Clinical Policy: Somatropin (Human Growth Hormone)

Reference Number: CP.CPA.84
Effective Date: 11.16.16
Last Review Date: 05.18
Line of Business: Commercial

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®, Genotropin Miniquick®, Humatrope®, Humatrope Combo Pack®, Norditropin FlexPro®, Nutropin AQ® NuSpin®, Omnitrope®, Saizen®, Serostim®, Zomacton™, Zorbtive™).

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

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)) **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;
   b. Idiopathic Short Stature as defined by > 2.25 standard deviations below the normal adult height for gender (5' 3" for a male and 4' 11" for a female);
   c. SHOX deficiency with Shoxdna Dx® genetic test that detects mutations and deletions in the SHOX gene;
   d. Growth failure secondary to chronic kidney disease in pre-transplantation;
   e. Prader-Willi syndrome, Turner syndrome, Noonan syndrome;
   f. Neonatal hypoglycemia;
   g. Central nervous system tumor treated with radiation;
   h. Small for gestational age;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≤ 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 ≤ 15 years if girl or ≤ 17 years if boy;

7. Failure of Humatrope and Norditropin if requesting non-preferred products, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed the maximum indicated in Section V (Dosage and Administration).

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

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

1. Diagnosis of one of the following (a or b):
   a. Adult GHD;
   b. SBS;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with an endocrinologist;
4. For Adult GHD only: member has multiple pituitary hormone deficiencies resulting from structural hypothalamic/pituitary disease, radiation, defined CNS pathology, cranial radiation, trauma, pituitary surgery, or genetic defect affecting the GH axis with low IGF-1 and low IGFBP-3;
5. Failure of Humatrope and Norditropin if requesting non-preferred products, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed the maximum indicated in Section V (Dosage and Administration).

Approval Duration:
Adult GHD – 6 months or to member's renewal period whichever is longer
SBS – 4 weeks (not renewable)

C. Wasting or Cachexia in HIV Patients (must meet all)**:**

1. Diagnosis of HIV infection;
2. Age ≥ 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 ≥ 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. Failure of Humatrope and Norditropin if requesting non-preferred products, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed the maximum indicated in Section V (Dosage and Administration).

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

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): CP.CPA.09 for commercial.

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 one of the following (a or b):
   a. Increased growth rate by 2 cm over baseline in first year or 1 cm over baseline in 6 months for those patients undergoing a 6-month trial;
   b. For ISS treatment, the child's height continues to be > 2.25 standard deviations below the normal adult height for gender (5' 3" for a male and 4' 11" for a female);
3. Member's bone age is ≤ 15 years if girl or ≤ 17 years if boy;
4. If request is for a does increase, new dose does not exceed the maximum indicated in Section V (Dosage and Administration).

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

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 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 Section V (Dosage and Administration).

Approval Duration:
Adult GHD, HIV-Related Cachexia – 6 months or to member's renewal period whichever is longer
SBS – 4 weeks (not renewable)

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 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.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.

IV. Appendices/General Information

Appendix A: Abbreviation

CKD: chronic kidney disease
CNS: central nervous system
FDA: Food and Drug Administration
GHD: growth hormone deficiency
GH: 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
rhGH: recombinant human growth hormone
SGA: small for gestational age
SBS: short bowel syndrome
SHOX: short stature homeobox-containing gene
TS: Turner syndrome

Appendix B: Therapeutic Alternatives

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

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

- 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
  - Zorbtive: 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 products, where applicable: Humatrope and Norditropin
- Non-preferred products: Genotropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Zomacton, Zorbtive
- 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: (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
- 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.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
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, idiopathic short stature, Adults with growth hormone deficiency, SBS	Refer to prescribing information (*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*)	Refer to prescribing information
Serostim	Wasting or Cachexia in HIV patients	• < 35 kg = 0.1 mg/kg SC QHS • 35 to 45 kg = 4 mg SC QHS • 45 kg to 55 kg = 5 mg SC QHS • > 55 kg = 6 mg SC QHS	6 mg SC/day

VI. Product Availability

Drug	Availability
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

Drug	Availability
Serostim	Vial: 4 mg, 5 mg, 6 mg
Zomacton	Vial: 5 mg, 10 mg
Zorbtive	Vial: 8.8 mg

VII. References

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21. Romer T, Zabransky M, Walczak M, Szalecki M, and Balser S. Effect of switching recombinant human growth hormone: comparative analysis of phase 3 clinical data. Biol Ther 2011; 1(2):005. DOI 10.1007/s13554-011-0004-8.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	01.18.17	11.17
2Q 2018 annual review: added specialist requirement; Growth hormone use in children: added height requirement for ISS and bone age requirement for initial approval of all diagnoses for children; added requirement for baseline height documentation for initial approval of GH use in children in order to assess response at reauthorization; continued approval criteria for GH use in children was revised from: Continued growth rate exceeds 2.5 cm/year to 2 cm/year per NICE 2010 guidelines and 2008 Pediatric Endocrine Society; added bone age requirement for continued tx in children; combined CP.CPA.151 Somatropin (Serostim) into this grouped somatropin policy; added preferencing to dx of HIV-associated cachexia; references and appendices reviewed and updated.	02.20.18	05.18
No significant changes; added 4 newly FDA-approved pediatric indications for Zomacton; no change to usage criteria as policy already addressed use of Zomacton for these 4 indications.	09.26.18	
2Q 2019 annual review: added age requirement for wasting or cachexia in HIV patients; 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 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.

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