PRIOR AUTHORIZATION POLICY

POLICY: Growth Disorders – Skytrofa Prior Authorization Policy
- Skytrofa™ (lonapegsomatropin subcutaneous injection – Ascendis Pharma)

REVIEW DATE: 10/12/2022

OVERVIEW

Skytrofa, a weekly human growth hormone product, is indicated for the treatment of pediatric patients ≥ 1 year of age who weigh at least 11.5 kg and have **growth failure due to an inadequate secretion of endogenous growth hormone**.[1]

Disease Overview

Lonapegsomatropin is a prodrug of somatropin.[1] In children with growth hormone deficiency (GHD), somatropin is effective for increasing final adult height.[2] Somatropin therapy is recommended to normalize adult height and avoid extreme shortness in children and adolescents with GHD.[2] In addition to congenital causes, hypopituitarism may also be caused by radiation therapy; somatropin may be used to improve final height of children who have undergone radiation.[3,4]

Guidelines

Skytrofa is not yet addressed in published guidelines. Guidelines for growth hormone and insulin-like growth factor (IGF)-1 treatment in children and adolescents (2016) recommend the use of growth hormone to normalize adult height and avoid extreme shortness in pediatric patients with GHD.[2] These guidelines do not recommend one growth hormone product over another.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Skytrofa. All reviews will be directed to a clinician (i.e., pharmacist) for verification of criteria. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Skytrofa as well as monitoring required for adverse events and long-term efficacy, initial approval requires a Skytrofa patient to be evaluated by a physician who specializes in the condition being treated. Human growth hormone is FDA-approved for treatment of a limited number of conditions. The FDA has not approved the use of human growth hormone as therapy for anti-aging, longevity, cosmetic or performance enhancement. Federal law prohibits the dispensing of human growth hormone for non-approved purposes. A pharmacy's failure to comply with that law could result in significant criminal penalties to the pharmacy and its employees. Accordingly, a pharmacy may decline to dispense prescriptions for human growth hormone when written by a physician or other authorized prescribers who they believe may be involved in or affiliated with the fields of anti-aging, longevity, rejuvenation, cosmetic, performance enhancement, or sports medicine.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Skytrofa is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Growth Hormone Deficiency in a Pediatric Patient (≥ 1 year of age to < 18 years of age).** Approve for 1 year if the patient meets the following (A or B):
   - **A)** Initial Therapy with any Growth Hormone Agent. Approve if the patient meets one of the following (i, ii, iii, iv, or v):
     - **i.** Patient meets both of the following (a and b):
       - **a)** Patient meets one of the following (1 or 2):
         - **(1)** Patient has had two growth hormone stimulation tests performed with any of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND both tests show an inadequate response as defined by a peak growth hormone response which is below the normal reference range as determined by the testing laboratory; OR
         - **(2)** Patient meets BOTH of the following criteria (a and b):
           - **(a)** Patient has had at least one growth hormone stimulation test performed with any of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND the test shows an inadequate response as defined by a peak growth hormone response which is below the normal reference range as determined by the testing laboratory; AND
           - **(b)** Patient has at least one risk factor for growth hormone deficiency (for example, the height for age curve has deviated downward across two major height percentiles [e.g., from above the 25th percentile to below the 10th percentile]; the child's growth rate is less than the expected normal growth rate based on age and gender; low insulin-like growth factor (IGF)-1 and/or IGFBP-3 levels; the child has a very low peak growth hormone level on provocative testing as defined by the prescribing physician; the child's growth velocity is less than the 10th percentile for age and gender [height velocity percentile is NOT the same as height-for-age percentile]; the patient is status post craniopharyngioma resection; the patient has optic nerve hypoplasia; the patient has a growth hormone gene deletion); AND
       - **b)** Patient has been evaluated by an endocrinologist.
     - **ii.** Patient has undergone brain radiation or tumor resection AND meets both of the following (a and b):
       - **a)** Patient meets at least one of the following (1 or 2):
         - **(1)** Patient has had one growth hormone stimulation test with any of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND the test shows an inadequate response as defined by a peak growth hormone response which is below the normal reference range as determined by the testing laboratory; OR
         - **(2)** Patient has a deficiency in at least one other pituitary hormone (i.e., adrenocorticotropic hormone, thyroid-stimulating hormone, gonadotropin [luteinizing hormone and/or follicle stimulating hormone deficiency are counted as one deficiency], or prolactin); AND
       - **b)** Patient has been evaluated by an endocrinologist.
     - **iii.** Patient has congenital hypopituitarism AND meets both of the following (a and b):
       - **a)** Patient meets at least one of the following (1 or 2):
         - **(1)** Patient has had one growth hormone stimulation test with any of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND the test shows an inadequate response as defined by a peak growth hormone response which is below the normal reference range as determined by the testing laboratory; OR
         - **(2)** Patient has a deficiency in at least one other pituitary hormone (i.e., adrenocorticotropic hormone, thyroid-stimulating hormone, gonadotropin [luteinizing hormone and/or follicle stimulating hormone deficiency are counted as one

deficiency], or prolactin) and/or the patient has the imaging triad of ectopic posterior pituitary and pituitary hypoplasia with abnormal pituitary stalk; AND

b) Patient has been evaluated by an endocrinologist.

iv. Patient has panhypopituitarism and meets both of the following (a and b):

a) Patient meets at least one of the following (1, 2, or 3):

(1) Patient has pituitary stalk agenesis, empty sella, sellar or supra-sellar mass lesion, or ectopic posterior pituitary "bright spot" on magnetic resonance imaging or computed tomography; OR

(2) Patient has three or more of the following pituitary hormone deficiencies: somatropin (growth hormone), adrenocorticotropic hormone, thyroid-stimulating hormone, gonadotropin (luteinizing hormone and/or follicle stimulating hormone deficiency are counted as one deficiency), and prolactin; OR

(3) Patient has had one growth hormone stimulation test with any of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND the test shows an inadequate response as defined by a peak growth hormone response which is below the normal reference range as determined by the testing laboratory; AND

b) Patient has been evaluated by an endocrinologist.

v. Patient has had a hypophysectomy (surgical removal of pituitary gland).

B) Patient is Currently Receiving Skytrofa or is switching to Skytrofa from another Growth Hormone Agent (Patient has been established on either therapy for ≥ 10 months). Approve if the patient meets one of the following (i or ii):

i. Patient is < 12 years of age: Height has increased by ≥ 2 cm/year in the most recent year; OR

ii. Patient is ≥ 12 years of age and < 18 years of age: Patient meets both of the following (a and b):

a) Height has increased by ≥ 2 cm/year in the most recent year; AND

b) Patient's epiphyses are open.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Skytrofa is not recommended in the following situations:

1. **Athletic Ability Enhancement.**[5] Somatropin and related agents are not FDA-approved for athletic performance enhancement or for body building in non-athletes. Federal law prohibits the distribution or dispensing of somatropin or related agents for non-FDA approved uses.

2. **Central Precocious Puberty.** Children with precocious puberty are often treated with gonadotropin releasing hormone (GnRH) agonists (Lupron® [leuprolide acetate injection]) to suppress pituitary gonadal activity, to slow the advancement of bone age (prevent premature fusion of the epiphyseal growth plates), and to improve adult height. In some patients, GnRH agonist therapy may result in marked deceleration of bone growth and may result in adult height that is less than the midparental height. Somatropin has been used in girls when growth velocity decreases or if it appears that the targeted adult height will not be attained.[6] There are no large well-controlled trials on the efficacy and safety of adding somatropin to GnRH agonist therapy in these children or the effect on final height.[6,7]

3. **Congenital Adrenal Hyperplasia (CAH).**[8,9] The Endocrine Society clinical practice guidelines on CAH due to steroid 21-hydroxylase deficiency recommend against the use of experimental treatment approaches outside of formally approved clinical trials.[9] Children with predicted adult height standard deviation ≤ -2.25 may be considered for growth-promoting treatments in appropriately controlled trials.

4. **Constitutional Delay of Growth and Puberty.** These children have delayed skeletal maturation and pubertal development. Administering somatropin does not increase adult height (which is usually normal).[10] Short-term androgen therapy accelerates growth and the rate of pubertal advancement in boys.

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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