DRUG DETERMINATION POLICY

Title: DDP-05 Growth Hormone

Effective Date: 10/25/23

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. Note that Genotropin is the preferred somatropin branded agent.

3.0 Clinical Determination Guidelines:

Document the following with chart notes.

I. General Considerations

A. Appropriate medication use [must meet all listed below]:

1. Diagnosis: meets standard diagnostic criteria that designate signs, symptoms, and test results to support specific diagnosis.

2. Food and Drug Administration (FDA) approval status [must meet one listed below]:

a. FDA approved: product, indication, and/or dosage regimen.

b. Non-FDA approved use: Compendium support (Lexicomp®) for use of a drug for a non-FDA approved indication or dosage regimen.

3. Place in therapy: sequence of therapy supported by national or internationally accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

B. Pharmaceutical sample use: The Plan does not recognize samples as a medication trial or for continuation of therapy.

C. Adherence to requested medication required for re-approval [must meet one listed below]:

1. Medications processed on the medical benefit: consistent utilization (at least 80% of days covered) history documented in claims history or chart notes.

2. Medications processed on the pharmacy benefit: consistent (at least 80% of days covered) fill history electronically or verbally from pharmacy.

II. Pediatric growth failure.

A. General: diagnosis and severity [must meet both listed below]:

1. Prescriber: pediatric endocrinologist.

2. Auxology: height/growth [must meet one listed below]:

a. Height for age curve has deviated downward across two major height percentage curves (e.g., from 25th to 10th)

b. Height velocity.

Age	Height Velocity
2 to 4 years	<5.5 cm/year (<2.2inches/year)
4 to 6 years	<5 cm/year (<2 cm/year)
6 years to puberty	Boys: <4 cm/year (<1.6 inches/year) Girls: <4.5 cm/year (<1.8 inches/year)

B. Specific growth failure disorders.

1. Diagnosis and severity [must meet all listed below]:

a. Covered diagnoses: chronic renal failure without transplant, Turners syndrome or Prader-Willi syndrome.

b. Bone: confirmed open epiphyses.

c. Deficiency of at least one additional pituitary hormone.

2. Dosage regimen: Genotropin (see Appendix I).

3. Approval:

a. Initial: six months.

b. Re-approval [must meet one listed below]:

- Growth response: pre-pubertal at least 4.5cm per year or post-pubertal at least 2.5cm per year.

- Prader-Willi Syndrome: increased lean body fat or decreased fat mass.

C. Growth Hormone Deficiency.

1. Diagnosis and severity [must meet both listed below]:

a. Bone age: at least two years behind chronological age with confirmed open epiphyses.

b. Standard GH stimulation tests: failed two tests with peak GH value of less than 10ng per 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 at least 4.5cm per year or post-pubertal at least 2.5cm per year.

D. Exclusions.

1. Excluded brands: Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Zomacton.

a. Preferred agent contraindicated, inadequate response or had significant adverse effects.

b. Specific brand coverage exception may be made for continuation of therapy.

2. Diagnoses: 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).

III. Transitional and Adult Growth Hormone Deficiency:

A. General [must meet all listed below]:

1. Prescriber: endocrinologist.

2. Transitional patients [must meet both listed below]:

a. Bone: confirmed closed epiphyses (age range 15 to 18 years); AND

b. Re-evaluated one to three months after stopping growth hormone with standard growth hormone stimulation test.

3. Stimulation test indicating treatment [must meet one listed below]:

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

**Arginine stimulation test preferred*

B. Hypothalamic disorder or insult: non-organic disease [must meet both listed below]:

1. Etiology: idiopathic growth hormone deficiency, head injury, cranial irradiation or subarachnoid hemorrhage.

2. Test/Labs [must meet both listed below]:

   a. Low Insulin-like Growth Factors: less than 0 standard deviation score; AND

   b. Growth hormone stimulation test indicating peak growth hormone result below the value stated in the table above.

C. Multiple hormone deficiencies: organic disease.

1. Three or more hormone deficiencies [must meet both listed below]:

   a. Low insulin-like growth factor 1 less than 2.5 percentile

   b. No stimulation test required.

2. None to two hormone deficiencies [must meet both listed below]:

   a. Low insulin-like growth factor 1 below 50 percentile

   b. Growth hormone stimulation test indicating peak growth hormone below the value stated in the table above.

D. Dosage regimen: Genotropin (see Appendix II).

E. Approval.

1. Initial: six months.

2. Re-approval:

   a. Duration: one year.

   b. Outcome: must demonstrate increase in total lean body mass, increased insulin-like growth factor 1 levels or increase in exercise capacity from baseline.

F. Exclusions.

1. Growth hormone products: Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Zomacton.

   a. Preferred agent contraindicated, inadequate response after or had significant adverse effects.

2. Diagnosis.

   a. All growth hormones: aging, enhancement of body mass/strength, catabolic illness (except human immunodeficiency viruses), wound healing, obesity, cystic fibrosis, idiopathic dilated cardiomyopathy.

4.0 Coding: None.

5.0 References, Citations & Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.;Humatrope, Norditropin, Nutropin AQ, Genotropin, Omnitrope, Saizen, Zomactonbtive, I, Serostim, accessed September 2021.
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.
9. Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline*The Journal of Clinical Endocrinology & Metabolism*, Volume 96, Issue 6, 1 June 2011, Pages 1587–1609, https://doi.org/10.1210/jc.2011-0179
10. Hormonal Replacement in Hypopituitarism in Adults: An Endocrine Society Clinical Practice Guideline*The Journal of Clinical Endocrinology & Metabolism*, Volume 101, Issue 11, 1 November 2016, Pages 3888–3921, https://doi.org/10.1210/jc.2016-2118

6.0 Appendices:

See pages 6-8.

7.0 Revision History:

Original Effective Date: August 26, 2011

Next Review Date: 11/01/2024

Revision Date	Reason for Revision
2/19	Transitioned to new format
9/19	Annual review; replaced abbreviations, clarified preferred and excluded products
12/19	Annual review; formatting done, references updated.
8/20	Annual review; no significant content change, replaced abbreviations, formatting, clarification of preferred products
8/21	Annual review; replaced abbreviations; added appropriate use section; deleted Norditropin dosing in text and moved it in table to excluded agents
10/22	Annual review; modified pediatric growth failure diagnosis with growth chart or height velocity changes
8/23	Annual review

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

DRUG	DOSAGE	FORMULATION
Preferred Products		
Genotropin® (somatropin [rDNA origin] for injection), for subcutaneous use	• Idiopathic Short Stature: up to 0.47mg/kg/week • Pediatric GHD*:* 0.16 to 0.24mg/kg/week • Prader-Willi Syndrome*:* 0.24mg/kg/week • Small for Gestational Age*:* up to 0.48mg/kg/week • Turner Syndrome*:* 0.33mg/kg/week	Genotropin lyophilized powder in a 2-chamber cartridge: 5mg and 12mg (with preservative) Genotropin Miniquick Growth Hormone Delivery Device containing a 2-chamber cartridge (without preservative): 0.2mg, 0.4mg, 0.6 mg, 0.8mg, 1.0mg, 1.2 mg, 1.4mg, 1.6mg, 1.8mg, and 2.0mg
Excluded Products		
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)	5mg vial and 5mL vial of diluent 6mg, 12mg and 24g cartridge, and prefilled syringe
Norditropin® Cartridges [somatropin (rDNA origin) injection], for subcutaneous use	• Idiopathic Short Stature: up to 0.47mg/kg/week • Pediatric GHD: 0.17mg/kg/week to 0.24mg/kg/week • Prader-Willi Syndrome: 0.24mg/kg/week • Noonan Syndrome*: u*p to 0.46mg/kg/week • Small for Gestational Age: up to 0.47mg/kg/week • Turner Syndrome: up to 0.47mg/kg/week	Norditropin is preloaded in the Norditropin FlexPro or Norditropin NordiFlex pens, or cartridges for use with the corresponding NordiPens: • 5mg/1.5mL: FlexPro and NordiFlex pens, and cartridges • 10mg/1.5mL: FlexPro and NordiFlex pens • 15mg/1.5mL: FlexPro and NordiFlex pens, and cartridges • 30mg/3mL: Norditropin NordiFlex pen only
Nutropin AQ® somatropin (rDNA origin) injection], for subcutaneous use	Chronic Kidney Disease: up to: • 0.35mg/kg/week (divided into daily injections)	Nutropin AQ® is a sterile liquid available in: • Pen Cartridge: 10mg/2mL and 20mg/2mL • NuSpin: 5mg/2mL (clear device), 10mg/2mL and 20mg/2 mL.

Appendix II: Adult Growth Hormone Dosing and Formulations (Not All Inclusive)

DRUG	DOSAGE	FORMULATION
Genotropin® (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: • Non weight based dosing: initial: 0.2mg/day (range 0.15-0.30mg/day), titration: increase gradually every 1-2 months by increments of 0.1-0.2mg/day. • Weight based dosing: initial: ≤0.04mg/kg/week; titration: increase as tolerated to ≤0.08mg/kg/week at 4–8-week intervals.	Genotropin lyophilized powder in a 2-chamber cartridge: 5mg and 12mg (with preservative) Genotropin Miniquick Growth Hormone Delivery Device containing a 2-chamber cartridge (without preservative): 0.2mg, 0.4mg, 0.6mg, 0.8mg, 1.0mg, 1.2mg, 1.4mg, 1.6mg, 1.8mg, and 2.0mg

Appendix III Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Growth Hormone Genotropin, Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Tev-Tropin, Zorbtive (somatotrpin)	• Central Nervous System (CNS): paresthesia (9.6%), • Musculoskeletal: arthralgia (17%), limb stiffness (8%), myalgia (24%) • Miscellaneous: edema (11%), limb pain (15%) • Pregnancy Category: B-C	• Labs: thyroid, urine glucose, insulin-like growth factor-1 (IGH) level, serum phosphate, ALT, parathyroid hormone • Neurologic: intracranial hypertension • Musculoskeletal: slipped capital femoral epiphysis & progression of scoliosis • Miscellaneous: growth curve, tanner staging	Not needed