



Division: Pharmacy Policy	Subject: Prior Authorization Criteria
Original Development Date: Original Effective Date: Revision Date:	June 8, 2012; April 4, 2013; July 8, 2013, February 25, 2015, June 11, 2015, January 21, 2016, February 12, 2016, May 19, 2016, July 5, 2016, March 7, 2017, August 18, 2017, March 6, 2018

GROWTH HORMONE TREATMENT IN CHILDREN and ADULTS

LENGTH OF AUTHORIZATION: UP TO ONE YEAR

REVIEW CRITERIA FOR CHILDREN:

Required for Approval:

- Must have approved diagnosis with supporting documentation (if the preferred product listed below is FDA indicated, trial of the preferred product is required)

Product Name	FDA Indication
Genotropin® (preferred) or Norditropin® (preferred)	Idiopathic Short Stature, Pediatric Growth Hormone deficiency, Prader–Willi Syndrome, Small for Gestational Age, Turner Syndrome,
Humatrope®	Short stature homeobox-containing gene (SHOX)
Norditropin®(preferred)	Short stature due to Noonan Syndrome
Nutropin AQ®	Growth failure due to chronic renal insufficiency (CRI)
Omnitrope®/Zomacton®/Saizen®	Refer to preferred agents

- Must be ≤ 16 years of age
- Must be prescribed by an endocrinologist, pediatric endocrinologist or pediatric nephrologist

Idiopathic Short Stature: ❖ Genotropin®, Norditropin®
<p>Growth velocity: ≥ 2.25 standard deviations (SD) below the mean for age and gender</p> <p>Bone age: Minimum of one year behind chronological age</p> <p>Epiphyses: Confirmation of open growth plates</p> <p>Diagnostic Evaluation:</p> <ul style="list-style-type: none"> • A mixed or normal response >10ng/ml to two Growth Hormone provocation tests (e.g., arginine, clonidine, glucagon, insulin, or levodopa) • Growth velocity must be less than 5cm/year • Other pituitary hormone deficiencies (e.g., hypothyroidism, chronic ischemic disease) have been ruled out.



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Pediatric Growth Hormone Deficiency (GHD):

❖ Genotropin®, Norditropin®

Growth velocity: ≥ 2 standard deviations (SD) below the mean for age and gender (or at less than the 10th percentile)

Present height: Less than the 5th percentile for age and sex, or the mid-parental height

Bone age: Minimum of one year behind chronological age

Epiphyses: Confirmation of open growth plates

Diagnostic Evaluation:

- **Two** subnormal responses to GH provocation tests (e.g., arginine, clonidine, glucagon, insulin and levodopa): Confirmation of stimulation test(s) with peak serum GH concentration less than 10 ng/ml;
or
- One abnormal GH test is sufficient for children with defined CNS pathology, multiple pituitary hormone deficiency (MPHD), history of irradiation, or a genetic defect affecting the GH axis;
or
- **One** subnormal response to a GH provocation test with peak serum GH concentration less than 10ng/ml **and subnormal** serum levels of insulin-like growth factor 1 (IGF-I) **and** insulin-like growth factor binding protein 3 (IGFBP3), greater than 2 standard deviations below the mean for age and gender, based on specific lab reference values.
- ***Idiopathic Short Stature (ISS) has been ruled out (normal birth weight and GH sufficient)***
- Other pituitary hormone deficiencies (e.g., hypothyroidism, chronic ischemic disease) have been ruled out.

Prader-Willi Syndrome:

❖ Genotropin®, Norditropin®

Growth velocity: ≥ 2 standard deviations (SD) below the mean for age and gender

Diagnosis: Confirmed diagnosis of Prader-Willi Syndrome (*micro-deletion in the long arm of chromosome 15 or 2 maternal chromosome 15 and no paternal chromosome 15, or nonfunctional paternal chromosome 15*)

Epiphyses: Confirmation of open growth plates



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Small for Gestational Age (SGA):

❖ Genotropin®, Norditropin®

Age: Greater than 2 years old

Birth weight/length: ≥ 2 standard deviations (SD) below the mean for gestational age

Growth velocity: Failure to manifest catch-up growth by two years of age, defined as 2 standard deviations (SD) below the mean for age and gender

Epiphyses: Confirmation of open growth plates

Turner Syndrome:

❖ Genotropin®, Norditropin®

Age/Gender: Females greater than 2 years old

Growth velocity: ≥ 2 standard deviations (SD) below the mean for age and gender

Bone age: Less than 14 years

Diagnosis: Confirmed diagnosis of Turner Syndrome (*peripheral blood karyotype showing a 45, XO genotype*)

Epiphyses: Confirmation of open growth plates

For short stature in children with SHOX (short stature homeobox-containing gene) deficiency:

❖ Humatrope®

- ✓ **Growth velocity:** ≥ 2 standard deviations (SD) below the mean for age and gender
- ✓ **Bone age:** Minimum of one year behind chronological age
- ✓ **Diagnosis:** Confirmed diagnosis of SHOX Syndrome
- ✓ **Epiphyses:** Confirmation of open growth plates

For short stature in children with Noonan Syndrome:

❖ Norditropin®

- ✓ **Growth velocity:** ≥ 2 standard deviations (SD) below the mean for age and gender
- ✓ **Bone age:** Minimum of one year behind chronological age
- ✓ **Diagnosis:** Confirmed diagnosis of Noonan Syndrome
- ✓ **Epiphyses:** Confirmation of open growth plates



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For growth failure associated with chronic renal failure up to the time of transplantation:

❖ **Nutropin AQ®**

- ✓ **Renal function:** Documentation of chronic renal insufficiency (serum creatinine < 30mg/dl), up to the time of renal transplant
- ✓ **Growth velocity:** ≥ 2 standard deviations (SD) below the mean for age and gender
- ✓ **Bone age:** Minimum of one year behind chronological age
- ✓ **Epiphyses:** Confirmation of open growth plates
- ✓ Prior to initiation of GH treatment, existing metabolic derangements such as malnutrition, zinc deficiency, and secondary hyperparathyroidism should be corrected.

❖ **Discontinuation of growth hormone therapy in children:**

- ✓ Expected final adult height has been reached; or
- ✓ If there is a poor response to treatment, generally defined as an increase in growth velocity of less than 50 % from baseline, in the 1st year of therapy ; or
- ✓ Increase in height velocity is less than 2 cm total growth in 1 year of therapy; or
- ✓ There are persistent and uncorrectable problems with adherence to treatment

❖ **Criteria for continuation of growth hormone therapy in children:**

- ✓ FDA approved diagnosis
- ✓ Prescribed by an endocrinologist, pediatric endocrinologist or pediatric nephrologist
- ✓ Growth velocity ≥ 2.5 cm/year **AND**
- ✓ Bone age is less than 16 years in males; 14 years in females (indicated in x-ray of fingers, hands, or wrists) **AND**
- ✓ Growth (epiphyseal) plates must be open (evidenced by x-ray) – linear growth can no longer occur in patients with epiphyseal closure



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DRUG	DOSAGE	FORMULATION
Genotropin® (somatropin [rDNA origin] for injection), for subcutaneous use	<ul style="list-style-type: none"> • Idiopathic Short Stature: up to 0.47 mg/kg/week • Pediatric GHD: 0.16 to 0.24 mg/kg/week • Prader-Willi Syndrome: 0.24 mg/kg/week • Small for Gestational Age: Up to 0.48 mg/kg/week • Turner Syndrome: 0.33 mg/kg/week 	<p>Genotropin lyophilized powder in a two-chamber color-coded cartridge: 5 mg (green tip) and 12 mg (purple tip) (with preservative)</p> <p>Genotropin Miniquick Growth Hormone Delivery Device containing a two chamber cartridge (without preservative): 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</p>
Humatrope® [somatropin (rDNA ORIGIN)] for injection, for subcutaneous use	SHOX deficiency: 0.35mg/kg/week (given in divided doses 6 to 7 times per week)	5 mg vial and 5-mL vial of diluent 6 mg (gold), 12 mg (teal) and 24 mg (purple) cartridge, and prefilled syringe
Norditropin® Cartridges [somatropin (rDNA origin) injection], for subcutaneous use	<ul style="list-style-type: none"> • Idiopathic Short Stature: Up to 0.47 mg/kg/week • Pediatric GHD: 0.17 mg/kg/week to 0.24 mg/kg/week • Prader-Willi Syndrome: 0.24 mg/kg/week • Noonan Syndrome: Up to 0.46 mg/kg/week • Small for Gestational Age: Up to 0.47 mg/kg/week • Turner Syndrome: Up to 0.47 mg/kg/week 	<p>Norditropin is preloaded in the Norditropin FlexPro or Norditropin NordiFlex pens, or cartridges for use with the corresponding NordiPens:</p> <ul style="list-style-type: none"> • 5 mg/1.5 mL (orange): FlexPro and NordiFlex pens, and cartridges • 10 mg/1.5 mL (blue): FlexPro and NordiFlex pens • 15 mg/1.5 mL (green): FlexPro and NordiFlex pens, and cartridges • 30 mg/3 mL (purple): Norditropin NordiFlex pen only
Nutropin AQ® somatropin (rDNA origin) injection], for subcutaneous use	Chronic Kidney Disease: Up to 0.35 mg/kg/week (divided into daily injections)	<p>Nutropin AQ® is a sterile liquid available in:</p> <ul style="list-style-type: none"> • Pen Cartridge: 10 mg/2 mL (yellow color band), and 20 mg/2 mL (purple color band). • NuSpin: 5 mg/2 mL (clear device), 10 mg/2 mL (green device), and 20 mg/2 mL (blue device).



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GROWTH HORMONE TREATMENT IN ADULTS

Product Name	FDA Indication
Genotropin[®] (preferred) or Norditropin[®] (preferred)	Growth hormone deficiency (GHD)
Omnitrope[®], Nutropin[®], Humatrope[®] Saizen[®], Zomacton[®]	<i>(Refer to preferred agents)</i>

PRADER WILLI

- Growth hormone therapy is not approved in Prader Willi unless the beneficiary meets the growth hormone deficiency criteria for adults.

REVIEW CRITERIA FOR ADULTS:

- Must have approved diagnosis (see chart above for requested medication).
- The prescriber of the requested growth hormone must be an endocrinologist.
- Patients with childhood-onset growth hormone deficiency (COGHD) previously treated with GH replacement in childhood should be retested after final height is achieved and GH therapy discontinued for at least 3 months to ascertain their GH status before considering restarting GH therapy (**at the reduced dose level recommended for growth hormone deficient adults**). (A repeat stimulation test may be required at the beginning of the next age increment in which a variation of IGF-1 occurs).
- For childhood GH treatment of conditions other than GHD, such as Turner's syndrome and idiopathic short stature, there is no proven benefit to continuing GH treatment in adulthood.
- A negative response to a standard growth hormone stimulation test is a maximum peak of < 5 ng/ml, when measured by radioimmunoassay (RIA) (polyclonal antibody) or < 2.5 ng/ml when measured by immunoradiometric assay (monoclonal antibody).



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- The preferred stimulation test agent is the Insulin Tolerance Test (ITT). Alternative provocative tests may be used in patients with contraindication to ITT. Other alternatives include glucagon, and rarely the arginine test alone. The glucagon stimulation test is associated with good performance and great diagnostic accuracy for GHD diagnosis:
 - *If a **single agent test (arginine)** is used there may be a requirement for a second stimulation test depending on the IGF-1. If the IGF-1 is subnormal with the presentation of a hypothalamic disorder(s) then one stimulation test would be required. However, if the IGF-1 is normal with hypothalamic pituitary disorder(s) then two stimulation tests may be required.*
 - ***ITT** is contraindicated in cases with coronary artery disease or seizures, abnormal EKG with history of Ischemic Heart Disease or Cardiovascular Disease, and not advised for those > age 60.*
- Levodopa and Clonidine are not adequate agents for adult testing.
- The practitioner must correct for TSH deficiency prior to completing a stimulation test.
- A Growth Hormone stimulation test is not required when there is documented deficiencies of 3-4 pituitary hormones or documented deficiency of two pituitary hormones and IGF-1 < 84ng/ml. The anterior pituitary hormone deficiencies accepted for this exception to stimulation testing include: FSH and/or LH (subnormal results in both FSH and LH, simultaneously, would count as one deficiency), TSH, ACTH, and arginine vasopressin (AVP).
- Low IGF-1 alone is not an indicator of growth hormone deficiency.
- For diagnosis of short bowel syndrome the prescriber must submit documentation to verify the diagnosis and the use of specialized nutrition support such as a high carbohydrate, low fat diet, enteral feedings, parenteral nutrition, fluid, and micronutrient supplements. Zorbtive[®] therapy is indicated under these conditions.
 - NOTE: Changes to concomitant medications should be avoided during Zorbtive[®] therapy.
 - Subcutaneous dosage (Zorbtive[®] only):
*Adults and the elderly: 0.1 mg/kg SC once daily **for 4 weeks**. Do not exceed a maximum of 8 mg/day. Dosage selection for the elderly should usually start at the lower end of the dosage range. In clinical trials, Zorbtive[®] (plus a specialized oral diet without glutamine) vs. diet alone significantly decreased the total amount of intravenous parenteral nutrition (TPN) by 2.1L/week. The addition of glutamine to the diet/Zorbtive[®] group resulted in a significant decrease in IPN of 3.9 L/week. Other clinical reports have also documented a reduction in TPN usage.*



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DRUG	DOSAGE	FORMULATION
Genotropin® (somatropin [rDNA origin] for injection), for subcutaneous use	<p>Adult GHD: Either a non-weight based or a weight based dosing regimen may be followed, with doses adjusted based on treatment response and IGF-I concentrations :</p> <ul style="list-style-type: none"> • Non-weight based dosing: 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 0.1-0.2 mg/day. • Weight based dosing: The recommended initial dose is not more than 0.04 mg/kg/week; the dose may be increased as tolerated to not more than 0.08 mg/kg/week at 4–8 week intervals. 	<p>Genotropin lyophilized powder in a two-chamber color-coded cartridge: 5 mg (green tip) and 12 mg (purple tip) (with preservative)</p> <p>Genotropin Miniquick Growth Hormone Delivery Device containing a two chamber cartridge (without preservative): 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</p>
Norditropin® [somatropin (rDNA origin) for injection], for subcutaneous injection	<p>Adult GHD: 0.004 mg/kg/day to be increased as tolerated to not more than 0.016 mg/kg/day after approximately 6 weeks, or a starting dose of approximately 0.2 mg/day (range, 0.15 to 0.30 mg/day) increased gradually every 1 to 2 months by increments of approximately 0.1 to 0.2 mg/day (2.2)</p> <ul style="list-style-type: none"> • <input type="checkbox"/> Injection sites should always be rotated to avoid lipatrophy (2.3)mg/kg/day after 4 weeks. 	<p>Norditropin is preloaded in the Norditropin FlexPro or Norditropin NordiFlex pens, or cartridges for use with the corresponding NordiPens:</p> <ul style="list-style-type: none"> • 5 mg/1.5 mL (orange): FlexPro and NordiFlex pens, and cartridges • 10 mg/1.5 mL (blue): FlexPro and NordiFlex pens • 15 mg/1.5 mL (green): FlexPro and NordiFlex pens, and cartridges • 30 mg/3 mL (purple): Norditropin NordiFlex pen only



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