Clinical Policy: Somatropin (Recombinant Human Growth Hormone)
Reference Number: ERX.SPMN.17
Effective Date: 07/16
Last Review Date: 06/16

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

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that somatropin (recombinant human growth hormone (rhGH): Genotropin®, Humatrope®, Norditropin®, Nutropin AQ®, Omnitrope®, Saizen®, Serostim®, Zomacton™, Zorbtive®) is medically necessary for the following indications when the corresponding criteria is met:

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I. Initial Approval Criteria

A. Neonatal Hypoglycemia (must meet all)
   1. Prescribed by or in consultation with an endocrinologist;
   2. Diagnosis of neonatal hypoglycemia;
   3. Brain MRI shows risk for hypopituitarism;
   4. Random growth hormone (GH) measurement of < 20 µg/L;
   5. Causes of hypoglycemia, other than growth hormone deficiency (GHD), have been ruled out;
   6. Prescribed rhGH dose does not exceed 0.4 mg/kg/week;
   7. If prescription 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 intolerance to Norditropin.

Approval duration: up to 12 months total

B. Growth Hormone Deficiency - Children (must meet all)
   1. Prescribed by or in consultation with an endocrinologist;
   2. Epiphyses are open;
   3. Evidence of short stature/growth failure per Appendix B;
   4. Diagnosis of GHD;
   5. Other causes of growth failure have been ruled out (e.g., chronic systemic disease, undernutrition, hypothyroidism, Turner syndrome - in girls, skeletal disorders);
   6. Intracranial tumor is excluded by MRI or CT;
   7. Low or low normal IGF-I or IGFBP-3 level and one of the following:
      a. Two GH stimulation tests with peak levels ≤ 10 µg/mL;
      b. Evidence of ≥ 3 pituitary hormone deficiencies;
      c. History of surgery or irradiation in the region of the hypothalamus and pituitary;
      d. Defined central nervous system pathology documented by MRI or CT;
      e. Documented genetic cause of GHD;
   8. Prescribed rhGH dose does not exceed either of the following:
      a. 0.7 mg/kg/week if pubertal;
      b. 0.4 mg/kg/week if prepubertal;
   9. If prescription 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 intolerance to Norditropin.

Approval duration: 12 months

C. Growth Hormone Deficiency – Adults and Transition Patients (must meet all)
   1. Prescribed by or in consultation with an endocrinologist;
   2. Diagnosis of adult onset (AO) or childhood onset (CO) GHD;
   3. One of the following (a, b or c):
      a. Two GH stimulation tests with peak levels ≤ 5 µg/mL;
b. Both of the following:
   i. One GH stimulation test with a peak level ≤ 5 µg/ml;
   ii. One low IGF-I level;

c. One low IGF-I level and one of the following:
   i. Hypothalamic-pituitary structural lesions;
   ii. Evidence of ≥ 3 pituitary hormone deficiencies;
   iii. Documented genetic cause of GHD;

4. If prescription 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 intolerance to Norditropin.

Approval duration: 12 months

D. Genetic Diseases with Primary Effects on Growth - Children (must meet all)
   1. Prescribed by or in consultation with an endocrinologist;
   2. Epiphyses are open;
   3. One of the following diagnoses:
      a. Prader-Willi syndrome (PWS):
         i. Confirmed by genetic testing;
         ii. None of the following apply:
            a) Severe obesity;
            b) History of upper airway obstruction;
            c) History of sleep apnea;
            d) Severe respiratory impairment;
         iii. Prescribed rhGH dose does not exceed 0.3 mg/kg/week;
      b. Turner syndrome:
         i. Confirmed by genetic testing;
         ii. Evidence of short stature or growth failure per Appendix B;
         iii. Prescribed rhGH dose does not exceed 0.5 mg/kg/week;
      c. Noonan syndrome:
         i. Confirmed by genetic testing or diagnosis by geneticist;
         ii. Evidence of short stature or growth failure per Appendix B;
         iii. Prescribed rhGH dose does not exceed 0.5 mg/kg/week;
      d. Short stature homeobox-containing gene (SHOX) deficiency:
         i. Confirmed by genetic testing;
         ii. Evidence of short stature or growth failure per Appendix B;
         iii. Prescribed rhGH dose does not exceed 0.4 mg/kg/week;

4. If prescription 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 intolerance to Norditropin.

Approval duration: 12 months

E. Born Small for Gestational Age - Children (must meet all)
   1. Prescribed by or in consultation with an endocrinologist;
2. Epiphyses are open;
3. Diagnosis of small for gestational age (SGA);
4. Birth weight or length > 2 SD below the mean for gestational age;
5. Failure to manifest catch-up growth to reach normal height range by age 2;
6. Prescribed rhGH dose does not exceed 0.5 mg/kg/week;
7. If prescription 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 intolerance to Norditropin.

**Approval duration: 12 months**

**F. Chronic Kidney Disease - Children** (must meet all)
1. Prescribed by or in consultation with an endocrinologist or nephrologist;
2. Epiphyses are open;
3. Evidence of short stature or growth failure per Appendix B;
4. Diagnosis of chronic kidney disease (CKD) as evidenced by one of the following:
   a. Structural or functional abnormalities of the kidney for ≥ 3 months;
   b. GFR < 60 mL/min per 1.73 m² for ≥ 3 months;
   c. Both a and b with no 3-month duration requirement;
5. Prescribed in conjunction with optimal CKD management (e.g., metabolic, endocrine, and nutritional abnormalities have been treated and stabilized);
6. Member does not have a functioning renal allograft;
7. Prescribed rhGH dose does not exceed 0.4 mg/kg/week;
8. If prescription 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 intolerance to Norditropin.

**Approval duration: 12 months**

**G. Short Bowel Syndrome - Adults** (must meet all)
1. Prescribed by or in consultation with a gastroenterologist;
2. Age ≥ 18 years;
3. Diagnosis of short bowel syndrome (SBS);
4. Member’s SBS therapeutic plan requires specialized nutritional support;
5. Prescribed rhGH dose does not exceed 8 mg/day;
6. If prescription 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 intolerance to Norditropin.

**Approval duration: 3 months**

**H. HIV-Related Wasting or Cachexia - Adults** (must meet all)
1. Prescribed by or in consultation with a physician specializing in HIV diagnosis and management;
2. Age ≥ 18 years;
3. Diagnosis of HIV-related wasting or cachexia;
4. Unexplained weight loss of > 10% body weight from baseline;
5. Treatment with therapies other than rhGH have been suboptimal;
6. Alternate causes of wasting or cachexia have been ruled out;
7. Currently receiving antiretroviral therapy;
8. Prescribed rhGH dose does not exceed 6 mg/day;
9. If prescription 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 intolerance to Norditropin.

**Approval duration: 3 months**

I. Conditions Considered Not Medically Necessary
GH therapy is considered not medically necessary for:
1. Idiopathic short stature (ISS);
2. Constitutional growth delay;
3. Obesity;
4. Adult short stature or altered body habitus associated with antiviral therapy;
5. Anabolic therapy to enhance body mass or strength for non-medical reasons (e.g., athletic gains);
6. For other off-label uses not listed.

II. Continued Approval
A. Neonatal Hypoglycemia (must meet all)
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Positive therapeutic response;
   3. Prescribed rhGH dose does not exceed 0.4 mg/kg/week.

   **Approval duration: up to 12 months total**

B. Growth Hormone Deficiency - Children (must meet all)
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Documented adherence and therapeutic response to rhGH therapy;
   3. If treatment for ≥ 1 year (a and b):
      a. Height velocity > 2 cm/year;
      b. Bone age ≤ 15 years if girl or ≤ 17 years if boy;
   4. Prescribed rhGH dose does not exceed:
      a. If pubertal - 0.7 mg/kg/week;
      b. If non-pubertal - 0.4 mg/kg/week.

   **Approval duration: 12 months**

C. Growth Hormone Deficiency - Adults (must meet all)
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Documented adherence to rhGH therapy;
3. Normalization of IGF-1 levels if low prior to rhGH therapy;
4. One of the following:
   a. Decreased body fat;
   b. Increased bone density;
   c. Improved endurance;
   d. Less fatigue.

Approval duration: 12 months

D. Genetic Diseases with Primary Effects on Growth - Children (must meet all)
1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Documented adherence to rhGH therapy;
3. If treatment for ≥ 1 year (a and b):
   a. Height velocity > 2 cm/year;
   b. Bone age ≤ 15 years if girl or ≤ 17 years if boy;
4. Prescribed rhGH dose does not exceed:
   a. PWS - 0.3 mg/kg/week;
   b. Turner syndrome - 0.5 mg/kg/week;
   c. SHOX deficiency - 0.4 mg/kg/week;
   d. Noonan syndrome - 0.5 mg/kg/week.

Approval duration: 12 months

E. Born Small for Gestational Age - Children (must meet all)
1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Documented adherence to rhGH therapy;
3. If treatment for ≥ 1 year (a and b):
   a. Height velocity > 2 cm/year;
   b. Bone age ≤ 15 years if girl or ≤ 17 years if boy;
4. Prescribed rhGH dose does not exceed 0.5 mg/kg/week.

Approval duration: 12 months

F. Chronic Kidney Disease – Children (must meet all)
1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Documented adherence to rhGH therapy;
3. If treatment for ≥ 1 year (a and b):
   a. Height velocity > 2 cm/year;
   b. Bone age ≤ 15 years if girl or ≤ 17 years if boy;
4. Member does not have a functioning renal allograft;
5. Prescribed rhGH dose does not exceed 0.4 mg/kg/week.
Approval duration: 12 months

G. **Short Bowel Syndrome: Adults** (must meet all)
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Documented adherence to rhGH therapy;
   3. Decreased specialized nutritional requirement as measured by total volume, total calories, or infusion frequency;
   4. Prescribed dose does not exceed 8 mg/day.

   **Approval duration: up to 6 months total**

H. **HIV-Related Wasting or Cachexia: Adults** (must meet all)
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Documented adherence to rhGH therapy;
   3. One of the following:
      a. Partial recovery of weight loss documented at baseline;
      b. Improvement in body mass;
      c. Improvement in nutritional status;
   4. Currently receiving antiretroviral therapy;
   5. Prescribed rhGH dose does not exceed 6 mg/day.

   **Approval duration: up to 3 months total**

I. **Other diagnoses/indications**
   1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy.

**Background**

*Description/Mechanism of Action:*
Somatropin is a purified polypeptide hormones of recombinant DNA origin; somatropin contains the identical sequence of amino acids found in human growth hormone; human growth hormone assists growth of linear bone, skeletal muscle, and organs by stimulating chondrocyte proliferation and differentiation, lipolysis, protein synthesis, and hepatic glucose output; stimulates erythropoietin which increases red blood cell mass; exerts both insulin-like and diabetogenic effects; enhances the transmucosal transport of water, electrolytes, and nutrients across the gut.

**Formulations:**
Solution, Subcutaneous:
   - Norditropin FlexPro: 5 mg/1.5 mL (1.5 mL); 10 mg/1.5 mL (1.5 mL); 15 mg/1.5 mL (1.5 mL); 30 mg/3 mL (3 mL) [contains phenol]
   - Nutropin AQ NuSpin 5: 5 mg/2 mL (2 mL) [contains phenol]
   - Nutropin AQ NuSpin 10: 10 mg/2 mL (2 mL) [contains phenol]
   - Nutropin AQ NuSpin 20: 20 mg/2 mL (2 mL) [contains phenol]
Nutropin AQ Pen: 10 mg/2 mL (2 mL)
Nutropin AQ Pen: 20 mg/2 mL (2 mL) [contains phenol]
Omnitrope: 5 mg/1.5 mL (1.5 mL) [contains benzyl alcohol]
Omnitrope: 10 mg/1.5 mL (1.5 mL) [contains phenol]
Solution Reconstituted, Injection (Subcutaneous):
Humatrope: 5 mg (1 ea)
Humatrope: 6 mg (1 ea); 12 mg (1 ea); 24 mg (1 ea) [contains glycerin, metacresol]
Saizen: 5 mg (1 ea); 8.8 mg (1 ea)
Saizen Click.Easy: 8.8 mg (1 ea)
Solution Reconstituted, Subcutaneous:
Humatrope: 5 mg (1 ea); 12 mg (1 ea) [contains metacresol]
Omnitrope: 5.8 mg (1 ea)
Serostim: 4 mg (1 ea); 5 mg (1 ea); 6 mg (1 ea)
Zomacton: 5 mg (1 ea) [contains benzyl alcohol]
Zomacton: 10 mg (1 ea) [contains metacresol]
Zorbtive: 8.8 mg (1 ea) [contains benzyl alcohol]
Solution Reconstituted, Subcutaneous [preservative free]:
Genotropin MiniQuick: 0.2 mg (1 ea); 0.4 mg (1 ea); 0.6 mg (1 ea); 0.8 mg (1 ea); 1 mg (1 ea); 1.2 mg (1 ea); 1.4 mg (1 ea); 1.6 mg (1 ea); 1.8 mg (1 ea); 2 mg (1 ea)

**FDA Approved Indications:**

Somatropin is a recombinant human growth hormone/subcutaneous injectable formulation indicated for treatment of the following conditions in children and adults:

- **Children:**
  - Growth failure due to inadequate endogenous growth hormone secretion
  - Short stature associated with Turner syndrome
  - Prader-Willi syndrome
  - Growth failure associated with chronic renal insufficiency (CRI) up until the time of renal transplantation
  - Growth failure in children born small for gestational age who fail to manifest catch-up growth by 2-4 years of age
  - Idiopathic short stature (non-growth hormone-deficient short stature) defined by height SDS ≤ -2.25 and growth rate not likely to attain normal adult height
  - Short stature or growth failure associated with SHOX deficiency
  - Short stature associated with Noonan syndrome

- **Adults:**
  - Adult GHD who meet both of the following criteria:
    - Biochemical diagnosis of adult GHD by means of a subnormal response to a standard GH stimulation test (peak GH ≤ 5 mcg/L). Confirmatory testing may not be required in patients with congenital/genetic GHD or multiple pituitary hormone deficiencies due to organic diseases.
    - Adult- or childhood-onset GHD:
      - Adult-onset: Patients who have adult GHD whether alone or with multiple hormone deficiencies (hypopituitarism) as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma
      - Childhood-onset: Patients who were GH deficient during childhood, confirmed as an adult before replacement therapy is initiated
  - HIV patients with wasting or cachexia with concomitant antiviral therapy
  - Short-bowel syndrome
Appendices

Appendix A: Abbreviation Key

- Adult onset: AO
- Childhood onset: CO
- CKD: chronic kidney disease
- GFR: glomerular filtration rate
- GH: growth hormone
- GHD: growth hormone deficiency
- HIV: human immunodeficiency virus
- IGF-1: insulin-like growth factor-1
- IGFBP-3: insulin-like growth factor binding protein-3
- ISS: idiopathic short stature
- PWS: Prader-Willi syndrome
- SBS: short bowel syndrome
- SD: standard deviation
- SGA: small for gestational age
- SHOX deficiency: short stature homeobox-containing gene deficiency

Appendix B: Short Stature/Growth Failure Criteria

Short stature/growth failure prior to rhGH therapy is evidenced by one of the following:

1. Height > 3 SD below the mean
2. Height > 2 SD below the mean (and a or b)
   a. Height velocity > 1 SD below the mean over 1 year
   b. Decrease in height SD > 0.5 over 1 year in children > 2 years of age
3. Height > 1.5 SD below midparental height
4. Height velocity > 2 SD below the mean over 1 year
5. Height velocity > 1.5 SD below the mean over 2 years

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.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tr>
<td>J2941</td>
<td>Injection, somatropin, 1mg</td>
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</tbody>
</table>

Reviews, Revisions, and Approvals

Policy created.  
Date: 06/16  
Approval Date: 06/16
References
2. Humatrope Prescribing Information. Indianapolis, IN: Eli Lilly and Company; April 2015.
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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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