Division: Pharmacy Policy	Subject: State of Florida's Agency for Health Care Administration's 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, July 9, 2020, September 23, 2020, October 15, 2020, September 22, 2021, January 7, 2022

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, Short stature due to Noonan Syndrome (Norditropin only), Small for Gestational Age, Turner Syndrome,
Humatrope®	Short stature homeobox-containing gene (SHOX)
Nutropin AQ®	Growth failure due to chronic renal insufficiency (CRI)
Omnitrope®/Zomacton®/Saizen®/Skytrofa™	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®

Height: ≥ 2.25 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 if age 10 and older
Diagnostic Evaluation:

- 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 5 cm/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: < 5 cm/year **Present height:** ≥ 2 standard deviations (SD) below the mean for age and gender or less than the 5th percentile for age and gender **Bone age:** Minimum of one year behind chronological age **Epiphyses:** Confirmation of open growth plates if age 10 and older **Diagnostic Evaluation (one of the following):** • **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 and the patient has 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) **plus subnormal** serum levels of insulin-like growth factor 1 (IGF-I) ***and/or*** insulin-like growth factor binding protein 3 (IGFBP3) **Exclusionary Conditions**: • ***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®**
Height: ≥ 2 standard deviations (SD) below the mean for age and gender or less than the 5th percentile 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 if age 10 and older

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 if age 10 and older

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Turner Syndrome: ❖ **Genotropin®, Norditropin®**
Age/Gender: Females greater than 2 years old **Height:** ≥ 2 standard deviations (SD) below the mean for age and gender or less than the 5th percentile for age and gender **Growth Velocity:** < 5 cm/year **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 if age 10 and older

For short stature in children with SHOX (short stature homeobox containing gene) deficiency: ❖ **Humatrope®**
Height: ≥ 2 standard deviations (SD) below the mean for age and gender or less than the 5th percentile for age and gender **Growth Velocity:** < 5 cm/year **Bone age:** Less than 14 years **Diagnosis:** Confirmed diagnosis of SHOX Syndrome **Epiphyses:** Confirmation of open growth plates if age 10 and older

For short stature in children with Noonan Syndrome: ❖ **Norditropin®**
Height: ≥ 2 standard deviations (SD) below the mean for age and gender or less than the 5th percentile for age and gender **Growth Velocity:** < 5 cm/year **Bone age:** Minimum of one year behind chronological age **Diagnosis:** Confirmed diagnosis of Noonan Syndrome **Epiphyses:** Confirmation of open growth plates if age 10 and older

For growth failure associated with chronic renal failure up to the time of transplantation: ❖ **Nutropin AQ®**
Renal function: Documentation of chronic renal insufficiency (glomerular filtration rate < 30 mL/min/1.73m^2), up to the time of renal transplant **Height:** ≥ 2 standard deviations (SD) below the mean for age and gender or less than the 5th percentile for age and gender **Growth Velocity:** < 5 cm/year **Bone age:** Minimum of one year behind chronological age **Epiphyses:** Confirmation of open growth plates if age 10 and older Confirmation that existing metabolic derangements such as malnutrition, zinc deficiency, and secondary hyperparathyroidism have been corrected prior to initiation of GH treatment

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❖ 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 ≥ 2.5cm/year **AND** • If age 10 and older confirmation that the bone age is less than 16 years in males; 14 years in females (indicated in x-ray of fingers, hands, or wrists) **AND** • If age 10 or older, confirmation that the growth (epiphyseal) plates must be open (evidenced by x-ray) – linear growth can no longer occur in patients with epiphyseal closure

DOSING AND ADMINISTRATION:

- Refer to product labeling at https://www.accessdata.fda.gov/scripts/cder/daf/

GROWTH HORMONE TREATMENT IN ADULTS

Product Name	FDA Indication
Genotropin® (preferred) or Norditropin® (preferred)	Growth hormone deficiency (GHD)
Omnitrope®, Nutropin®, Humatrope® Saizen®, Sogroya®, Skytrofa™, Zomacton®	*(Refer to preferred agents)*

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 or gastroenterologist (for a diagnosis of short bowel syndrome).

- 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 that 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).
- 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.

DOSING AND ADMINISTRATION:

- Refer to product labeling at https://www.accessdata.fda.gov/scripts/cder/daf/

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