I. POLICY

It is the policy of UPMC Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, as defined in CRM.015-Medical Necessity, and approval by the Pharmacy & Therapeutics Committee of the criteria for prior authorization, as described in RX.003-Prior Authorization Process.

The Growth Hormone drugs are subject to the prior authorization process.

II. DEFINITIONS

N/A

III. PURPOSE

The purpose of this policy is to define the Prior Authorization Process for Growth Hormone.

IV. SCOPE

This policy applies to the Pharmacy Services Department.
V. **PROCEDURE**

**Criteria for Growth Hormone**

UPMC Health Plan recognizes the use of growth hormone (GH) as appropriate and consistent with good medical practices, thus eligible for payment when used ONLY for those members who meet the criteria set forth below:

A. **Initial Authorization**

1. **Children and Adolescents with Classic Growth Hormone Deficiency (GHD)**
   GH replacement is considered medically necessary for members with GHD and growth failure who meet all of the following criteria:
   a. Documented failure to respond to 2 GH provocative tests, defined as a serum GH level (peak level) <10ng/mL. Unless contraindicated, one of the tests must be the insulin tolerance test; others include levodopa, arginine, clonidine, propranolol, and glucagon. One abnormal GH test is sufficient in children with a history of irradiation or multiple pituitary hormone deficiency; and
   b. Insulin-like growth factor-I (IGF-I) levels below normal for bone age and sex; and
   c. At least two of the following:
      i. Present height is <5th percentile for age/sex
      ii. Pretreatment growth velocity is <10th percentile for bone age and gender or <4.5cm/yr
      iii. Comparison of skeletal (bone) age by x-ray of left hand and wrist is > 2 standard deviations below the chronological age.
   d. GH therapy in children must be prescribed by a pediatric endocrinologist and must be used with appropriate physician follow-up; and
   e. GH request must include a treatment plan outlining the dose, monitoring parameters such as when the member will be seen for follow-up, methods for determining treatment response and anticipated duration of use.

Authorization is granted for any of the formulary GH products indicated for this medical condition if all of the above criteria are met. Authorization will be granted for up to one (1) year of therapy.

2. **Children with growth retardation due to chronic renal insufficiency (CRI)**
   GH replacement prior to renal transplantation is considered medically necessary for children with CRI and growth retardation who meet all of the following criteria:
   a. Members with documented diagnosis of CRI up to the time of renal transplant; and
   b. At least one of the following:
      i. Present height is <5th percentile for age/sex
      ii. Growth velocity is <10th percentile for bone age and gender or <4.5cm/yr
   c. GH therapy in children must be prescribed by a pediatric endocrinologist or a pediatric nephrologists, and must be used with appropriate physician follow-up
   d. GH request must include a treatment plan outlining the dose, monitoring, and parameters such as when the member will be seen for follow-up, methods for determining treatment response and anticipated duration of use.
Authorization is granted for any of the formulary GH products for this medical condition if all of the above criteria are met. Authorization will be granted for up to one (1) year of therapy.

3. Turner syndrome/Noonan Syndrome
GH replacement is considered medically necessary for female children with Turner’s syndrome or children with Noonan Syndrome who have growth retardation and who meet all of the following criteria:
   a. Documented diagnosis of Turner’s syndrome or Noonan Syndrome; and
   b. At least one of the following:
      i. Present height is <5th percentile for age/sex
      ii. Growth velocity is <10th percentile for bone age and gender or <4.5cm/yr
   c. GH therapy in children must be prescribed by a pediatric endocrinologist and must be used with appropriate physician follow-up; and
   d. GH request must include a treatment plan outlining the dose, monitoring parameters such as when the member will be seen for follow-up, methods for determining treatment response and anticipated duration of use.

Authorization is granted for any of the formulary GH products for this medical condition if all of the above criteria are met. Authorization will be granted for up to one (1) year of therapy.

4. Children with Prader-Willi Syndrome
GH replacement is considered medically necessary for children with Prader-Willi syndrome who meet all of the following criteria:
   a. Documented diagnosis of Prader-Willi Syndrome; and
   b. At least one of the following:
      i. Present height is <5th percentile for age/sex
      ii. Growth velocity is <10th percentile for bone age and gender or <4.5cm/yr
   c. GH therapy in children must be prescribed by a pediatric endocrinologist and must be used with appropriate physician follow-up; and
   d. GH request must include a treatment plan outlining the dose, monitoring parameters such as when the member will be seen for follow-up, methods for determining treatment response and anticipated duration of use.

Authorization is granted for any of the formulary GH products for this medical condition if all of the above criteria are met. Authorization will be granted for up to one (1) year of therapy.

5. Children with extreme short stature
GH replacement will be considered for children with extreme short stature who meet all of the following criteria:
   a. Documentation that includes specific examples of how basic activities of daily life (ADL) are affected; and
   b. Height Standard Deviation Score must be <-2.25 cm/yr; and

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c. Documentation that associated growth rates are unlikely to permit attainment of adult height within the target height range calculated based on parental heights; and

d. Documentation that children with short stature born small for gestational age (SGA) have not shown catch-up growth by age two (2) years; and

e. GH therapy in children must be prescribed by a pediatric endocrinologist and must be used with appropriate physician follow-up; and

f. GH request must include a treatment plan outlining the dose, monitoring parameters such as when the member will be seen for follow-up, methods for determining treatment response and anticipated duration of use.

For these cases, UPMC Health Plan’s Medical Director will consult with a pediatric endocrinologist(s) to determine if authorization will be granted. Refer to CRM.015 - (Medical Necessity). A trial of six (6) months of GH therapy would be authorized to children with extreme short stature fulfilling the above mentioned criteria to determine if the response justifies continuation of treatment.

6. Adult Growth Hormone Deficiency – Childhood Onset
GH replacement will be considered medically necessary for adults with childhood-onset GHD who meet all of the following criteria:

a. Members who were diagnosed with GHD during childhood who have GH deficiency reconfirmed as an adult; GH treatment should be stopped for 2-3 months after completion of linear growth, and then GH levels should be reassessed by stimulation test; and

b. Member has a biochemical diagnosis of GH deficiency determined by a negative response to a standard GH stimulation test defined as a peak GH level of <3ng/ml. The insulin tolerance test (ITT) is required unless contraindicated. Growth Hormone Releasing Hormone (GHRH)-arginine stimulation test results may be submitted for those members with a documented contraindication to ITT; and

c. Member has NOT reached adult peak bone mass (between 25 and 30 years of age). After adult peak bone mass has been reached, then the Adult GHD – Adult Onset criteria should be followed; and

d. GH therapy in adults must be prescribed by an endocrinologist; and

e. GH request must include a treatment plan outlining the dose, monitoring parameters such as when the member will be seen for follow-up, methods for determining treatment response and anticipated duration of use.

Authorization is granted for any of the formulary GH products for this medical condition if all of the above criteria are met. Authorization will be granted for up to one (1) year of therapy.

7. Adult Growth Hormone Deficiency – Adult Onset
GH replacement will be considered medically necessary for adults with childhood-onset GHD who meet all of the following criteria:

a. Members who were diagnosed with GHD during childhood who have GH deficiency reconfirmed as an adult; GH treatment should be stopped for 2-3
months after completion of linear growth, and then GH levels should be reassessed by stimulation test; and

b. Member has a biochemical diagnosis of GH deficiency determined by a negative response to a standard GH stimulation test defined as a peak GH level of <3ng/ml. The ITT is required unless contraindicated. GHRH-arginine stimulation test results may be submitted for those members with a documented contraindication to ITT; and

c. Member has NOT reached adult peak bone mass (between 25 and 30 years of age). After adult peak bone mass has been reached, then the Adult GHD – Adult Onset criteria should be followed; and

d. GH therapy in adults must be prescribed by an endocrinologist; and

e. GH request must include a treatment plan outlining the dose, monitoring parameters such as when the member will be seen for follow-up, methods for determining treatment response and anticipated duration of use; and

f. Member has a biochemical diagnosis of GH deficiency determined by a negative response to a standard growth hormone stimulation test defined as a peak GH level of <3ng/ml. The ITT is required unless contraindicated. GHRH-arginine stimulation test results may be submitted for those members with a documented contraindication to ITT. If GHRH-arginine test results are not available, then the results of two other stimulation tests, including clonidine, L-Dopa, or arginine stimulation, should be submitted; OR

g. If the cause of pituitary disease is known AND if three or more pituitary hormones are deficient (Adrenocorticotropic hormone (ACTH), Thyroid Stimulating Hormone (TSH) and gonadotropins), an Insulin-like Growth Factor (IGF)-1 level of < 84 ng/mL is sufficient to diagnose GH deficiency. Additional GH stimulation tests are not required in these members; OR

h. If the cause of GH deficiency is unknown, evidence of hypothalamic-pituitary disease, defined as documented deficiencies in at least two of the following: TSH, ACTH or gonadotropins, must be provided in addition to the GH levels from the stimulation test; and

i. If the member has a pituitary adenoma, documentation must be submitted that the tumor size has remained stable for a period of one (1) year prior to initiating GH therapy; and

j. No evidence of active malignancy; and

k. The member does not have poorly controlled diabetes or diabetes with unstable proliferative retinopathy, as GH therapy is contraindicated in these members; and

l. GH therapy in adults must be prescribed by an endocrinologist; and

m. GH request must include a treatment plan outlining the dose, monitoring parameters such as when the member will be seen for follow-up, methods for determining treatment response and anticipated duration of use.

Authorization is granted for any of the formulary GH products for this medical condition if all of the above criteria are met. Authorization will be granted for up to one (1) year of therapy.
8. **Adult members with HIV-associated wasting** or cachexia may be considered for GH therapy with Serostim®. Please refer to RX-PA-007 for Serostim® prior authorization criteria.

9. **Adult members with short bowel syndrome may be considered for GH therapy with Zorbtive®.** Please refer to RX-PA-042 for Zorbtive® prior authorization criteria.

**B. Continued Authorization**

- Reauthorization for pediatric indications shall be done at least annually to check for therapy benefit by reviewing a progress report, indicating growth and maturation. GH replacement will not be considered medically necessary if *one of any* of the following discontinuation criteria is met:
  - Growth velocity while on therapy is < 2.5cm/year (indicating non response to therapy); or
  - Expected final adult height has been reached; or
  - Growth plates have fused; or
  - Bone age in females reaches age 14, in males age 16; or
  - Renal transplantation for CRI
- Reauthorization for adult GHD shall be done on an annual basis to monitor for response to therapy, adverse effects, and compliance. GH replacement will not be considered medically necessary if an adult with Childhood Onset GHD has reached adult peak bone mass.

**C. Diagnoses Not Covered**

GH has not been proven to be effective for the following conditions, and thus will not be covered by UPMC Health Plan:

1. Children with:
   a) Constitutionally delayed growth and development (i.e., delayed skeletal maturation with normal growth velocities and rates of bone age advancement, members who are at the lowest 5% of the growth curve at age three)
   b) Steroid-induced growth failure
   c) Kidney transplant recipients
   d) Down syndrome
   e) Fanconi’s syndrome
   f) Bloom syndrome
   g) Chromosomal and genetic disorders

2. Adults with:
   a) Chronic fatigue syndrome
   b) Fibromyalgia
   c) Obesity
   d) Athletic performance enhancer
   e) Anti-aging treatment
   f) Sepsis
   g) Burns
   h) Trauma

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i) Surgery
j) End stage renal disease (ESRD)
k) Wasting associated with:
   i. Cancer
   ii. Organ failure

D. Additional Information
1. UPMC Health Plan will only cover FDA-approved dosing recommendations.
2. New growth hormone products will be reviewed based on FDA approval.
3. This policy applies to commercially available and formulary growth hormone products: Genotropin®, Humatrope®, Norditropin®, Nutropin®, Nutropin AQ®, Nutropin Depot®, Saizen®, and Tev-Tropin®
4. All documentation requested must be provided for review. If requested documentation is not provided, the prior authorization will be denied.
5. If the member has a diagnosis other than those listed in this document, the clinical pharmacist will review the request for appropriate use of GH and may approve the request based on their clinical judgment. The UPMC Health Plan’s Medical Director, and if needed, an endocrinologist may be consulted if necessary.
6. If a member does not meet the above approval criteria, the request will be referred to a UPMC Health Plan Medical Director for review.

E. Bibliography


