DRUG DETERMINATION POLICY

Title: DDP-05 Growth Hormone

Effective Date: 06/24/2019

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve Benefits. Coverage depends on the specific Benefit plan. Pharmacy Benefit Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Growth hormone (GH) products are specialty drugs indicated for a number of diagnoses and are associated with untoward effects. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses.

3.0 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 two 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 ≥1 additional pituitary hormone.

2. Dosage regimen: see Appendix I.

3. Approval:

a. Initial: six months.

b. Re-approval:

- Growth response: pre-pubertal ≥4.5 cm/year or post-pubertal ≥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 two tests with peak GH value of <10ng/mL

2. Dosage regimen: see Appendix II.

3. Approval

a. Initial: six months.

b. Re-approval:

- Six months to one 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 one to three months after stopping GH with standard GH stimulation test.
3. Stimulation test indicating treatment (one 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: six months.
2. Re-approval: one year; must demonstrate increase in total lean body mass, increased IGF-1 levels, or increase in exercise capacity from baseline.

F. 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: three months.
    b. Re-approval: six months; weight stabilization or increase.

G. 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 (e.g., chronic diarrhea, malignancy; Kaposi's Sarcoma).

4.0 Coding:

COVERED CODES		
Code	**Description**	**Prior Approval**
J2941	Injection, somatropin, 1 mg	Y

5.0 Unique Configuration/Prior Approval/Coverage Details:

None.

6.0 References, Citations & 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.

2. A review of guidelines for use of growth hormone in pediatric and transition patients. Pituitary 2012; 15:301-310.

3. Evaluation and treatment of adult growth hormone deficiency: An endocrine society clinical practice guidelines. J Clin Endocrinol Metab, 2011; 96(6):1587-1609.

4. Curr Opin Endocrinol, Diabetes Obes 2012; 19:300-305.

5. Diagnosing growth hormone deficiency in adults. International Journal of Endocrinology 2012; 1D 972617:7 pages.

6. American Association of Clinical Endocrinologists 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.

7. Growth hormone treatment for growth hormone deficiency and idiopathic short stature: New guidelines shaped by the presence and absence of evidence. Curr Opin Pediatr 2017.29:466-471.

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.

7.0 Appendices:

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 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, 12 mg and 24 mg cartridge, and prefilled syringe

DRUG	DOSAGE	FORMULATION
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 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)	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	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

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

8.0 Revision History:

Original Effective Date: August 26, 2011

Last Approval Date: 06/24/2019

Next Review Date: 06/24/2020

Revision Date	**Reason for Revision**
2/19	Transitioned to new format