BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

INCRELEX® (mecasermin) subcutaneous solution Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Increlex (mecasermin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist

2. Individual is 2-17 years of age

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Growth failure from severe primary insulin-like growth factor-1 deficiency (IGFD) and **ALL** of the following:
        i. Height is 3 standard deviations or more below normal for age and sex of the individual

ii. Basal IGF-1 level is 3 standard deviations or more below normal for age and sex of the individual
iii. Normal or elevated growth hormone (GH) level

b. Growth hormone gene deletion with development of neutralizing antibodies to growth hormone

4. Individual has completed **ALL** the following **baseline tests** before initiation of treatment and will have continued monitoring as clinically appropriate:
   a. Funduscopic examination
   b. Pre-prandial glucose

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Requested agent will not be used in a neonate and infant due to benzyl alcohol preservative used in the solution

7. There is documentation of open epiphyses on most recent bone radiograph

8. There is no concurrent use with any growth hormone product

9. Requested agent will not be used as a substitute for growth hormone for approve growth hormone indications

10. Individual does not have renal impairment or hepatic impairment

11. There is **NO** evidence of secondary forms of IGF deficiency (e.g., growth hormone deficiency, malnutrition, hypothyroidism, chronic treatment with systemic anti-inflammatory steroids)

12. There are **NO** FDA-label contraindications such as:
    a. Malignant neoplasia
    b. History of malignancy
    c. Closed epiphyses (growth plates)

Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Increlex (mecasermin) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist

2. Individual has documentation of positive clinical response to therapy defined as the following:
   a. Individual's height has increased at least 2 cm total growth in one year over the previous year (*previous year and current year height values must be submitted with date they were done*)
   b. There is documentation of the expected goal adult height and that it has not been reached yet

c. The epiphyses are still open on most recent bone radiograph

3. Individual has been adherent with the medication

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
   a. Contraindications as listed in the criteria for initial therapy section
   b. Intracranial Hypertension
   c. Evidence of benign or malignant neoplasm
   d. Benzyl alcohol reaction – "gasping syndrome"

6. Requested agent will not be used in a neonate and infant due to benzyl alcohol preservative used in the solution

7. There is no concurrent use with any growth hormone product

8. Requested agent will not be used as a substitute for growth hormone for approve growth hormone indications

9. Individual does not have renal impairment or hepatic impairment

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-Cancer Medications**

  2. **Off-Label Use of Cancer Medications**

Description:

Increlex (mecasermin) is an injectable solution of human insulin-like growth factor-1 (IGF-1) produced by recombinant DNA technology. Increlex is used for the treatment of growth failure in children with severe primary IGF-1 deficiency, also referred to as primary IGFD. Primary IGFD is a growth hormone (GH)-resistant state characterized by lack of IGF-1 production in the presence of normal or elevated levels of endogenous GH.

These children have normal or elevated levels of growth hormone but due a deficiency of IGF-1, are unable to utilize the growth hormone resulting in extremely short stature. Increlex is also used in children with a growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH. It is not a substitute for GH for approved GH indications.

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Severe Primary IGFD includes classical and other forms of growth hormone insensitivity. Patients with Primary IGFD may have mutations in the GH receptor (GHR), post-GHR signaling pathway including the IGF-1 gene. However, they are not GH deficient, and therefore, they are not expected to respond adequately to exogenous GH treatment.

Increlex is not intended for use in subjects with secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids. Thyroid and nutritional deficiencies should be corrected before initiating Increlex treatment. Increlex is not a substitute for GH treatment.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Increlex (mecasermin) product information, revised by manufacturer Eton Pharmaceuticals, Inc. 05-2025 Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2025.

Richmond Padilla EJ, Rogol AD. Growth hormone insensitivity syndromes. In: UpToDate, Geffner ME, Kremen J (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2025. Topic last updated July 09, 2025. Accessed September 28, 2025.

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