Original Effective Date: 08/01/2003
Current Effective Date: 10/02/2025
Last P&T Approval/Version: 07/30/2025
Next Review Due By: 07/2026
Policy Number: C8891-A

Increlex (mecasermin)

PRODUCTS AFFECTED

Increlex (mecasermin)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Growth failure in children with Primary insulin-like growth factor-1 deficiency

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. GROWTH FAILURE:
   1. Documented diagnosis of Primary insulin-like growth factor deficiency (IGFD) OR growth hormone (GH) gene deletion with neutralizing antibodies to GH
      AND

2. Other reasons for short stature have been ruled out, such as hypothyroidism, chronic system disease, chronic illnesses, skeletal disorders, and medications (i.e., chronic anti-inflammatory steroid therapy)
   AND
3. Documentation member has short stature with a height greater than or equal to 3 standard deviations below the mean for age and gender
   AND
4. Documentation member has an IGF-1 greater than or equal to 3 standard deviations below the mean for age and gender
   AND
5. Documentation member has normal or elevated growth hormone levels (for Primary IGFD) as evidenced by normal response to at least two provocative stimuli of GH release (normal response is generally accepted to be a peak GH level of more than 7 ng/ml as measured by radioimmunoassay (RIA))
   AND
6. Documentation member has projected adult height more than 1.5 standard deviations below the mid-parental height.
   AND
7. Documentation member has clinically determined growth failure as defined by a growth rate velocity < 7cm/year if < 3yrs old, and < 5cm/year if > 3 yrs. old.
   NOTE: During puberty normal growth is about 7-10 cm/year and after puberty about 1-3 cm/year.
   AND
8. FOR MEMBERS 12 YEARS OF AGE AND OLDER ONLY: Documentation of open epiphyses confirmed by bone age X-ray (taken within 6 months of request) of the left hand and wrist showing one of the following:
   a. Males: not to exceed 16 0/12 years of age
   b. Females: not to exceed 14 0/12 years of age
   AND
9. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Increlex include known hypersensitivity to mecasermin, do not administer intravenously, closed epiphysis, and malignant neoplasia].

CONTINUATION OF THERAPY:

A. GROWTH FAILURE:

1. Member is 18 years of age or younger
   AND
2. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
3. Prescriber attests or clinical reviewer has found that member's epiphyses are open
   AND
4. Documentation of a growth rate velocity greater than or equal to 2.5 cm/year
   NOTE: Should see a doubling of pretreatment growth rate or an increase of 3 cm/yr or more in the first year and 2.5 cm/yr thereafter
   AND
5. Documentation expected adult height has not been reached defined as 5th percentile for adults (65 inches for men and 60 inches for women) or 50th percentile for height based on age calculated using mid-parental height
   AND
6. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified pediatric endocrinologist, or physician experienced in the diagnosis and management of growth disorders. [If prescribed in consultation, consultation notes must be submitted with initial request and with reauthorization requests.]

AGE RESTRICTIONS:
2 years of age and older to less than 18 years of age

QUANTITY:
0.12 mg/kg twice daily

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Insulin-Like Growth Factors (Somatomedins)

FDA-APPROVED USES:
Indicated for the treatment of growth failure in pediatric patients 2 years of age and older with severe primary IGF1 deficiency or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to growth hormone (GH).

Limitations of use: Increlex is not a substitute to GH for approved GH indications.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Centers for Disease Control and Prevention: http://www.cdc.gov/growthcharts/
Height standard deviation score: The CDC website includes growth charts for children indicating heights (lengths) with curves down to 2 standard deviations (approximately 3rd percentile).

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Primary insulin-like growth factor 1 (IGF-1) deficiency is characterized by an inadequate production of IGF-1, in spite of sufficient secretion of growth hormone (GH). This leads to a serious growth disorder. The classic form of severe primary IGF-1 deficiency (SPIGFD) is Laron syndrome, where a genetic defect in the GH receptor (GHR) leads to low or undetectable IGF-1 levels in the body.
More recently, genetic abnormalities in the GH signal transduction (STAT5b) and in the IGF-1 gene, which also lead to primary IGF-1 deficiency and very small stature, have been described.

Patients with severe primary IGFD have extremely short stature (defined as height standard deviation score not exceeding -3), low serum concentrations of IGF-I (defined as standard deviation score not exceeding -3), and normal or elevated GH secretion Primary IGFD may be associated with abnormalities of the GH receptor, post-GH-receptor signaling pathway, or the IGF-I gene resulting in GH insensitivity exogenously administered GH not expected to elicit an adequate response in these patients.

Patients with GH gene deletion are likely to develop GH-neutralizing antibodies following exposure to exogenous GH preparations (secondary GH insensitivity syndrome, isolated GH deficiency type IA).

Not intended for use in children with secondary forms of IGF-I deficiency (e.g., GH deficiency [not including those with GH gene deletion], malnutrition, hypothyroidism, corticosteroid-induced growth failure). Correct thyroid and nutritional deficiencies prior to initiation of mecasermin therapy. Not a substitute for GH therapy. Mecasermin is an IGF-1 produced using recombinant DNA technology to replace endogenous IGF-1

1. Endogenous IGF-1 circulates predominately bound to IGF-binding protein-3 (IGFBP-3) and a GH-dependent acid-labile subunit (ALS). Acting at receptors in the liver and other tissues, endogenous cGH stimulates the synthesis and secretion of IGF-1. In patients with primary severe IGF-1 deficiency, GH receptors in the liver are unresponsive to GH, leading to reduced endogenous IGF-I concentrations and decreased growth (skeletal, cell, organ). Endogenous IGF- 1 also suppresses liver glucose production, stimulates peripheral glucose utilization, and has an inhibitory effect on insulin secretion.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Increlex (mecasermin) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Increlex (mecasermin) include: known hypersensitivity to mecasermin, do not administer intravenously, closed epiphysis, and malignant neoplasia.

Exclusions/Discontinuation:

Do not use concurrently with growth hormone.
Increlex is not indicated for use in patients with secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of antiinflammatory corticosteroids.

OTHER SPECIAL CONSIDERATIONS:

Severe hypoglycemia leading to hypoglycemic seizures has been observed with Increlex treatment. Because Increlex has insulin-like hypoglycemic effects it should be administered shortly before or after (± 20 minutes) a meal or snack. Patients should avoid engaging in any high-risk activities within 2 – 3 hours after dosing, particularly at the initiation of treatment, until a well-tolerated dose has been established. Increlex should not be administered when the meal or snack is omitted. The dose of Increlex should never be increased to make up for one or more omitted doses. Preprandial glucose monitoring is recommended at treatment initiation and until a well-tolerated dose is established. If frequent symptoms of hypoglycemia or severe hypoglycemia occur, preprandial glucose monitoring should continue, and glucose monitoring should also occur at the time of event if possible. If hypoglycemia occurs with recommended doses despite adequate food intake, the dose should be reduced. Patients and caregivers should be educated on how to recognize and treat the signs and symptoms of hypoglycemia.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize*

industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:
Increlex SOLN 40MG/4ML multiple dose vial

REFERENCES

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4. Roelfsema V, Clark RG. The growth hormone and insulin-like growth factor axis: its manipulation for the benefit of growth disorders in renal failure. Journal of the American Society of Nephrology 2001 Jun;12(6):1297-306
5. Cohen J, Blethen S, Kuntze J, Smith SL, Lomax KG, Mathew PM. Managing the Child with Severe Primary Insulin-Like Growth Factor-1 Deficiency (IGFD): IGFD Diagnosis and Management. Drugs in R&D. 2014;14(1):25-29. doi:10.1007/s40268-014-0039-7.
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7. Backeljauw PF, Underwood LE, GHIS Collaborative Group. Therapy for 6.5–7.5 years with recombinant insulin-like growth factor I in children with growth hormone insensitivity syndrome: a clinical research center study. J Clin Endocrinol Metab. 2001; 86:1504-10. [PubMed 11297575]
8. Chernausek SD, Backeljauw PF, Frane J et al. Long-term treatment with recombinant insulin- like growth factor (IGF)-I in children with severe IGF-I deficiency due to growth hormone insensitivity. J Clin Endocrinol Metab. 2007; 92:902-10. [PubMed 17192294]
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10. Chernausek SD, Backeljauw PF, Frane J, Kuntze J, Underwood LE, GH Insensitivity Syndrome Collaborative Group. Long-term treatment with recombinant insulin-like growth factor (IGF)-I in children with severe IGF-I deficiency due to growth hormone insensitivity. JClin Endocrinol Metab. 2007;92(3):902-10.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Contraindications/Exclusions/ Discontinuation References	Q3 2025

REVISION- Notable revisions: Required Medical Information Continuation of Therapy Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q3 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity Drug Class FDA-Approved Uses Available Dosage Forms	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Contraindications/Exclusions/Discontinuation	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file