PRIOR AUTHORIZATION POLICY

POLICY: Growth Disorders – Increlex Prior Authorization Policy
- Increlex® (mecasermin [rDNA origin] subcutaneous injection – Ipsen)

REVIEW DATE: 12/13/2023

OVERVIEW

Increlex, an insulin-like growth factor (IGF-1), is indicated for the treatment of growth failure in pediatric patients ≥ 2 years of age with the following conditions:[1]

- **Primary IGF-1 deficiency**, for patients with severe disease, defined as:
  - Height standard deviation score ≤ -3.0; AND
  - Basal IGF-1 standard deviation score ≤ -3.0; AND
  - Normal or elevated growth hormone level.
- **Growth hormone gene deletion**, in patients who have developed neutralizing antibodies to growth hormone.

Increlex is given by subcutaneous injection twice daily, shortly before or after a meal or snack. Treatment with Increlex should continue until the epiphyses fuse indicating full growth potential has been achieved.[2] It is a limitation of use that Increlex is not a substitute to growth hormone for approved growth hormone indications. Increlex is not indicated in secondary forms of IGF-1 deficiency, such as growth hormone deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory corticosteroids.[1]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Increlex. Because of the specialized skills required for evaluation and diagnosis of patients treated with Increlex as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Increlex to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Insulin-Like Growth Factor-1 (IGF-1) Deficiency – Severe, Primary Disease.** Approve for 1 year if the patient meets ONE of the following conditions (A or B):
   - **A)** Initial Therapy or Patient Has Been on Increlex < 1 Year. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, iv, v, vi, and vii):
     - **i.** Patient is ≥ 2 years of age; AND
     - **ii.** The epiphyses are open; AND
     - **iii.** Height standard deviation score is ≤ -3.0 at baseline; AND
     - **iv.** Basal IGF-1 standard deviation score is ≤ -3.0 at baseline; AND

Note: Baseline is prior to initiation of treatment with Increlex. Reference ranges for IGF-1 vary among laboratories and are dependent upon age, gender, and puberty status.

v. Growth hormone concentration is normal or increased at baseline; AND
vi. Patient will not be receiving concurrent treatment with growth hormone; AND
vii. The medication is prescribed by or in consultation with a pediatric endocrinologist.

B) Patient Has Been Receiving Increlex for ≥ 1 Year. Approve if the patient meets ALL of the following (i, ii, and iii):
i. Patient's height has increased by ≥ 2 cm/year in the most recent year; AND
ii. The epiphyses are open; AND
iii. Patient will not be receiving concurrent treatment with growth hormone.

2. Growth Hormone Gene Deletion. Approve for 1 year if the patient meets ONE of the following conditions (A or B):

A) Initial Therapy or Patient Has Been on Increlex < 1 Year. Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):
i. Patient is ≥ 2 years of age; AND
ii. The epiphyses are open; AND
iii. Patient has developed neutralizing antibodies to growth hormone; AND
iv. Patient will not be receiving concurrent treatment with growth hormone; AND
v. The medication is prescribed by or in consultation with a pediatric endocrinologist.

B) Patient Has Been Receiving Increlex for ≥ 1 Year. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
i. Patient's height has increased by ≥ 2 cm/year in the most recent year; AND
ii. The epiphyses are open; AND
iii. Patient has developed neutralizing antibodies to growth hormone; AND
iv. Patient will not be receiving concurrent treatment with growth hormone.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Increlex is not recommended in the following situations:

1. Idiopathic Short Stature. Increlex has not been fully evaluated for this indication. Small studies have suggested some patients may respond to IGF-1 therapy[3]; however, patients with idiopathic short stature also respond to somatropin. Somatropin (monotherapy) is indicated for idiopathic short stature[4] and there is insufficient evidence to determine the risks and benefits of Increlex for this indication.

2. Growth Hormone Deficiency. Increlex is not a substitute to somatropin for approved somatropin uses and is not indicated for use in patients with secondary forms of IGF-1 deficiency, such as growth hormone deficiency.[1]

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

REFERENCES

1. Increlex® subcutaneous injection [prescribing information]. Cambridge, MA: Ipsen; October 2023.
2. Cohen J, Blethen S, Kuntze J, et al. Managing the child with severe primary insulin-like growth factor-1 deficiency (IGFD): IGFD diagnosis and management. *Drugs R D*. 2014;14(1):25-29.
3. Midyett LK, Rogol AD, VanMeter QL, et al. Recombinant insulin-like growth factor (IGF)-1 treatment in short children with low IGF-1 levels: First-year results from a randomized clinical trial. *J Clin Endocrinol Metab*. 2010;95(2):611-9.
4. Norditropin subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; March 2020.