Premier Health Plan

POLICY AND PROCEDURE

POLICY TITLE: ***Growth Hormones***
DEPARTMENT: **Clinical Pharmacy Services – Utilization Management**
ORIGINAL DATE: ***November 2001 (as adopted from UPMC Health Plan)***

Last P & T Committee Approval Date: *June 2018*

Product Applicability: *mark all applicable products below:*

COMMERCIAL	[ ] HMO [ ] PPO *Products*: [ ] Small [ ] Indiv. [ ] Large *Exchange*: [ ] Shop [ ] Indiv. [x] All
OTHER	[x] Self-funded/ASO

PURPOSE

The purpose of this policy is to define the prior authorization process for Growth Hormone products.

Growth Hormones are indicated for the following:

- Treatment of children with growth failure due to:
  - Growth hormone deficiency (GHD)
  - Chronic kidney disease (CKD) up until the time of renal transplantation
  - Idiopathic short stature (ISS)
  - Noonan syndrome
  - Prader-Willi syndrome
  - SHOX deficiency
  - Turner syndrome
  - Being born small for gestational age with no catch-up growth by age 2 to 4 years
- Treatment of adults with either adult-onset or childhood-onset GHD

DEFINITIONS

N/A

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POLICY

It is the policy of the 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 formulary Growth Hormone products are subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

Must meet all of the criteria listed under the respective diagnosis:

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:

- Must have documented failure to respond to 2 GH provocative tests, defined as a serum GH level (peak level) <10ng/mL, using the following stimulation tests: insulin, levodopa, arginine, clonidine, and glucagon. One abnormal GH test is sufficient in children with a history of irradiation or multiple pituitary hormone deficiency
- Must have at least TWO of the following:
    - Present height is <3rd percentile or >2 standard deviations (SD) below the mean for gender and age
    - Pretreatment growth velocity is <7 cm per year for children aged <3 years and <4 cm per year for children aged 3 and older OR for a child of any age the growth velocity is <10th percentile for gender and age based on at least 6 months of growth data
    - Comparison of skeletal (bone) age by x-ray of left hand and wrist is >2 standard deviations below the chronological age
- Must have no evidence of active malignancy for the past year
- Must not have active proliferative or severe non-proliferative diabetic retinopathy
- Must be prescribed by a pediatric endocrinologist and must be used with appropriate physician follow-up
- Must include a treatment plan outlining the dose, monitoring parameters such as when the member is seen for follow up, methods for determining treatment response and anticipated duration of use

2. Neonates with Classic Growth Hormone Deficiency (GHD)

GH replacement is considered medically necessary for neonates with GHD who meet *all* of the following criteria:

- Must be 30 days old or less at time of diagnosis
- Must have presence of neonatal hypoglycemia in the absence of a metabolic disorder. Chart documentation indicating that other metabolic disorder have been ruled out as a cause of hypoglycemia through clinical work-up must be submitted.
- Must have a random growth hormone level of <20 ng/mL (µg/L)
- Must have no evidence of active malignancy for the past year
- Must not have active proliferative or severe non-proliferative diabetic retinopathy
- Must be prescribed by a pediatric endocrinologist or a pediatric nephrologist, and must be used with appropriate physician follow-up
- Must include a treatment plan outlining the dose, monitoring, and parameters such as when the member is seen for follow-up, methods for determining treatment response and anticipated duration of use

3. 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:

- Must have documented diagnosis of CRI up to the time of renal transplant; growth hormone is not approved post-transplant
- Must have at least ONE of the following:
    - Present height is <3rd or percentile or >2 standard deviations (SD) below the mean for gender and age
    - Pretreatment growth velocity is <7 cm per year for children aged <3 years and <4 cm per year for children aged 3 and older OR for a child of any age the growth velocity is <10th percentile for gender and age based on at least 6 months of growth data
- Must have no evidence of active malignancy for the past year
- Must not have active proliferative or severe non-proliferative diabetic retinopathy
- Must be prescribed by a pediatric endocrinologist or a pediatric nephrologists, and must be used with appropriate physician follow-up
- Must include a treatment plan outlining the dose, monitoring, and parameters such as when the member is seen for follow-up, methods for determining treatment response and anticipated duration of use

4. 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:

- Must have documented diagnosis of Turner's syndrome or Noonan Syndrome
- Must have at least ONE of the following:
  - Present height is <5th percentile for age/sex
  - Pretreatment growth velocity: is <7 cm per year for children aged <3 years and <4 cm per year for children aged 3 and older OR for a child of any age the growth velocity is <10th percentile for gender and age based on at least 6 months of growth data
- Must have no evidence of active malignancy for the past year
- Must not have active proliferative or severe non-proliferative diabetic retinopathy
- Must be prescribed by a pediatric endocrinologist and must be used with appropriate physician follow-up
- Must include a treatment plan outlining the dose, monitoring parameters such as when the member is seen for follow-up, methods for determining treatment response and anticipated duration of use

5. Children with Prader-Willi Syndrome

GH replacement is considered medically necessary for children with Prader-Willi syndrome who meet *all* of the following criteria:

- Must have documented diagnosis of Prader-Willi Syndrome
- Must have at least ONE of the following:
  - Present height is <3rd or percentile or >2 standard deviations (SD) below the mean for gender and age
  - Pretreatment growth velocity is <7 cm per year for children aged <3 years and <4 cm per year for children aged 3 and older OR for a child of any age the growth velocity is <10th percentile for gender and age based on at least 6 months of growth data
- Must not be severely obese [defined as a body mass index (BMI) ≥97th percentile for age and gender OR a BMI ≥35], have a history of upper airway obstruction, or sleep apnea, or have severe respiratory impairment
- Must have no evidence of active malignancy for the past year
- Must not have active proliferative or severe non-proliferative diabetic retinopathy
- Must be prescribed by a pediatric endocrinologist and must be used with appropriate physician follow-up
- Must include a treatment plan outlining the dose, monitoring parameters such as when the member is seen for follow-up, methods for determining treatment response and anticipated duration of use

6. Children with Short Stature Homeobox-containing Gene (SHOX) deficiency

GH replacement is considered medically necessary for children with short stature homeobox-containing gene deficiency and who meet *all* of the following criteria:

- Must have documented diagnosis of SHOX deficiency
  - Documentation of lab result confirming SHOX mutation is required
- Must have at least ONE of the following:
  - Present height is <3rd or percentile or >2 standard deviations (SD) below the mean for gender and age
  - Pretreatment growth velocity is <7 cm per year for children aged <3 years, and <4 cm per year for children aged 3 and older, OR for a child of any age the growth velocity is <10th percentile for gender and age based on at least 6 months of growth data
- Must have no evidence of active malignancy for the past year
- Must not have active proliferative or severe non-proliferative diabetic retinopathy
- Must be prescribed by a pediatric endocrinologist and must be used with appropriate physician follow-up
- Must include a treatment plan outlining the dose, monitoring parameters such as when the member is seen for follow-up, methods for determining treatment response and anticipated duration of use

7. Children born Small for Gestational Age (SGA)

GH replacement is considered medically necessary for treatment of growth failure in children born small for gestational age (SGA) who meet *all* of the following criteria:

- Must be born SGA, as defined has ONE of the following:
  - Must have a birth weight of less than 2,500 g at a gestational age of more than 37 weeks
  - Must have a birth weight or length below the 3rd percentile or < -2 SD for gestational age
- Must have failed to achieve catch-up growth by ages two to four
  - Must have baseline pre-treatment height SDS < -2.5 SD for age and gender
- Must have no evidence of active malignancy for the past year
- Must not have active proliferative or severe non-proliferative diabetic retinopathy
- Must be prescribed by a pediatric endocrinologist and must be used with appropriate physician follow-up
- Must include a treatment plan outlining the dose, monitoring parameters such as when the member is seen for follow-up, methods for determining treatment response and anticipated duration of use

8. Adult Growth Hormone Deficiency – Childhood Onset

GH replacement is considered medically necessary for adults with childhood-onset GHD who meet *all* of the following criteria:

- Must have been growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes. Chart documentation confirming member's history of growth hormone deficiency is required.
- Must have GH treatment stopped for at least 1 month after completion of linear growth, and then GH levels should be reassessed by stimulation test
- GH reassessment through stimulation testing is **not** required for members with a high likelihood of GHD, as defined as having a serum IGF-I level <84µg/L while not receiving growth hormone therapy **AND** at least ONE of the following:
    - Severe GHD in childhood due to a genetic cause
    - Structural hypothalamic-pituitary disease
    - Central nervous system tumors
    - Deficiencies in at least 3 of the following pituitary hormones: adrenocorticotropin hormone (ACTH), thyroid stimulating hormone (TSH), gonadotropin deficiency (leutinizing hormone [LH] and/or follicle stimulating hormone [FSH] are counted as 1 deficiency), prolactin, or arginine vasopressin (VAP) deficiency
    - Severe GHD and the receipt of high-dose cranial radiation therapy
- For members with only a serum IGF-I level <84µg/L while not receiving growth hormone therapy, biochemical diagnosis of GH deficiency must be demonstrated on reassessment as determined by a negative response to **one** of the following standard GH stimulation tests (see below)
- For members with serum IGF-levels within the given laboratory range while not on growth hormone therapy, biochemical diagnosis of GH deficiency must be demonstrated on reassessment as determined by a negative response to **two** of the following standard GH stimulation tests:
    - The insulin tolerance test (ITT) is required unless contraindicated. Negative response to the ITT is defined as a peak GH level of ≤5.0µg/L. Contraindications to the ITT include patients with known or who are at high risk for coronary artery disease or patients with a history of seizures, and severe panhypopituitarism/hypoadrenalism.
    - If ITT is contraindicated, the glucagon test is required unless contraindicated. Negative response to the glucagon test is defined as a peak GH level of ≤3µg/L. Contraindications to the glucagon test include patients who are malnourished or who have not eaten in 48 hours, patients with pheochromocytoma or insulinoma, and severe hypocortisolemia.

    - If both ITT and glucagon tests are contraindicated, the arginine test is required. Negative response to arginine test is defined as a peak GH level of ≤0.4 µg/L
- Must have no evidence of active malignancy for the past year
- Must not have active proliferative or severe non-proliferative diabetic retinopathy
- Must submit documentation that the tumor size has remained stable for a period of one (1) year prior to initiating GH therapy if the member has a pituitary adenoma
- Must be prescribed by an endocrinologist
- Must include a treatment plan outlining the dose, monitoring parameters such as when the member is seen for follow-up, methods for determining treatment response and anticipated duration of use

9. Adult Growth Hormone Deficiency – Adult Onset

GH replacement is considered medically necessary for adults with adult-onset GHD who meet *all* of the following criteria:

- Must have a diagnosis of growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma
- For members with panhypopituitarism, growth hormone stimulation testing is **not** necessary to verify the diagnosis if member has **both**:
    - Deficiencies in at least 3 of the following pituitary hormones: adrenocorticotropin hormone (ACTH), thyroid stimulating hormone (TSH), gonadotropin deficiency (luteinizing hormone [LH] and/or follicle stimulating hormone [FSH] are counted as 1 deficiency), prolactin, or arginine vasopressin (VAP) deficiency
    - Serum IGF-I level <84 µg/L while not receiving growth hormone therapy
- For members without panhypopituitarism with low IGF levels, biochemical diagnosis of GH deficiency must be determined by a negative response to **two** of the following growth hormone stimulation tests:
    - The ITT is required unless contraindicated. Negative response to the ITT is defined as a peak GH level of ≤5.0µg/L.
    - If ITT is contraindicated, the glucagon test is required unless contraindicated. Negative response to the glucagon test is defined as a peak GH level of ≤3µg/L
    - If both ITT and glucagon tests are contraindicated, the arginine test is required. Negative response to arginine test is defined as a peak GH level of ≤0.4µg/L
    - If all other stimulation tests are contraindicated AND the member has a BMI of less than or equal to 40 kg/m^2, the macimorelin stimulation test (via

MacrilenTM) is required. Negative response to macimorelin stimulation test is defined as a peak GH level of < 2.8 ng/mL
    - For members with a deficiency in at least 1 other pituitary hormone AND a serum IGF-I level <84µg/L, only **one** growth hormone stimulation test is required
- Must submit documentation that the tumor size has remained stable for a period of one (1) year prior to initiating GH therapy if the member has a pituitary adenoma
- Must have no evidence of active malignancy for the past year
- Must not have active proliferative or severe non-proliferative diabetic retinopathy
- Must be prescribed by an endocrinologist
- Must include a treatment plan outlining the dose, monitoring parameters such as when the member is seen for follow-up, methods for determining treatment response and anticipated duration of use

Reauthorization Criteria:

1. Pediatric Indications

Prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals based upon chart documentation from the prescriber that the member's condition has improved based upon the prescriber's assessment while on therapy. GH replacement for pediatric indications is **not** considered medically necessary if any of the following discontinuation criteria are met:

- Growth velocity while on therapy is <2.5cm/year (indicating non response to therapy)
- Expected final adult height has been reached
- Growth plates have fused
- Bone age in females reaches age 14, in males age 16
- Renal transplantation for CRI

2. Adult Indications

Prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorizations may be extended at 1-year intervals based upon:

- Chart documentation demonstrating that the member continues to benefit from growth hormone therapy. Specific examples of benefit must be included (e.g. normalization of IGF-1 levels, improvements in cardiovascular risk markers, bone

mineral density, body composition, physical exercise tolerance, quality of life, etc.)

- Evaluation of whether or not there have been any major changes in clinical status affecting the medical necessity of GH supplementation
- Verification that the member continues to be compliant with GH therapy and recommended follow-up with provider

Diagnoses Not Covered

GH has not been proven to be effective for the following conditions, and thus is not covered for:

1. Children with:

- Idiopathic short stature
- 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)
- Steroid-induced growth failure
- Kidney transplant recipients
- Down syndrome
- Fanconi's syndrome
- Bloom syndrome

2. Adults with:

- Chronic fatigue syndrome
- Fibromyalgia
- Obesity
- Athletic performance enhancer
- Anti-aging treatment
- Sepsis
- Burns
- Trauma
- Surgery
- End stage renal disease (ESRD)
- Wasting associated with:
    - Cancer
    - Organ failure

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	Up to 1 year
Reauthorization	Same as initial

If the established criteria are not met, the request is referred to a Medical Director for review.

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RECORD RETENTION

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Annual Review	*02/16, 02/17, 02/18*
Criteria Update	*06/18*