Effective Date: 6/2016
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SPECIALTY GUIDELINE MANAGEMENT

NUTROPIN AQ (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Pediatric patients with growth failure due to any of the following:
      a. Growth hormone (GH) deficiency
      b. Turner syndrome
      c. Chronic kidney disease (CKD)
      d. Idiopathic short stature (ISS)
   2. Adults with childhood-onset or adult-onset GH deficiency

B. Compendial Uses
   1. Human immunodeficiency virus (HIV)-associated wasting/cachexia

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review for both initial and continuation of therapy requests (where applicable):

A. Medical records supporting the diagnosis of neonatal GH deficiency
B. Pretreatment growth hormone provocative test result(s) (laboratory report or medical record documentation)
C. Pretreatment and/or current IGF-1 level (laboratory report or medical record documentation)*
D. Diagnostic karyotype results in Turner syndrome
E. The following information must be provided for all continuation of therapy requests if not previously approved by Neighborhood Health Plan of Rhode Island:
   1. Total duration of treatment (approximate duration is acceptable)
   2. Date of last dose administered
   3. Approving health plan/pharmacy benefit manager

* IGF-1 levels vary based on the laboratory performing the analysis. Laboratory-specific values must be provided to determine whether the value is within the normal range.

III. PRESCRIBER SPECIALTIES

For all diagnoses excluding HIV-associated wasting/cachexia, therapy must be prescribed by or in consultation with any of the following specialists:

A. Endocrinologist
B. Pediatric endocrinologist
C. Geneticist
D. Pediatric nephrologist (CKD only)

IV. INITIAL CRITERIA FOR APPROVAL

A. Pediatric GH Deficiency

Authorization of 12 months may be granted to members with pediatric GH deficiency when EITHER criteria 1. or 2. below is met:

1. Member is a neonate or was diagnosed with GH deficiency as a neonate. Medical records must be available to support the diagnosis of neonatal GH deficiency (e.g., hypoglycemia with random GH level, evidence of multiple pituitary hormone deficiency, chart notes, or magnetic resonance imaging [MRI] results).
2. Member meets ALL of the following:
    a. Member has EITHER:
        i. Two pretreatment pharmacologic provocative GH tests with both results demonstrating a peak GH level < 10 ng/mL, OR
        ii. A documented pituitary or CNS disorder (refer to Appendix A) and a pretreatment IGF-1 level > 2 standard deviations (SD) below the mean
    b. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below the mean and growth velocity is slow
    c. For members ≥ 2.5 years of age at initiation of treatment:
        i. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
        ii. Pretreatment 1-year height velocity is > 2 SD below the mean
    d. Epiphyses are open

B. Idiopathic Short Stature

Authorization of 12 months may be granted to members with ISS when ALL of the following criteria are met:

1. Pretreatment height is > 2.25 SD below the mean
2. Predicted adult height is < 5'3" for boys and < 4'11" for girls
3. Pediatric GH deficiency has been ruled out with a provocative GH test (peak GH level ≥ 10 ng/mL)
4. Epiphyses are open

C. Turner Syndrome

Authorization of 12 months may be granted to members with Turner syndrome when ALL of the following criteria are met:

1. Diagnosis was confirmed by karyotyping
2. Patient's pretreatment height is less than the 5th percentile for age
3. Epiphyses are open

D. Growth Failure Associated with Chronic Kidney Disease

Authorization of 12 months may be granted to members with CKD when ALL of the following criteria are met:

1. For members < 2.5 years of age at initiation of treatment, the pretreatment height is > 2 SD below the mean and growth velocity is slow
2. For members ≥ 2.5 years of age at initiation of treatment:
   a. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
   b. Pretreatment 1-year height velocity is > 2 SD below the mean
3. Epiphyses are open

E. Adult GH Deficiency

Authorization of 12 months may be granted to members with adult GH deficiency when ANY of the following criteria is met:

1. Member has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated GH levels < 5 ng/mL, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD
2. Member has had 1 pretreatment pharmacologic provocative GH test that demonstrated a GH level < 5 ng/mL AND has a pretreatment IGF-1 level that is low for age and gender, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD
3. Member has a structural abnormality of the hypothalamus or pituitary (refer to Appendix A) and ≥ 3 documented pituitary hormone deficiencies (refer to Appendix B)
4. Member has childhood-onset GH deficiency and a congenital abnormality of the hypothalamus or pituitary (refer to Appendix A)

F. HIV-Associated Wasting/Cachexia

Authorization of 12 weeks may be granted to members with HIV-associated wasting or cachexia when ALL of the following criteria are met:

1. Member has tried and had a suboptimal response to alternative therapies (e.g., cyproheptadine, dronabinol, megestrol acetate or testosterone if hypogonadal) unless the member has a contraindication or intolerance to alternative therapies
2. Member is currently on antiretroviral therapy
3. Pretreatment BMI is < 18.5 kg/m^2 (see Appendix C)

V. CONTINUATION OF THERAPY

A. Pediatric GH Deficiency, Turner Syndrome, CKD, ISS

Authorization of 12 months may be granted for continuation of therapy when ALL of the following criteria are met:

1. Epiphyses are open (confirmed by X-ray or X-ray is not available)
2. Member's growth rate is > 2 cm/year unless there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty)

B. Adult GH Deficiency

Authorization of 12 months may be granted for continuation of therapy when all criteria for initial authorization are met (refer to Section IV.E. above).

C. HIV-Associated Wasting/Cachexia

Authorization of 12 weeks may be granted for continuation of therapy when ALL of the following criteria are met:

1. Member is currently on antiretroviral therapy.
2. Current BMI is < 27 kg/m^2 (see Appendix C).

VI. APPENDICES

A. Appendix A: Examples of Hypothalamic/Pituitary/CNS Disorders

1. Congenital genetic abnormalities
   a. Known mutations in growth-hormone-releasing hormone (GHRH) receptor, GH gene, GH receptor, or pituitary transcription factors
2. Congenital structural abnormalities
   a. Optic nerve hypoplasia/septo-optic dysplasia
   b. Agenesis of corpus callosum
   c. Empty sella syndrome
   d. Ectopic posterior pituitary
   e. Pituitary aplasia/hypoplasia
   f. Pituitary stalk defect
   g. Anencephaly or prosencephaly
   h. Other mid-line defects
   i. Vascular malformations
3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
   a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma, pituitary adenoma)
   b. Cysts (Rathke cleft cyst or arachnoid cleft cyst)
   c. Surgery
   d. Radiation
   e. Chemotherapy
   f. CNS infections
   g. CNS infarction (e.g., Sheehan's syndrome)
   h. Inflammatory lesions (e.g., autoimmune hypophysitis)
   i. Infiltrative lesions (e.g., sarcoidosis, histiocytosis)
   j. Head trauma/traumatic brain injury
   k. Aneurysmal subarachnoid hemorrhage

B. Appendix B: Pituitary Hormones (Other than Growth Hormone)

1. Adrenocorticotropic hormone (ACTH)
2. Antidiuretic hormone (ADH)
3. Follicle stimulating hormone (FSH)
4. Luteinizing hormone (LH)
5. Thyroid stimulating hormone (TSH)
6. Prolactin

C. Appendix C: Calculation of BMI

$$\text{BMI} = \frac{\text{Weight (pounds)} \times 703}{[\text{Height (inches)}]^2} \quad \text{OR} \quad \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}$$

BMI classification:	Underweight	< 18.5 kg/m^2
	Normal weight	18.5 – 24.9 kg/m^2
	Overweight	25 – 29.9 kg/m^2
	Obesity (class 1)	30 – 34.9 kg/m^2
	Obesity (class 2)	35 – 39.9 kg/m^2
	Extreme obesity	≥ 40 kg/m^2