due to preservatives or dosing increment limitations) or member has a contraindication or experienced clinically significant adverse effects to Norditropin;
8. Dose does not exceed the maximum indicated in the prescribing information.

**Approval Duration: 12 months**

**B. Adult GHD or Short Bowel Syndrome (must meet all)**

1. Diagnosis of one of the following (a or b):
  - a. Adult GHD as evidenced by one of the following (i or ii):
    - i. Two insulin tolerance test (ITT) GH stimulation tests with peak levels  $\leq$  5  $\mu\text{g/L}$ ;
    - ii. One low IGF-I level and one of the following (a, b, c, d, e, f, or g):
      - a) One ITT GH stimulation test with a peak level levels  $\leq$  5  $\mu\text{g/L}$ ;
      - b) One glucagon GH stimulation test with peak level  $\leq$  3  $\mu\text{g/L}$ ;
      - c) One arginine GH stimulation test with peak level  $\leq$  0.4  $\mu\text{g/L}$ ;
      - d) Hypothalamic-pituitary structural lesions;
      - e) Growth hormone releasing hormone/Arginine test with peak GH levels:
        - 1)  $\leq$  11.0  $\mu\text{g/L}$  in members with BMI < 25  $\text{kg/m}^2$ ;
        - 2)  $\leq$  8.0  $\mu\text{g/L}$  in members with BMI  $\geq$  25 and < 30  $\text{kg/m}^2$ ;
        - 3)  $\leq$  4.0  $\mu\text{g/L}$  in members with BMI  $\geq$  30  $\text{kg/m}^2$ ;
      - f) Evidence of  $\geq$  3 pituitary hormone deficiencies (*see Appendix D*);
      - g) Documented genetic cause of GHD;
    - b. SBS;
  2. Age  $\geq$  18 years;
  3. Prescribed by or in consultation with an endocrinologist;
  4. If request is for an rhGH product other than Norditropin, the Norditropin formulations are inappropriate (e.g., due to preservatives or dosing increment limitations) or member has a contraindication or experienced clinically significant adverse effects to Norditropin;
  5. Dose does not exceed the maximum indicated in the prescribing information.

**Approval Duration:**

**Adult GHD** – 12 months

**SBS** – 4 weeks

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1. Diagnosis of HIV infection;
2. Age  $\geq$  18 years;
3. Member is on concomitant anti-viral therapy for the treatment of HIV;
4. Involuntary weight loss of  $>10\%$  of body weight;
5. One of the following (a or b) unless contraindicated or clinically significant adverse effects are experienced:
  - a. If inadequate appetite, failure of megestrol acetate or dronabinol to stimulate appetite;
  - b. If inadequate intake due to nausea, failure of  $\geq$  1 preferred agent(s) for nausea (*see Appendix B*);
6. Failure of a therapeutic trial of testosterone in combination with an anabolic steroid in males unless contraindicated or clinically significant adverse effects are experienced;
7. If request is for an rhGH product other than Norditropin, the Norditropin formulations are inappropriate (e.g., due to preservatives or dosing increment limitations) or member has a contraindication or experienced clinically significant adverse effects to Norditropin;
8. Dose does not exceed the maximum indicated in the prescribing information.

**Approval duration: 3 months**

**D. 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): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

**II. Continued Therapy****A. Growth Hormone Use in Children (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 as evidenced by increased growth rate by 2 cm over baseline in first year;
3. Member's bone age is  $\leq$  15 years if girl or  $\leq$  17 years if boy;
4. If request is for a dose increase, new dose does not exceed the maximum indicated in the prescribing information.

**Approval duration: 12 months**

**B. Adult GHD, HIV-Related Cachexia, or Short Bowel Syndrome (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. If request is for a dose increase, new dose does not exceed the maximum indicated in the prescribing information.

**Approval duration: 12 months**

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**C. 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): HIM.PHAR.21 for health insurance marketplace and 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.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.
- B. Idiopathic short stature (ISS);
- C. Constitutional growth delay;
- D. Obesity;
- E. Adult short stature or altered body habitus associated with antiviral therapy;
- F. Anabolic therapy to enhance body mass or strength for non-medical reasons (e.g., athletic gains).

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CKD: chronic kidney disease	PWS: Prader-Willi syndrome
FDA: Food and Drug Administration	rhGH: recombinant human growth hormone
GFR: glomerular filtration rate	SBS: short bowel syndrome
GH: growth hormone	SD: standard deviation
GHD: growth hormone deficiency	SGA: small for gestational age
HIV: human immunodeficiency virus	SHOX: short stature homeobox-containing gene
IGF-1: insulin-like growth factor-1	TS: Turner syndrome
IGFBP-3: insulin-like growth factor binding protein-3	
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>
<i>Appetite stimulants</i>		
Megestrol (Megace®)	400 - 800 mg PO daily (10 – 20 ml/day)	800 mg/day
Dronabinol (Marinol®)	2.5 mg PO bid	20 mg/day

Drug	Dosing Regimen	Dose Limit/Maximum Dose
<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 <sup>®</sup> (testosterone transdermal)	2.5 – 7.5 mg patch applied topically QD	7.5 mg/day
Androgel <sup>®</sup> (testosterone gel)	5 - 10 gm gel (delivers 50 – 100 mg testosterone) applied topically QD	10 gm/day gel (100 mg/day testosterone)
Testim <sup>®</sup> (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 <sup>®</sup> )	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
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<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*\*preferred status may differ based on specific formulary used*

#### *Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Genotropin, Genotropin Miniquick, Humatrope, Humatrope Combo Pack, Norditropin FlexPro, Nutropin AQ NuSpin, Omnitrope, Saizen, Zomacton: acute critical illness; children with Prader-Willi syndrome who are severely obese or have severe respiratory impairment (reports of sudden death); active malignancy; hypersensitivity; active proliferative or severe non-proliferative diabetic retinopathy; children with closed epiphyses
  - Zorbitive: acute critical illness; active malignancy; hypersensitivity; active proliferative or severe non-proliferative diabetic retinopathy
  - Serostim: acute critical illness; active malignancy; diabetic retinopathy; hypersensitivity
- Boxed warning(s): none reported

#### *Appendix D: General Information*

- Preferred product: Norditropin

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- 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 somatropin, 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 somatropin 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:  $(\text{father's height} + \text{mother's height} + 13 \text{ cm})/2$  or  $(\text{Father's Height} + \text{Mother's Height} + 5 \text{ inches})/2$
    - b) Girls:  $(\text{father's height} + \text{mother's height} - 13 \text{ cm})/2$  or  $(\text{Father's Height} - 5 \text{ inches} + \text{Mother's Height}) / 2$
  - Height velocity > 2 SD below the mean over 1 year
  - Height velocity > 1.5 SD below the mean over 2 years
- 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, 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: lutenizing hormone
  - PrL: Prolactin
  - Melatnocyte-stimulating hormone (MSH)
  - Oxytocin
  - ADH: Antidiuretic hormone

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**V. Dosage and Administration**

<b>Drug Name</b>	<b>Indication</b>	<b>Dosing Regimen</b>	<b>Maximum Dose</b>
Somatropin (Genotropin, Genotropin Miniquick, Humatrope, Humatrope Combo Pack, Norditropin Flexpro, Nutropin Aq Nuspin, Omnitrope, Saizen, Zomacton, Zorbtive)	Children and adolescents with GHD, small for gestational age, Turner syndrome, Prader- Willi syndrome, Noonan syndrome, SHOX deficiency, growth failure secondary to CKD, Adults with growth hormone deficiency, SBS	Refer to prescribing information ( <i>Somatropin, rh-GH doses must be individualized and are highly variable depending on the nature and severity of the disease, the formulation being used, and on patient response</i> )	Refer to prescribing information
Serostim	Wasting or Cachexia in HIV patients	<ul style="list-style-type: none"> <li>• &lt; 35 kg = 0.1 mg/kg SC QHS</li> <li>• 35 to 45 kg = 4 mg SC QHS</li> <li>• 45 kg to 55 kg = 5 mg SC QHS</li> <li>• &gt; 55 kg = 6 mg SC QHS</li> </ul>	6 mg SC/day

**VI. Product Availability**

<b>Drug</b>	<b>Availability</b>
Genotropin lyophilized powder	Dual-chamber syringe: 5 mg, 12 mg
Genotropin Miniquick (without preservative)	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	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	Cartridge: 5 mg/2 mL Pen: 10 mg/2 mL, 20 mg/2 mL
Omnitrope	Cartridge: 5 mg/1.5 mL, 10 mg/1.5 mL Dual-chamber syringe: 5.8 mg
Saizen	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

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#### VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>Appendix K: deleted low-fat diet, added low oxalate diet.</p> <p>Appendix F: changed age of 2 to age of 4. Changed “normal range is typically considered <math>\geq 10^{\text{th}}</math> percentile to (height velocity SDS less than 0 during the past year.</p> <p>Growth failure due to CRI algorithm: fixed typo Appendix E</p> <p>PWS algorithm: changed first year response to GH therapy: Does patient change in height SDS <math>&gt;0.3</math>, a 1 year height velocity <math>\geq 3</math> cm/y, or a height velocity SDS <math>\geq +1</math></p> <p>SGA algorithm: changed to Verify: Birth weight or length <math>&lt; 2</math> SDS for gestational age. Changed to Did patient fail to manifest catch-up growth by 3years of age.</p> <p>Removed delayed bone age requirement in Figure 2 for diagnosis of GHD</p>	10.13	12.13
<p>Combined “management challenges” and “current standards of practice” into one background section</p> <p>Figure 1: restructured review process to proceed to figure 2 or 10 depending on age of patient; added brain MRI or CT if pediatric</p> <p>Figure 2: allowed specific disease states to skip stimulation test questions since they are not relevant</p> <p>Figures 5 – 9: directed to re-auth algorithm if currently on med through Centene benefit to reduce redundancy</p> <p>Added Figure 16 to reduce redundancy in other algorithms</p> <p>Reformatted safety section</p> <p>Added Table 3</p> <p>Updated Appendix D &amp; F</p> <p>Added Appendix Q: Assessment of bone age</p> <p>Added Appendix R: Calculation of midparental height</p>	12.14	12.14
<p>Policy converted to new template.</p> <p>Increlex transferred to new policy.</p> <p>Tev-Tropin and Nutropin removed – no longer available.</p>	11.15	Updates requested

Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>Criteria arranged by pediatric then adult initial/continuation therapy; in both sections, documentation requests and dose titration questions removed.</p> <p>Pediatric GH criteria – neonatal hypoglycemia/GHD as an indication is removed – considered off-label per Norditropin; specific growth failure/short stature requirements removed per expert review; midparental height removed per expert review; CKD criteria changed from GFR&lt;75 to definition of CKD per KDOQI; changed initial and re-authorization approval periods to 12 months in response to CPC comment that was not in line with efficacy criteria measured after one year for re-auth.</p> <p>Adult GHD criteria – for childhood and adult onset GHD, require only low IGF-1 if defined structural lesions, multiple hormone deficiencies, etc. per expert review recommending no need for provocation test here.</p>		
<p>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, 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.</p>	01.16	02.16
<p>Added table of contents and minor edit for clarity, no criteria changes</p>	03.16	
<p>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</p>	04.16	
<p>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.</p>	05.16	06.16

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<p>Adult age requirement is required for HIV and SBS only; open epiphyses are required for all childhood diagnoses other than neonatal hypoglycemia.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>Removed requirement for normalized IGF-1 levels on continued approval for childhood GHD.</p> <p>Specialist reviewed.</p>		
<p>Added criteria for adult and transition PWS to initial and continuation criteria per the GH Research Society PWS 2013 consensus statement.</p>	09.16	09.16
<p>Converted to new template. Re-auth: removed reasons to discontinue. Removed preexisting papilledema and concomitant administration of GH and Increlex from Appendix B.</p>	05.17	06.17
<p>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 <math>\geq 3</math> months, GFR <math>&lt; 60</math> mL/min per <math>1.73</math> m<sup>2</sup> for <math>\geq 3</math> 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 <math>&gt; 10\%</math> body weight from baseline, treatment with therapies other than</p>	02.20.18	05.18

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
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 $\leq 5 \mu\text{g/mL}$ to $\leq 5 \mu\text{g/L}$ ; aligned labs required for diagnosis with 2009 AACE guidelines; for Child/adolescent GHD: corrected peak GH level $\leq 10 \mu\text{g/L}$ to 10; GH use in children: added requirement for documentation of baseline height for initial approval.		
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 $\leq 15$ years if girl or $\leq 17$ years if boy, consistent with existing requirement for continued therapy; references reviewed and updated.	02.06.19	05.19

**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

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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.

**For Health Insurance Marketplace members**, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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