

Prior Authorization DRUG Guidelines

SOMATOTROPIN/Recombinant human growth hormone

(Genotropin, Humatrope, Norditropin, Nutropin, Omnitrope, Saizen, Serostim, Tev-Tropin, Zorbtive)

Effective Date: 1/28/14

Date Developed: 1/28/14 by Catherine Sanders, MD

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Genotropin, and other recombinant human growth hormones (somatotropins) are purified polypeptide hormones of recombinant DNA origin; somatotropin 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

Pre-Authorization Criteria:

Somatotropin is covered for the following indications: (Note: different formulations may apply to different conditions)

- 1) Children:
 - a) Treatment of growth failure due to inadequate endogenous growth hormone secretion (Genotropin[®], Humatrope[®], Norditropin[®], Nutropin[®], Nutropin AQ[®], Omnitrope[®], Saizen[®], Tev-Tropin[®])
 - b) Treatment of short stature associated with Turner syndrome (Genotropin[®], Humatrope[®], Norditropin[®], Nutropin[®], Nutropin AQ[®], Omnitrope[®])
 - c) Treatment of Prader-Willi syndrome (Genotropin[®], Omnitrope[®])
 - d) Treatment of growth failure associated with chronic renal insufficiency (CRI) up until the time of renal transplantation (Nutropin[®], Nutropin AQ[®])
 - e) Treatment of growth failure in children born small for gestational age who fail to manifest catch-up growth by 2 years of age (Genotropin[®], Omnitrope[®]) or by 2-4 years of age (Humatrope[®], Norditropin[®])
 - f) Treatment of idiopathic short stature (nongrowth hormone-deficient short stature) defined by height standard deviation score (SDS) ≤ -2.25 and growth rate not likely to attain normal adult height (Genotropin[®], Humatrope[®], Nutropin[®], Nutropin AQ[®], Omnitrope[®])
 - g) Treatment of short stature or growth failure associated with short stature homeobox gene (SHOX) deficiency (Humatrope[®])
 - h) Treatment of short stature associated with Noonan syndrome (Norditropin[®])
- 2) Adults:
 - a) HIV patients with wasting or cachexia with concomitant antiviral therapy (Serostim[®])
 - b) Replacement of endogenous growth hormone in patients with adult growth hormone deficiency who meet both of the following criteria (Genotropin[®], Humatrope[®], Norditropin[®], Nutropin[®], Nutropin AQ[®], Omnitrope[®], Saizen[®]):

-Biochemical diagnosis of adult growth hormone deficiency 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.

And

-Adult-onset: Patients who have adult growth hormone deficiency 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

c) Treatment of short-bowel syndrome (Zorbitive[®])

Dosing: Adult:

Growth hormone deficiency: Adjust dose based on individual requirements: To minimize adverse events in older or overweight patients, reduced dosages may be necessary. During therapy, dosage should be decreased if required by the occurrence of side effects or excessive IGF-I levels.

Weight-based dosing:

Norditropin[®]: SubQ: Initial dose ≤ 0.004 mg/kg/day; after 6 weeks of therapy, may increase dose up to 0.016 mg/kg/day

Nutropin[®], Nutropin[®] AQ: SubQ: ≤ 0.006 mg/kg/day; 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

Humatrope[®]: SubQ: ≤ 0.006 mg/kg/day; dose may be increased up to a maximum of 0.0125 mg/kg/day

Genotropin[®], Omnitrope[®]: SubQ: Weekly dosage: ≤ 0.04 mg/kg divided into equal doses 6-7 days per week; dose may be increased at 4- to 8-week intervals to a maximum of 0.08 mg/kg/week

Saizen[®]: SubQ: ≤ 0.005 mg/kg/day; dose may be increased to not more than 0.01 mg/kg/day after 4 weeks

Nonweight-based dosing: SubQ: Initial: 0.2 mg/day (range: 0.15-0.3 mg/day); may increase every 1-2 months by 0.1-0.2 mg/day based on response and/or serum IGF-I levels

Dosage adjustment with estrogen supplementation (growth hormone deficiency): Larger doses of somatotropin may be needed for women taking oral estrogen replacement products; dosing not affected by topical products

HIV-associated adipose redistribution syndrome (HARS) (unlabeled use): *Serostim[®]*: SubQ: Induction: 4 mg once daily at bedtime for 12 weeks; Maintenance: 2 mg or 4 mg every other day at bedtime for 12-24 weeks. Note: Every-other-day dosing during induction has also been studied. Although a greater response was seen with daily dosing, it was associated with an increased incidence of adverse events.

HIV patients with wasting or cachexia:

Serostim[®]: SubQ: 0.1 mg/kg once daily at bedtime (maximum: 6 mg/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; rotate injection sites to avoid lipodystrophy. Adjust dose if needed to manage side effects.

Daily dose based on body weight:

< 35 kg: 0.1 mg/kg

35-45 kg: 4 mg

45-55 kg: 5 mg

> 55 kg: 6 mg

Short-bowel syndrome: *Zorbtive*®: SubQ: 0.1 mg/kg once daily for 4 weeks (maximum: 8 mg/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.

Dosing: Pediatric:

Growth hormone deficiency:

Genotropin®, *Omnitrope*®: SubQ: Weekly dosage: 0.16-0.24 mg/kg divided into equal doses 6-7 days per week

Humatrope®: SubQ: Weekly dosage: 0.18-0.3 mg/kg divided into equal doses 6-7 days per week

Norditropin®: SubQ: 0.024-0.034 mg/kg/day, 6-7 days per week

Nutropin®, *Nutropin*® AQ: SubQ: Weekly dosage: 0.3 mg/kg divided into equal daily doses; pubertal patients: ≤0.7 mg/kg divided into equal daily doses

Tev-Tropin®: SubQ: Up to 0.1 mg/kg/dose administered 3 days per week

Saizen®: I.M., SubQ: Weekly dosage: 0.18 mg/kg divided into equal daily doses or as 0.06 mg/kg/dose administered 3 days per week or as 0.03 mg/kg/dose administered 6 days per week

Note: Therapy should be discontinued when patient has reached satisfactory adult height, when epiphyses have fused, or when the patient ceases to respond. Growth of 5 cm/year or more is expected, if growth rate does not exceed 2.5 cm in a 6-month period, double the dose for the next 6 months; if there is still no satisfactory response, discontinue therapy

Chronic renal insufficiency (CRI): *Nutropin*®, *Nutropin*® AQ: SubQ: Weekly dosage: 0.35 mg/kg divided into daily injections; continue until the time of renal transplantation

Dosage recommendations in patients treated for CRI who require dialysis:

Hemodialysis: Administer dose at night prior to bedtime or at least 3-4 hours after hemodialysis to prevent hematoma formation from heparin

CCPD: Administer dose in the morning following dialysis

CAPD: Administer dose in the evening at the time of overnight exchange

Turner syndrome:

Genotropin®, *Omnitrope*®: SubQ: Weekly dosage: 0.33 mg/kg divided into equal doses 6-7 days per week

Humatrope®: SubQ: Weekly dosage: 0.375 mg/kg divided into equal doses 6-7 days per week

Norditropin®: SubQ: Up to 0.067 mg/kg/day

Nutropin®, *Nutropin*® AQ: SubQ: Weekly dosage: ≤0.375 mg/kg divided into equal doses 3-7 days per week

Prader-Willi syndrome: *Genotropin*®, *Omnitrope*®: SubQ: Weekly dosage: 0.24 mg/kg divided into equal doses 6-7 days per week

Small for gestational age:

Genotropin®, *Omnitrope*®: SubQ: Weekly dosage: 0.48 mg/kg divided into equal doses 6-7 days per week

Humatrope®: SubQ: Weekly dosage: 0.47 mg/kg divided into equal doses 6-7 days per week

Norditropin®: SubQ: Up to 0.067 mg/kg/day

Alternate dosing (small for gestational age): In older/early pubertal children or children with very short stature, consider initiating therapy at higher doses (0.067 mg/kg/day) and then consider reducing the dose (0.033 mg/kg/day) if substantial catch-up growth observed. In younger children (<4 years) with less severe short stature, consider initiating therapy with lower doses (0.033 mg/kg/day) and then titrating the dose upwards as needed.

Idiopathic short stature:

Genotropin®, *Omnitrope*®: SubQ: Weekly dosage: 0.47 mg/kg divided into equal doses 6-7 days per week

Humatrope®: SubQ: Weekly dosage: 0.37 mg/kg divided into equal doses 6-7 days per week
Nutropin®, *Nutropin AQ*®: SubQ: Weekly dosage: Up to 0.3 mg/kg divided into equal daily doses
SHOX deficiency: *Humatrope*®: SubQ: Weekly dosage: 0.35 mg/kg divided into equal doses 6-7 days per week
HIV patients with wasting or cachexia (unlabeled use): *Serostim*®: SubQ: Limited data; doses of 0.04 mg/kg/day were reported in five children, 6-17 years of age; doses of 0.07 mg/kg/day were reported in six children, 8-14 years of age
Noonan syndrome: *Norditropin*®: SubQ: Up to 0.066 mg/kg/day

Dosing: Geriatric:

Patients ≥65 years of age may be more sensitive to the action of growth hormone and more prone to adverse effects; in general, dosing should be cautious, beginning at low end of dosing range.

Dosing: Renal Impairment:

No dosage adjustment provided in manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment:

No dosage adjustment provided in manufacturer's labeling (has not been studied).

Dosage Forms: U.S.:

Excipient information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product

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) [contains phenol]

Norditropin NordiFlex Pen: 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:

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:

Genotropin: 5 mg (1 ea); 12 mg (1 ea) [contains metacresol]

Nutropin: 10 mg (1 ea [DSC]) [contains benzyl alcohol]

Omnitrope: 5.8 mg (1 ea)

Serostim: 4 mg (1 ea); 5 mg (1 ea); 6 mg (1 ea)

Tev-Tropin: 5 mg (1 ea)

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)

Generic Equivalent Available: U.S.-No

Administration:

Do not shake; administer SubQ or I.M. (not all products are approved for I.M. administration). Rotate administration sites to avoid tissue atrophy. When administering to newborns, do not reconstitute with a diluent that contains benzyl alcohol; sterile water for injection may be used as an alternative.

Norditropin® cartridge must be administered using the corresponding color-coded NordiPen® injection pen.

Omnitrope®: Solution in the cartridges must be administered using the Omnitrope® pen; when installing a new cartridge, prime pen prior to first use.

Humatrope®: When administering for growth hormone deficiency, SubQ route is preferred

Tev-Tropin®: SubQ injections of solutions >1 mL not recommended.

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2/18/20	No	Howard Taekman, MD; Robert Sterling, MD	Annual review

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