JOHNS HOPKINS HEALTH PLANS	Johns Hopkins Health Plans **Pharmacy Public** **Pharmacy Management Drug Policies**	*Policy Number*	MEDS008
		Effective Date	01/19/2022
		Approval Date	01/19/2022
	Subject **Growth Hormone Products: Somatropin (Genotropin, Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Zomacton, Zorbtive); Lonapegsomatropin (Skytrofa)**	*Supersedes Date*	N/A
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This document applies to the following Participating Organizations:

Priority Partners

Keywords: Genotropin, Growth Hormone, Humatrope, Lonapegsomatropin, Norditropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Skytrofa, Somatropin, Zomacton, Zorbtive

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I. POLICY

A. Growth Hormone Products (somatropin: [Genotropin, Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Zomacton, Zorbtive]; Lonapegsomatropin: [Skytrofa]) will require prior authorization to ensure appropriate use. The process for initiating a prior authorization request can be found in policy PHARM 20. Growth hormone will require prior authorization for outpatient prescription drug benefit coverage to ensure this medication is used only when clinically appropriate.

1. PPMCO members are subject to the Priority Partners formulary, available at www.ppmco.org.
2. USFHP members are subject to prior authorization criteria, step-edits and days-supply limits outlined in the Tricare Policy Manual. Tricare Policy supersedes JHHP Medical/Pharmacy Policies. Tricare limits may be accessed at: http://pec.ha.osd.mil/formulary_search.php?submenuheader=1

II. POLICY CRITERIA

A. **Coverage for Children**:

1. Growth Hormone may be approved for use in children who meet the following criteria:
   a. Documented diagnosis of **Growth Hormone Deficiency (GHD)** with ONE the following:
      I. Diminished growth hormone response (peak growth hormone concentration level less than 10 nanograms/mL) to at least two different stimulation tests.Acceptable tests included: Insulin, Glucagon, Clonidine, Arginine, and L-dopa
      II. Low IGF-1 (insulin-like growth factor) for age, sex, and pubertal status in children 6 years of age or older in the absence of chronic disease (such as, malnutrition, hepatic disease, renal insufficiency, diabetes, and hypothyroidism) in combination with height velocity (HV) less than 25th percentile in 6-12 months prior to GH therapy, AND at least 2 of the following:
         i. Growth velocity less than 7 cm/year before 3 year of age, or less than 4-5 cm/year if between 3 years of age and puberty onset. (Severe short stature is defined as a height more than 2 standard deviations (SD) below the population mean.)

ii. Delayed bone age greater than 2 S.D. below mean for chronological age, generally greater than 2 years delayed in patients with radiographic evidence of epiphyses not closed.

iii. Documentation of a known risk factor for GHD, such as:

A. Craniofacial anomalies

B. Central nervous system structural abnormalities

C. Congenital hypopituitarism

D. Panhypopituitarism, or syndromes associated with hypopituitarism

E. History of hypophysectomy (surgical removal of pituitary gland)

F. History of central nervous system irradiation, including brain radiation

b. Documented diagnosis of **Turner Syndrome** with confirmation by karyotyping

c. Documented diagnosis of **Short Stature with renal insufficiency(CKD)** with the following:

I. Height less than 3rd percentile for chronological age with renal insufficiency defined as serum creatinine of greater than 3.0 mg/dl or a creatinine clearance between 5 and 75/ml/min per 1.73m2 before renal transplant. (Not approvable for post-transplant usage)

d. Documented diagnosis of **Prader-Willi Syndrome** with short stature or growth failure without severe respiratory impairment or severe obesity

e. Documented diagnosis of **Noonan Syndrome** with short stature with the following:

I. Height greater than 2 SD below the mean for gender & age

f. Documented diagnosis of **Short Stature homeobox-containing gene (SHOX) deficiency** with supporting chromosome analysis

g. Documented diagnosis of **Intrauterine growth retardation (including those with Russell –Silver syndrome)** or **small for gestational age (SGA)** with all the following:

I. Evaluation by a pediatric endocrinologist

II. Evidence that patient was born SGA. SGA is defined as birth weight of less than 2500 grams at a gestational age of more than 37 weeks or length below the 3rd percentile for gestational age or birth weight and/or length at least 2 SDs below the mean for gestational age and gender

III. Therapy is being initiated between the ages of 2 and 8 years

i. *Consideration for patients greater than 8 years of age will only be given for the following:

A. Child is prepubertal

B. Therapy will be discontinued when growth velocity is less than 5cm/yr, or evidence of epiphyseal fusion is present

B. **Coverage for Adults:**

1. Growth Hormone may be approved for use in adults who meet the following criteria:

a. Documented diagnosis of **GHD** and confirmation with one of the following:

I. An Insulin Tolerance Test(ITT) of less than 5 nanograms/mL*

i. *However, an alternative combination of arginine and GH-releasing hormone (GHRH) is recommended in patients with the following characteristics due to ITT contraindication:

A. 65 years of age and older

B. History of seizure disorders

C. History of ischemic heart disease or cerebrovascular disease

D. Abnormal EKG

II. Documentation of 3 or more pituitary hormone deficiencies

b. Documented diagnosis of **GHD** with the following:

I. Diminished growth hormone response (peak growth hormone concentration level less than 5 nanograms/ mL) to at least two different stimulation tests. Acceptable tests included: Insulin, Glucagon, Clonidine, Arginine, and L-dopa

II. Evidence of clinical symptoms such as:
   i. Increased weight and body fat mass with decreased lean body mass
   ii. Decreased exercise capacity
   iii. Decreased muscle mass and strength
   iv. Reduced cardiac performance
   v. Reduced bone density and increased fracture rate
   vi. Poor sleep, impaired sense of well-being, lack of motivation

III. One of the following characteristics:
   i. Adult onset due to hypothalamic disease, pituitary disease or surgery, or radiation therapy involving the pituitary gland
   ii. History of GHD in childhood
   iii. Sheehan's syndrome (pituitary infarction)
   iv. Autoimmune hypophysitis
   v. Other hypophysitis related inflammatory conditions (sarcoidosis)

2. **Serostim** may be approved for patients meeting the following:
   a. Documented diagnosis of AIDS wasting, or HIV associated failure to thrive
   b. Documentation that the patient is being simultaneously treated with antiretroviral medication
   c. Documentation showing one of the following:
      I. Chronic diarrhea (at least 2 loose stools per day for at least 30 days)
      II. Chronic weakness that cannot be explained by a concurrent illness other than HIV infection
3. **Zorbtive** may be approved for patients meeting the following:
   a. Documented diagnosis of short bowel syndrome
   b. Documentation that the patient is being treated with specialized nutritional support (such as intravenous parenteral nutrition, nutritional supplement, fluid)

III. AUTHORIZATION PERIOD/LIMITATIONS

A. Initial approval of Genotropin, Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Skytrofa, and Zomacton will be for 6 months for both adults and children

B. Continuation of therapy may be approved in 12-month intervals when the following criteria have been met.
   1. For pediatric patients:
      1. Documentation has been submitted showing all of the following:
         1. Patient is younger that 18 years of age
         2. Patient's height is still below the 5th percentile
         3. Patient meets one of the current bone age with documentation showing the following criteria has been met:
            1. For Children:
               a. The child is less than 18 years of age and:
                  i. Growth hormone has not been effective thus far
                  ii. Child's height is still below 5th percentile
                  iii. Current bone age is less than 15 years for males and 14 years for females
            2. For Adults:

a. History of follow-up monitoring for treatment efficacy with IGF-1 testing being completed at least twice a year

3. *Discontinuation of Therapy:
   1. CHILDREN:
      a. GH therapy will be considered not medically necessary if any of the following discontinuation criteria are met:
         i. Increase in height velocity is less than 2cm total growth in one year of therapy
         ii. Expected final adult height has been reached
         iii. If there is a poor response to treatment, generally defined as increase in growth velocity of less than 50% from baseline, in the first year of therapy.
         iv. In children with Prader-Willi syndrome, evaluation of response to therapy should also take into account whether body composition (i.e. ratio of lean to fat mass) has significantly improved
         v. There are persistent and uncorrectable problems with adherence to treatment
   2. ADULTS:
      a. Transition patients are defined as patients who complete GH therapy for childhood onset GH deficiency and are being considered for adult GH replacement therapy. These patients must undergo retesting to determine whether the growth hormone deficiency persists. A stimulation test should be performed prior to reinstitution of growth hormone unless the member has persistent complete hypopituitarism.

C. Approval of Zorbtive will be limited to one month of therapy

IV. EXCLUSIONS

A. The following is a list of uses that are considered experimental at this time. Further peer-reviewed studies need to be performed and growth hormones proven effective.
   1. Growth retardation associated with:
      a. Down's syndrome
      b. Juvenile arthritis
      c. Post-renal transplant
   2. Infertility
   3. Hand-Schuller-Christian Disease
   4. Hyperinsulinism in infants
   5. Kwashiorkor
   6. Osteoporosis
   7. Autonomic neuropathy
   8. Carcinoid syndrome
   9. Chylothorax
   10. Diabetic foot ulcers
   11. Cardiomyopathy
   12. Crohn's Disease
   13. Dwarfism
   14. Gastrointestinal Hemorrhage
   15. Skeletal dysplasia
   16. Chronic Catabolic states

17. Burn injuries
18. Russell-Silver syndrome
19. Obesity
20. Hypophostamic rickets
21. Muscular dystrophy
22. Cystic Fibrosis
23. Spina bifida
24. Constitutional delay of growth and development
25. Corticosteroid induced pituitary ablation
26. Idiopathic short stature (ISS) [This non-GH deficient short stature is considered cosmetic use]

B. The use of physician samples, or manufacturer product discounts, does not guarantee coverage under the provisions of the medical and/or pharmacy benefit. All pertinent criteria must be met in order to be eligible for benefit coverage.

V. RECOMMENDED DOSE

A. Genotropin: Weekly dosage is divided into equal daily subcutaneous injections
   1. Pediatric:
      a. GHD: 0.16 to 0.24 mg/kg body weight/week
      b. Prader-Willi Syndrome: 0.24 mg/kg body weight/week
      c. Turner Syndrome: 0.33 mg/kg body weight/week
      d. ISS: up to 0.47 mg/kg body weight/week
      e. SGA: up to 0.48 mg/kg body weight/week
   2. Adult:
      a. Non-weight based: 0.2 mg/day initially; may be increased in increments of 0.1-0.2 mg/day every 4 to 8 weeks
      b. Weight based: up to 0.04 mg/kg/week initially; may be increased in 4 to 8-week intervals to a maximum of 0.08 mg/kg/week

B. Humatrope: Weekly dosage is divided into equal daily subcutaneous injections
   1. Pediatric:
      a. GHD: 0.18 mg/kg/week to 0.3 mg/kg/week
      b. Turner Syndrome: Up to 0.375 mg/kg/week
      c. ISS: Up to 0.37 mg/kg/week
      d. SHOX Deficiency: 0.35 mg/kg/week
      e. SGA: Up to 0.47 mg/kg/week
   2. Adult:
      a. Non-weight based: 0.2 mg/day initially; may be increased in increments of 0.1-0.2 mg/day every 4 to 8 weeks
      b. Weight based: 0.006 mg/kg daily; dose may be increased to a maximum of 0.0125 mg/kg daily

C. Norditropin: Weekly dosage is divided into equal daily subcutaneous injections
   1. Pediatric:
      a. GHD: 0.17 mg/kg/week to 0.24 mg/kg/week
      b. Prader-Willi Syndrome: 0.24 mg/kg/week
      c. Turner Syndrome: Up to 0.47 mg/kg/week
      d. Noonan Syndrome: Up to 0.46 mg/kg/week
      e. SGA: Up to 0.47 mg/kg/week
      f. ISS: Up to 0.47 mg/kg/week
   2. Adult:

a. Non-weight based: 0.2 mg/day initially; may be increased in increments of 0.1-0.2 mg/day every 4 to 8 weeks
b. Weight based: 0.004 mg/kg daily; dose may be increased to a maximum of 0.016 mg/kg daily

D. Nutropin AQ: Weekly dosage is divided into equal daily subcutaneous injections
1. Pediatric:
a. GHD: Up to 0.3 mg/kg/week; for pubertal patients: Up to 0.7 mg/kg/week
b. Turner Syndrome: Up to 0.375 mg/kg/week
c. ISS: Up to 0.3 mg/kg/week
d. Chronic Kidney Disease: Up to 0.35 mg/kg/week
2. Adult:
a. Non-weight based: 0.2 mg/day initially; may be increased in increments of 0.1-0.2 mg/day every 4 to 8 weeks
b. Weight based: 0.006 mg/kg daily; dose may be increased to a maximum of 0.025 mg/kg/daily in patients# 35 years old or 0.0125 mg/kg/day in patients > 35 years old

E. Omnitrope: Weekly dosage is divided into equal daily subcutaneous injections
1. Pediatric:
a. GHD: 0.16 to 0.24 mg/kg body weight /week
b. Prader-Willi Syndrome: 0.24 mg/kg/week
c. Turner Syndrome: 0.33 mg/kg/week
d. ISS: up to 0.47 mg/kg/week
e. SGA: up to 0.48 mg/kg/week
2. Adult:
a. Non-weight based: 0.2 mg/day initially; may be increased in increments of 0.1-0.2 mg/day every 4 to 8 weeks
b. Weight based: up to 0.04 mg/kg/week initially; may be increased in 4 to 8-week intervals to a maximum of 0.08 mg/kg/week

F. Saizen:
1. Pediatric:
a. GHD: 0.18 mg/kg/week, divided into equal doses given either on 3 alternate days, 6 times per week, or daily
2. Adult:
a. Non-weight based: 0.2 mg/day initially; may be increased in increments of 0.1-0.2 mg/day every 4 to 8 weeks
b. Weight based: up to 0.005 mg/kg daily initially; may be increased to a maximum of 0.01mg/kg/ daily after 4 weeks

G. Serostim: 0.1 mg/kg (up to 6mg) subcutaneously once daily at bedtime (or every other day if patient is at higher risk of adverse effects)

H. Skytrofa: Once-weekly dosing
1. Pediatric:
a. GHD: 0.24 mg/kg/week

I. Zomacton:Weekly dosage is divided into equal doses given subcutaneously 3, 6, or 7 days per week
1. Pediatric:
a. GHD: 0.18 mg/kg/week to 0.3 mg/kg/week
b. Turner syndrome: Up to 0.375 mg/kg/week
c. ISS: Up to 0.37 mg/kg/week
d. SHOX Deficiency: 0.35 mg/kg/week
e. SGA: Up to 0.47 mg/kg/week
2. Adult:
a. Non-weight based: 0.2 mg/day initially; may be increased in increments of 0.1-0.2 mg/day every 4 to 8 weeks

b. Weight based: up to 0.006 mg/kg daily initially; may be increased to a maximum of 0.0125mg/kg daily

J. Zorbtive: 0.1 mg/kg subcutaneously once daily to a maximum daily dose of 8 mg for 4 weeks

VI. REFERENCES

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VII. APPROVALS

Signature on file at JHHP

JOHNS HOPKINS HEALTH PLANS	Johns Hopkins Health Plans **Pharmacy Public** **Pharmacy Management Drug Policies**	*Policy Number*	MEDS008
		Effective Date	01/19/2022
		Approval Date	01/19/2022
	Subject **Growth Hormone Products: Somatropin (Genotropin, Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Zomacton, Zorbtive); Lonapegsomatropin (Skytrofa)**	*Supersedes Date*	N/A
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DATE OF REVISION	SUMMARY OF CHANGE
07/20/2016	Revised GH Criteria, updated layout
03/01/2017	Clarified the brand products covered under the PA criteria
07/27/2017	Updated Exclusion section regarding physician samples
8/31/2017	Updated the Recommended Dose section
07/01/2018	Removed EHP Line of Business
01/20/2021	Revised criteria layout, clarified criteria, updated recommended dosing parameters
05/13/2021	Updated authorization guidance
01/19/2022	Added Skytrofa as an applicable product

Review/Revision Dates: 5/01/06, 01/17/07, 1/13/09, 3/1/14, 7/20/16, 3/1/2017, 7/27/17, 8/31/17, 07/01/2018, 01/20/2021, 05/13/2021, 01/19/2022