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PHARMACY SOLUTIONS

HUMAN GROWTH HORMONE COVERAGE CRITERIA

DRUG CLASS: Somatotropin Agonists – AHFS 68:30.04
BRAND NAME: Genotropin®, Humatrope®, Norditropin®, Nutropin®, Nutropin AQ®, Omnitrope™, Saizen®, Serostim®, Tev-Tropin®, Zorbtive®
GENERIC NAME: somatropin
POLICY #: 4020
CATEGORY: Medicare Part D

FDA INDICATIONS:

Pediatric Patients:

- Treatment of growth failure due to inadequate secretion of endogenous growth hormone secretion. (Genotropin®, Humatrope®, Norditropin®, Nutropin®, Nutropin AQ®, Omnitrope™, Saizen®, Tev-Tropin®)
- Treatment of short stature associated with Turner syndrome. (Genotropin®, Humatrope®, Norditropin®, Nutropin®, Nutropin AQ®)
- Treatment of Prader-Willi syndrome. (Genotropin®)
- Treatment of growth failure associated with chronic renal insufficiency (CRI) up until the time of renal transplantation. (Nutropin®, Nutropin AQ®)
- Treatment of growth failure in children born small for gestational age who fail to manifest catch-up growth by 2 years of age. (Genotropin®, Humatrope®, Norditropin®)
- Treatment of idiopathic short stature (non-growth hormone-deficient short stature) defined by height standard deviation score (SDS) less than or equal to -2.25 and growth rate not likely to attain normal adult height. (Genotropin®, Humatrope®, Nutropin®, Nutropin AQ®)
- Treatment of short stature or growth failure associated with short stature homeobox gene (SHOX) deficiency. (Humatrope®)
- Treatment of short stature associated with Noonan syndrome. (Norditropin®)

Adult Patients:

- HIV patients with wasting or cachexia with concomitant antiviral therapy. (Serostim®)
- Treatment of short-bowel syndrome. (Zorbtive®)
- Replacement of endogenous growth hormone in patients with adult growth hormone deficiency (GHD) who meet both of the following criteria (Genotropin®, Humatrope®, Norditropin®, Nutropin®, Nutropin AQ®, Omnitrope™, Saizen®):

    - Biochemical diagnosis of adult GHD by means of a subnormal response to a standard growth hormone stimulation test (peak growth hormone ≤5 mcg/L). Confirmatory testing may not be required in patients with congenital/genetic growth hormone deficiency or multiple pituitary hormone deficiencies due to organic diseases.

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AND

- 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

OR

- Childhood-onset: Patients who were growth hormone deficient during childhood, confirmed as an adult before replacement therapy is initiated.

ICD-9 CODES:	CODE NAME	CODE NUMBER
	Human immunodeficiency virus	042-043
	Growth hormone deficiency	253.3
	Short bowel syndrome	579.3
	Cachexia	799.4

BENEFIT DESIGN:
Coverage for human growth hormone is determined through a prior authorization process for every claim.

COVERAGE CRITERIA:
Coverage is provided if **one** of the following bullets applies:

- Patient must have a diagnosis of wasting or cachexia associated with HIV.
- Patient must have a diagnosis of short bowel syndrome (Zorbtive only®).
- Patient must have a diagnosis of adult growth hormone deficiency (adult or childhood onset) **and** evidence of a subnormal response to a standard growth hormone stimulation test (peak growth hormone ≤5 mcg/L).

* If prior authorization is approved, coverage may be given for up to 12 months.

BLACK BOX WARNINGS:

- None

RATIONALE:

- To ensure appropriateness of therapy.

DOSAGE AND ADMINISTRATION:
Adults – Growth Hormone Deficiency (GHD)

- Norditropin® – initial dose ≤0.004 mg/kg/day subcutaneous injection. After 6 weeks of therapy, may increase dose up to 0.016 mg/kg/day. Alternatively, a starting dose of approximately 0.2mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1-2 months by increments of approximately 0.1-0.2mg/day.
- Nutropin®, Nutropin AQ® – initial dose ≤0.006 mg/kg/day subcutaneous injection. Dose may be increased up to a maximum of 0.025 mg/kg/day in patients <35 years of age, or up to a maximum of 0.0125 mg/kg/day in

patients ≥35 years of age. Alternatively, a starting dose of approximately 0.2mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1-2 months by increments of approximately 0.1-0.2mg/day.

- Humatrope® – initial dose ≤0.006 mg/kg/day subcutaneous injection. Dose may be increased up to a maximum of 0.0125 mg/kg/day. Alternatively, a starting dose of approximately 0.2mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1-2 months by increments of approximately 0.1-0.2mg/day.
- Genotropin®, Omnitrope™ – initial weekly dosage ≤0.04 mg/kg/week given as a daily subcutaneous injection. Dose may be increased at 4- to 8-week intervals to a maximum of 0.08 mg/kg/week. Alternatively, a starting dose of approximately 0.2mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight. This dose can be increased gradually every 1-2 months by increments of approximately 0.1-0.2mg/day, according to individual patient requirements based on the clinical response and serum IGF-I concentrations.
- Saizen® – initial dose ≤0.005 mg/kg/day subcutaneous injection. Dose may be increased to not more than 0.01 mg/kg/day after 4 weeks. Alternatively, a starting dose of approximately 0.2mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1-2 months by increments of approximately 0.1-0.2mg/day.

Adults – HIV patients with wasting or cachexia

- Serostim® – initial dose 0.1 mg/kg subcutaneous injection once daily at bedtime (maximum 6mg/day). Alternately, patients at risk for side effects may be started at 0.1 mg/kg every other day. Patients who continue to lose weight after 12 weeks should be re-evaluated for opportunistic infections or other clinical events.
  - Daily dose based on body weight:
    <35kg: 0.1mg/kg
    35-45kg: 4mg
    45-55kg: 5mg
    >55kg: 6mg

Adults – Short Bowel Syndrome

- Zorbtive® – initial dose 0.1 mg/kg subcutaneous injection once daily for 4 weeks (maximum 8mg/day)
  - Fluid retention (moderate) or arthralgias: treat symptomatically or reduce dose by 50%
  - Severe toxicity: discontinue therapy for up to 5 days. When symptoms resolve, restart at 50% of dose. If severe toxicity recurs or does not disappear within 5 days after discontinuation, permanently discontinue treatment.

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RISK FACTORS/CONTRAINDICATIONS:

Contraindications:

- Acute critical illness
- Children with Prader-Willi syndrome who are severely obese or have severe respiratory impairment – reports of sudden death.
- Active malignancy
- Active proliferation or severe non-proliferative diabetic retinopathy
- Children with closed epiphyses
- Known hypersensitivity to somatropin or diluent

Warnings/Precautions:

- **Acute Critical Illness** – potential benefit of treatment continuation should be weighed against the potential risk.
- **Prader-Willi Syndrome in Children** – evaluate for signs of upper airway obstruction and sleep apnea before initiation of treatment. Discontinue treatment if these signs occur.
- **Neoplasm** – monitor patients with preexisting tumors for progression or recurrence. Increased risk of a second neoplasm in childhood cancer survivors treated with somatropin – in particular meningiomas in patients treated with radiation to the head for their first neoplasm.
- **Impaired Glucose Tolerance and Diabetes Mellitus** – may be unmasked. Periodically monitor glucose levels in all patients. Doses of concurrent antihyperglycemic drugs in diabetics may require adjustment.
- **Intracranial Hypertension (IH)** – exclude preexisting papilledema. May develop and is usually reversible after discontinuation or dose reduction.
- **Fluid Retention** – may occur frequently. Reduce dose as necessary.
- **Hypothyroidism** – may first become evident or worsen.
- **Slipped Capital Femoral Epiphysis** – may develop. Evaluate children with the onset of a limp or hip/knee pain.
- **Progression of Preexisting Scoliosis** – may develop.

DRUG INTERACTIONS:

Moderate:

- Estrogen – larger doses of somatropin may be needed for women taking oral estrogen replacement products.
- Glucocorticoids – concurrent glucocorticoid therapy may inhibit growth promotion effects.
- Insulin – changes in blood glucose.
- Sulfonylureas – changes in blood glucose.

REFERENCES:

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2. Humatrope [package insert]. Indianapolis, IN: Eli Lilly and Company; 2009.
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4. Nutropin [package insert]. South San Francisco, CA: Genentech, Inc.; 2006.
5. Nutropin AQ [package insert]. South San Francisco, CA: Genentech, Inc.; 2008.
6. Omnitrope [package insert]. Princeton, NJ: Sandoz, Inc.; 2009.
7. Saizen [package insert]. Rockland, MA: Serono, Inc.; 2007.
8. Serostim [package insert]. Rockland, MA: EMD Serono, Inc.; 2007.
9. Tev-Tropin [package insert]. Sellersville, PA: Gate Pharmaceuticals; 2007.
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11. Blue Cross and Blue Shield of Alabama Medical Policy Reference Manual. Growth hormone and insulin-like growth factor-1 (IGF-1) analogues: mecasermin (Increlex) and mecasermin rinfabate (Iplex). Policy # 067. March 2008.
12. Micromedex Healthcare Series Web site. Available at: http://www.thomsonhc.com/hcs/librarian Accessed July 2, 2009.

POLICY HISTORY:

- Original Effective Date: July 2006
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