PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 01/08/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

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.

- **Increlex® (mecasermin [rDNA origin] subcutaneous injection - Ipsen)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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 (A or B):
   - **A)** Initial Therapy or Patient Has Been on Increlex < 1 Year. Approve if the patient meets ALL 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 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 (A or B):
   - **A)** Initial Therapy or Patient Has Been on Increlex < 1 Year. Approve if the patient meets ALL 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 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 COVERED

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is(are) considered experimental, investigational, or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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]

REFERENCES

1. Increlex® subcutaneous injection [prescribing information]. Cambridge, MA: Ipsen; March 2024.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	12/13/2023
Annual Revision	No criteria changes.	01/08/2025