Pharmacy Management Drug Policy

SUBJECT: Growth Hormone Policy **POLICY NUMBER: PHARMACY-18** **EFFECTIVE DATE: 08/03** **LAST REVIEW DATE: 05/09/2024**
If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application		
Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☐ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☐ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☐ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Human growth hormone (GH), also known as somatotropin, is synthesized in the somatotrophs of the anterior pituitary gland. Synthetic growth hormone is primarily used as replacement therapy in patients with growth hormone deficiency (GHD). It may also be used in chronic kidney disease, Turner syndrome, Prader-Willi syndrome, as anabolic therapy in patients with the wasting syndrome of AIDS, for patients suffering malnourishment due to short bowel syndrome and for patients suffering from third degree burns.

The synthetic growth hormones addressed in this policy include: Genotropin, Humatrope, Ngenla, Norditropin, Nutropin AQ, Omnitrope, Saizen, Serostim, Skytrofa, Sogroya, Zomacton, and Zorbtive

POLICY:

Coverage of **Ngenla**, **Serostim**, **Skytrofa**, **Sogroya,** and **Zorbtive** is limited to the corresponding Food and Drug Administration (FDA) approved indication. Please see Drug Specific Criteria for additional coverage information.

Based on our assessment and review of peer-reviewed literature, the administration of **Genotropin**, **Humatrope**, **Norditropin**, **Nutropin AQ**, **Omnitrope**, **Saizen**, **Zomacton** has been proven to be effective and therefore, **medically necessary** for the following conditions:

I. CHILDREN - INCLUSION CRITERIA

Only a pediatric endocrinologist should prescribe GH for children. In children with renal insufficiency, GH therapy can be managed by a pediatric nephrologist with expertise in growth hormone therapy.

If the FDA approved indication is:	**Then the criterion for review includes the following for medical necessary consideration:**
Growth Hormone Deficiency (GHD) diagnosis in children	Requires **ONE** of the following criteria: 1. Diminished Growth Hormone Response (level less than 10 ng/ml) to ***2 or more*** of the following provocative tests: *Note – must be *2 different* agents • Levodopa, • Insulin-induced hypoglycemia, • Arginine, • Clonidine, • Glucagon **OR** 2. Pituitary abnormality (secondary to congenital malformation, tumor, or irradiation) **AND** a known deficiency of at least one additional pituitary hormone **OR** 3. Newborn with a congenital pituitary abnormality (ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk) **OR** known deficiency of a pituitary hormone, along with hypoglycemia, at which time a simultaneous serum GH concentration is <5 mcg/L **OR**
	4. Low IGF-1 (insulin-like growth factor) for age, sex, and pubertal status in children aged 6 or greater 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. In the instance of discrepancy between IGF-1& HV (i.e., IGF-1 is normal & HV <25th percentile) growth hormone stimulation testing (#1) will be required. ***AND at least 2 of the following:*** a. Growth velocity less than 7 cm/year before age 3 years, **OR** less than 4-5 cm/year from age 3 years to onset of puberty. Severe short stature is defined as a height more than 2 standard deviations (SD) below the population mean. b. 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.* c. A known risk factor for Growth Hormone Deficiency such as craniofacial anomalies, central nervous system structural abnormalities, congenital hypopituitarism, panhypopituitarism, or syndromes associated with hypopituitarism, or children who have had hypophysectomy (surgical removal of pituitary gland) or history of central nervous system irradiation, including children who undergone brain radiation.

Turner Syndrome	• Treatment of short stature in Turner Syndrome defined as a 45, XO genotype or mosaic 45XO 46 XY. Treatment should be initiated, as soon as patients fall below the 5th percentile of the normal growth curve for girls but not younger than age 2 years old.
Short Stature **WITH** renal insufficiency (CKD)	• Children with 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 1.73m^2 before renal transplant. *Not recommended for post-transplant patients.*
Prader-Willi Syndrome with short stature or growth failure	• Children with Prader-Willi Syndrome with short stature or growth failure. Growth hormone is contraindicated in patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment.
Noonan Syndrome with short stature	• Patient's height must be greater than 2 SD below the mean for gender & age.
Short Stature homeobox- containing gene (SHOX)	• Children with SHOX (short stature homeobox-containing gene) deficiency demonstrated by chromosome analysis and whose epiphyses are not closed.

Intrauterine growth retardation (including those with Russell – Silver syndrome) or small for gestational age (SGA)	• Growth hormone is indicated for short stature associated with SGA in children who did not catch up by 2 years of age. These children do not exhibit GH deficiency.
	All the following criteria must be met:
	1. Patient must be evaluated by a pediatric endocrinologist **AND**
	2. Patient must have been 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. Most children born SGA will show catch up growth by age 2. **AND**
	3. Age - It is recommended that therapy be initiated between the ages of 2 and 8 years. The effect of GH on SGA children is greater when GH is given to those younger than 4 years of age.
	  • Consideration for patients greater than 8 years of age will only be given if the child is prepubertal. Efficacy has not been established in pubertal adolescents born SGA. **AND**
	  • Therapy should be discontinued when growth velocity is less than 5cm/year or evidence of epiphyseal fusion is present.

II. ADULTS - INCLUSION CRITERIA

GH treatment for adults must be requested and coordinated by an endocrinologist. Adults with somatotropin deficiency syndrome require **at least one** of the following criteria (**A or B**):

A. Diagnosis confirmed by chemical documentation:
   1. Insulin Tolerance Test (ITT) less than 5ng/mL. ITT is the test of choice. This test is contraindicated for patients with the following:
      - Age greater than 65 years **OR**
      - History of ischemic heart disease or cerebrovascular disease **OR**
      - Abnormal EKG **OR**
      - Seizure disorders
   2. If ITT is contraindicated then the following tests may be considered - IV arginine in combination with GH-releasing hormone (GHRH) less than 9-10ng/mL
   3. If there is laboratory documented deficiencies of 3 or more pituitary hormones, insulin tolerance and arginine tests are not required.
   4. Serum IGF-I below normal. However, a normal IGF-I does not exclude diagnosis of GHD. This test should be used in conjunction with other diagnostic tests to determine presence of GHD. Levels of IGF-I may be reduced by poor nutrition, severe hepatic disease, poorly controlled diabetes mellitus, and inadequately treated hypothyroidism **OR**

B. GH is considered **medically necessary** for adult patients who meet **both #1 and #2 along with one criterion from #3:**
   1. Biochemical diagnosis of somatropin deficiency syndrome, by means of a negative response to a standard growth hormone stimulation test as noted above maximum peak less than 5ng/mL (regardless of stimulation test or GH assay used, the cutoff point of 5mcg/mL is used for all provocative tests.) **AND**
   2. Exhibit clinical symptoms of somatotropin deficiency syndrome such as
      - Increased weight and body fat mass, decreased lean body mass,
      - Decreased exercise capacity,
      - Decreased muscle mass and strength,
      - Reduced cardiac performance,
      - Reduced bone density and increased fracture rate, and
      - Poor sleep, impaired sense of well-being, lack of motivation.
   3. **AND ONE** of the following:
      a. Adult onset: patients with somatotropin deficiency syndrome and multiple hormone deficiencies (hypopituitarism or panhypopituitarism) as a result of:
         - Pituitary disease **OR**
         - Hypothalamic disease **OR**
         - Pituitary surgery **OR**
         - Radiation therapy directly to or involving the pituitary gland.
      b. Child Onset: patients who were growth hormone deficient during childhood and who have somatropin deficiency confirmed as an adult
      c. Sheehan's syndrome (pituitary infarction)
      d. Autoimmune hypophysitis
      e. Hypophysitis associated with other inflammatory conditions (e.g., Sarcoidosis, etc.).

III. CHILDREN AND ADULT INCLUSION CRITERIA

GH therapy is medically necessary if the patient meets the following:

A. Patients suffering from third degree burns.

IV. DRUG SPECIFIC CRITERIA

A. Skytrofa coverage will require the following:
   1. Must be 1 year of age or older and less than 18 years of age
   2. Must weigh at least 11.5 kg
   3. Must meet criteria above for Growth Hormone Deficiency (GHD) diagnosis in children
      a. All other diagnoses will not be covered as Skytrofa has not been approved for any other indication
   4. Must have had severe, intolerable injection site reactions to daily growth hormone therapy that necessitates weekly dosing
   5. Quantity limit is 4 cartridges per 28 days
      a. Additional quantities will be granted based on FDA-approved dosing

B. Sogroya coverage will require the following
   1. Must be 2.5 years of age or older
   2. Must meet criteria above for Growth Hormone Deficiency (GHD) in children OR adults
      a. All other diagnoses will not be covered as Sogroya has not been approved for any other indications
   3. Must have had severe, intolerable injection site reactions to daily growth hormone therapy that necessitates weekly dosing
   4. Quantity limit is 6 mL per 28 days

C. Ngenla coverage will require the following:
   1. Must be between the age of 3 to 18 years
   2. Must meet criteria above Growth Hormone Deficiency (GHD) in children
      a. All other diagnoses will not be covered as Ngenla has not been approved for any other indications
   3. Must have had severe intolerable injection site reactions to daily growth hormone therapy that necessitates weekly dosing
   4. Quantity Limit is 4 mL per 28 days
      a. Additional quantities will be granted based on FDA-approved dosing

D. Serostim coverage requires the following:
   1. Patients with AIDS wasting or cachexia or children with HIV associated failure to thrive defined as a greater than 10% of baseline weight loss or weight of <90% of ideal body weight **AND**
      a. Chronic diarrhea (at least 2 loose stools per day for at least 30 days) **OR**
      b. Chronic weakness that cannot be explained by a concurrent illness other than HIV infection.
      c. Patients must be simultaneously treated with antiviral agents. Diet must provide at least 100% of estimated caloric requirement. Evaluate weight on a quarterly basis for patients being treated for HIV wasting
      d. **For recertification,** the patient must have gained at least 2 kg of body weight after 12 weeks of therapy (clinical trials averaged 3.2kg)

E. Zorbtive coverage requires the following:
   1. Patients with short bowel syndrome who are receiving specialized nutritional support, defined as, high carbohydrate low-fat diet that is adjusted for individual patient requirements and preferences. Patients with short bowel syndrome who are

experiencing malabsorption, malnutrition, weight loss, or dehydration. Approval will be limited to a 4-week course per year. Special consideration will be given to any request for therapy longer in duration than 4 weeks.

V. PREFERRED DRUG CRITERIA

A. All requests for growth hormone will be required to use Omnitrope except in the following instances:
   1. Serostim will be approved for wasting or cachexia associated with HIV if the corresponding criteria listed in section IV is met
   2. Zorbtive will be approved for the treatment of short bowel syndrome if the corresponding criteria listed in section IV is met
   3. Individuals who have a documented sensitivity to benzyl alcohol (a preservative in Omnitrope 5 Pen and Omnitrope 5.8mg/vial) and to phenol (a preservative in Omnitrope 10 Pen) will be authorized to use Genotropin or Humatrope (which contain a different preservative)

RECERTIFICATIONS

For children with Growth Hormone Deficiency, approval will be for 12 months at a time. There must be documented improvement for patients to continue receiving growth hormone replacement. The following documentation must be submitted for review every 12 months:

- The difference between the patient's current height and their predicted adult height
- The patient's current bone age and chronological age
- The patient's current height percentile on height/weight chart
- Puberty status
- Treatment Plans/Goals

1. In children, GH therapy is typically discontinued when the growth velocity is less than 5 cm per year, **OR** when epiphyseal fusion has occurred, **OR** when the predicted mid-parental height is reached.
2. Radiographic testing to determine if epiphyses are closed at age 14 in girls and at age 16 in boys is required.

POLICY GUIDELINES:

1. Utilization Management are contract dependent and coverage criteria may be dependent on the contract renewal date. Additionally, coverage of drugs listed in this policy are contract dependent. Refer to specific contract/benefit language for exclusions.
2. Benzyl alcohol should not be used in children under the age of 3. Omnitrope 10 should be used in children under the age of 3 as it does not contain benzyl alcohol.
3. In children with chronic renal insufficiency, GH therapy is discontinued at the time of the renal transplant. Continued growth failure after a successful renal transplant may indicate the need for re-initiation of growth hormone therapy.
4. Discontinue if growth rate is <5cm/yr.
5. Discontinue if body mass stores normalized in HIV patients.
6. This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference the Coverage Exception Evaluation Policy for All Lines of Business Formularies policy for review guidelines.
7. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of

the preferred drug(s) will not be required.

- The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
- The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
- The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
- The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
- The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
- The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.

8. Unless otherwise stated above within the individual drug criteria, approval time-period will be for 2 years.
   - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.
9. This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference the Coverage Exception Evaluation Policy for All Lines of Business Formularies policy for review guidelines.

INVESTIGATIONAL DIAGNOSES:

Conditions considered **investigational** due to lack of peer-reviewed literature for which efficacy or safety data is not yet available include, but are not limited to:

- Constitutional delay of growth and development,
- Skeletal dysplasia's,
- Osteogenesis Imperfecta,
- Anabolic therapy provided to counteract an acute or chronic catabolic illness (i.e., surgery outcomes, trauma, critical illnesses), except for AIDS
- Chronic Fatigue Syndrome
- Fibromyalgia
- Battered Wife Syndrome

- Obesity
- Cystic Fibrosis
- Crohn's disease
- Transplantation
- MSA, Multiple System Atrophy
- Delay of puberty in combination with GnRH to enhance linear growth with GH
- Acute Critical Illness
- Pregnancy/Infertility
- Down Syndrome and other syndromes associated with short stature and malignant diathesis
- Proliferative Diabetic Retinopathy
- Pseudotumor Cerebri
- Cardiomyopathy and heart failure
- Weight loss or medical weight loss programs (taken orally or injected)

THE FOLLOWING INDICATIONS ARE CONSIDERED NOT MEDICALLY NECESSARY DUE TO CONTRAINDICATION OR LACK OF PROVEN MEDICAL BENEFIT:

1. Anti-aging therapy
2. Idiopathic short stature and familial short stature will not be covered. Studies have failed to demonstrate a significant impact of height on psychosocial morbidity for pediatric patients who are non-GHD with short- stature (also known as ISS). The American Academy of Pediatrics (AAP) has pointed out that there will always be a population of individuals considered short based on the normal distribution of height, regardless of how the bell-shaped curve may be altered by GH therapy.
3. Anabolic therapy to enhance body mass or strength for professional, recreational, or social reasons.
4. GH is contraindicated in patients with an active malignant condition. If GHD results from an intracranial tumor, absence of tumor growth or tumor recurrence should be documented for 6 to 12 months before initiation of GH treatment.
5. GH is contraindicated for individuals with Prader-Willi syndrome who are severely obese or have severe respiratory impairment.
6. Omnitrope 5 & 5.8mg which contains benzyl alcohol as a preservative is contraindicated in children under the age of 3. Omnitrope 10 contains phenol as a preservative and is safe to use in children of all ages.

RATIONALE:

1. The technology must have final approval from appropriate government regulatory bodies (e.g., the FDA). The FDA has approved the labeled use of human growth hormone for specific indications.
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes. Numerous clinical trials have been published to demonstrate the efficacy and safety of GH for specific conditions (i.e., burn patients). The evidence is insufficient to permit conclusions concerning the effect of GH therapy on health outcomes on geriatric patients, patients with non-GH deficient short stature, and patients with cardiac disease, critically- ill patients, or other conditions where anabolic therapy has been suggested to counteract acute illness.
3. The technology must improve net health outcomes; and
4. The technology must be as beneficial as any established alternatives.
5. Published clinical trials have demonstrated that GH stimulates growth in children, increases body weight, increases lean body mass, decreases fat mass, increases bone density, and stimulates bone turnover when used in adults for specific conditions.
6. The improvement must be attainable outside the investigational settings. GH therapy has been

proven to improve net health outcomes outside the investigational setting in specific instances (i.e., children and adults with GHD, AIDS wasting).

UPDATES:

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05/09/2024	Revised
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12/06/2023	Revised
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08/13	Revised/P&T Approval
04/10	Reviewed
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07/09	Revised

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