Pharmacy Benefit Determination Policy

Policy Subject: Growth Hormone	**Dates:**
Policy Number: SHS PBD 28	**Effective Date:** August 26, 2011
Category: Immunology, Vaccines & Biotech.	**Revision Date:** January 23, 2018
Policy Type: ☐ **Medical** ☒ **Pharmacy**	**Approval Date:** February 27, 2019
Department: Pharmacy	**Next Review Date:** February 2020
Product (check all that apply):	**Clinical Approval By:**
☒ Group HMO/POS	**Medical Directors**
☒ Individual HMO/POS	PHP: Peter Graham, MD
☒ PPO	**Pharmacy and Therapeutics Committee**
☒ ASO	PHP: Peter Graham, MD

Policy Statement:

Physicians Health Plan, PHP Insurance and Service Company and Sparrow PHP, will cover Growth Hormone through the Pharmacy Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines:

Drugs and Applicable Coding:

Clinical Determination Guidelines:

Document the following with chart notes

I. Pediatrics
   A. General: Diagnosis and Severity (both below)
      1. Prescriber: Pediatric endocrinologist
      2. Height/growth:
         a. Less than third percentile for age and gender OR
         b. Greater than 2 standard deviations below norm for age and gender
   B. Specific Disorders
      1. Diagnosis and severity (all below)
         a. Covered diagnoses: Chronic renal failure (without transplant), Turners syndrome OR Prader-Willi syndrome
         b. Bone: Confirmed open epiphyses
         c. Deficiency of $\geq$ 1 additional pituitary hormone
      2. Dosage regimen: See Appendix I
      3. Approval
         a. Initial: 6 months
         b. Re-approval:
            - Growth response: Pre-pubertal $\geq$ 4.5 cm/year or post-pubertal $\geq$ 2.5 cm/year.
            - Prader-Willi Syndrome: Increased lean body fat or decreased fat mass

C. Growth Hormone Deficiency (GHD)
1. Diagnosis and severity (both below)
   a. Bone Age: ≥ 2 years behind chronological age with confirmed open epiphyses
   b. Standard GH stimulation tests: Failed 2 tests with peak GH value of < 10ng/mL
2. Dosage regimen: See Appendix II
3. Approval
   a. Initial: 6 months
   b. Re-approval:
      - 6 months - 1 year (dependent on patient age);
      - Growth response: Pre-pubertal ≥ 4.5 cm/year. or post-pubertal ≥ 2.5 cm/year.

D. Exclusions: Constitutional Delayed Growth, Partial Growth Hormone Deficiency, neurosecretory tumor, Small for Gestational Age, Growth Hormone Dysfunction, steroid-induced growth failure, short stature due to Down's or Noonan's syndrome and Idiopathic Short Stature (ISS)

II. Transitional and Adult Growth Hormone Deficiency (GHD)

A. General (all below)
1. Prescriber: Endocrinologist
2. Transitional Patients (both below)
   a. Bone: Confirmed closed epiphyses (age range 15-18 years) AND
   b. Re-evaluated 1-3 mons after stopping GH with standard GH stimulation test
3. Stimulation test indicating treatment (1 below)

Stimulation Test	Peak GH Results
Insulin tolerance Test (ITT)	≤ 5mcg/L
Glucagon	≤ 3mcg/L
Arginine (ARG)	< 4mcg/L

B. Hypothalamic Disorder or Insult: Non-organic disease (both below)
1. Etiology: Idiopathic GHD, head injury, cranial irradiation or subarachnoid hemorrhage
2. Test/Labs (both below)
   a. Low IGF: <0 SDS AND
   b. GH stimulation test indicating peak GH result less that amount stated in the table above

C. Multiple Hormone Deficiencies: Organic disease
1. Three or more hormone deficiencies (both below)
   a. Low IGF:< 2.5 percentile AND
   b. No stimulation test required
2. Zero to two hormone deficiencies (both below)
   a. Low IGF: <50 percentile AND
   b. GH stimulation test indicating peak GH result less that amount stated in the table above

D. Dosage regimen: See Appendix II

E. Approval
1. Initial: 6 months.
2. Re-approval: 1 year; Increase in total lean body mass, increased IGF-1 levels, or increase in exercise capacity.

C. Medication Specific: Serostim (both below)
   1. Age: ≥ 18 years
   2. Diagnosis: AIDS-related cachexia (both below)
      a. Confirmed wasting syndrome: Unintended weight loss of ≥ 10% of body weight AND
      b. Other therapies: Optimal antiretroviral therapy has been attempted
   3. Approval
      a. Initial approval: 3 months
      b. Re-approval: 6 months; weight stabilization or increase.

D. Exclusions:
   1. All growth hormones: Aging, enhancement of body mass/strength, catabolic illness (not HIV), wound healing, obesity, cystic fibrosis, idiopathic dilated cardiomyopathy
   2. Serostim: Non-HIV Wasting syndromes (eg. chronic diarrhea, malignancy, Kaposi's sarcoma)

Appendix I: Pediatric Growth Hormone Dosage and Formulations (not all inclusive)

DRUG	DOSAGE	FORMULATION
Genotropin® and Omnitrope (somatropin [rDNA origin] for injection), for subcutaneous use	• **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	Genotropin lyophilized powder in a 2-chamber cartridge: 5 mg and 12 mg (with preservative) Genotropin Miniquick Growth Hormone Delivery Device containing a 2-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
Humatrope® [somatropin (rDNA ORIGIN)] for injection, for subcutaneous	***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, 12 mg and 24 mg cartridge, and prefilled syringe
Norditropin® Cartridges [somatropin (rDNA origin) injection], for subcutaneous use	• **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	Norditropin is preloaded in the Norditropin FlexPro or Norditropin NordiFlex pens, or cartridges for use with the corresponding NordiPens: • 5 mg/1.5 mL: FlexPro and NordiFlex pens, and cartridges • 10 mg/1.5 mL: FlexPro and NordiFlex pens • 15 mg/1.5 mL: FlexPro and NordiFlex pens, and cartridges • 30 mg/3 mL: Norditropin
Nutropin AQ® somatropin (rDNA origin) injection], for subcutaneous use	***Chronic Kidney Disease:*** Up to 0.35 mg/kg/week (divided into daily injections)	Nutropin AQ® is a sterile liquid available in: • Pen Cartridge: 10 mg/2 mL and 20 mg/2 mL • NuSpin: 5 mg/2 mL (clear device), 10 mg/2 mL and 20 mg/2 mL.

Appendix II: Adult Growth Hormone Dosing and Formulations (not all inclusive)

DRUG	DOSAGE	FORMULATION
Genotropin® and Omnitrope (somatropin [rDNA origin] for injection), for subcutaneous use	**Adult GHD*:*** Either non- or weight based dosing regimen may be followed, with doses adjusted based on response and IGF-I concentrations: • **Nonweight based dosing**: Initial: 0.2mg/day (range 0.15-0.30 mg/day) Titration: increase gradually every 1-2 months by increments of 0.1-0.2 mg/day. • **Weight based dosing**: Initial: ≤ 0.04 mg/kg/week; Titration: increase as tolerated to ≤0.08 mg/kg/week at 4–8 week intervals.	Genotropin lyophilized powder in a 2-chamber cartridge: 5 mg and 12 mg (with preservative) Genotropin Miniquick Growth Hormone Delivery Device containing a 2-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
Norditropin® [somatropin (rDNA origin) for injection], for subcutaneous injection	**Adult GHD*:*** • **Nonweight based dosing**: Initial: 0.2mg/day (range 0.15-0.30 mg/day) Titration: increase gradually every 1-2 months by increments of 0.1-0.2 mg/day • **Weight based dosing**: Initial 0.004 mg/kg/day Titration: increase gradually as tolerated to ≤0.016 mg/kg/day after 6 weeks Note: Injection sites should always be rotated to avoid lipoatrophy.	Norditropin is preloaded in the Norditropin FlexPro or Norditropin NordiFlex pens, or cartridges for use with the corresponding NordiPens: • 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

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Appendix III Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Growth Hormone Genotropin, Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Tev-Tropin, Zorbtive (somatotrpin)	• CNS: Paresthesia (9.6%), • MS: Arthralgia (17%), limb stiffness (8%), myalgia (24%) • Misc: Edema (11%), limb pain (15%) • Preg. category: B-C	• Labs: thyroid, urine glucose, IGF-1 level, serum PO4, ALT, parathyroid hormone • Neuro: Intracranial hypertension • MSKL: Slipped capital femoral epiphysis & progression of scoliosis • Misc: growth curve, tanner staging	Not needed

References and Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.;Humatrope, Norditropin, Nutropin, Genotropin, Omnitrope, Saizen, Tev-Tropin, Zorbtive, Increlex, Serostim accessed December 2018.
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4. Curr Opin Endocrinol, Diabetes Obes 2012;19:300-305.
5. Diagnosing growth hormone deficiency in adults. International Journal of Endocrinology 2012;1D 972617:7pages.
6. American Association of Clinical Endcrinologists medical guidelines for clinical practice for growth hormone use in growth hormone-deficient adults & transition patients - 2009 update: Executive summary of recommendations. Endocrine Practice 2009;15(6):580-586.
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8. Guidelines for growth hormone and Insulin-Like growth factor-1 treatment in children and adolescents: Growth Hormone deficiency, idiopathic short statute, and primary insulin-like growth factor-1 deficiency. Hormone Research in Paediatrics 2016;86:361-97

Approved By:

2/27/19

Peter Graham, MD – PHP Executive Medical Director — Date

2/27/19

Kurt Batteen - Human Resources — Date