Effective Date: 8/1/2003
Last P&T Approval/Version: 7/28/2021
Next Review Due By: 7/2022
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:
A. GROWTH FAILURE:
1. Documented Severe Primary IGFD* (insulin-like growth factor deficiency) or GH gene deletion with neutralizing antibodies to GH.
AND
2. Prescriber attestation that 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 that member has no known malignancy and member with be monitored for and treatment will be discontinued if evidence of malignant neoplasia develops.
AND
3. Documentation member has short stature with a height less than or equal to 3 standard deviations below the mean for age and gender.
AND
4. Documentation member has an IGF-1 less 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): 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 RIA)
   AND
6. Documentation member has projected adult height more than 1.5 standard deviations below the mid-parental height.
   AND
7. Documentation of bone age(radiograph)
   AND
8. 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
9. Documentation of open epiphyses confirmed by bone age X-ray of the left hand and wrist (12 years of age and older only). Males: not to exceed 16 0/12 years of age; Females: not to exceed 14 0/12 years of age. X- ray must be taken within 6 months of request.
   AND
10. 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 hypersensitivityto mecasermin, intravenous administration, closed epiphysis, and malignant neoplasm].

CONTINUATION OF THERAPY:

A. GROWTH FAILURE:

1. Prescriber attests that member's epiphyses are not closed
   AND
2. Documentation of a growth rate velocity or greater than or equal to than 2.5cm/year (Note: Should see a doubling of pretreatment growth rate or an increase of 3cm/yr. or more in the first year and 2.5 cm/yr. thereafter)

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 patients with growth disorders. Submit consultation notes, if applicable.

If prescribed in consultation, consultation notes must be submitted with initial request and with reauthorization requests.

AGE RESTRICTIONS:

2 years of age or older, and not older than 18 years of age

QUANTITY:

Quantity limit: Dose must not exceed 0.12 mg/kg twice daily OR 0.24 mg/kg per day

PLACE OF ADMINISTRATION:

The recommendation is that medications in this policy will be for pharmacy benefit coverage and patient self-administered

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Endocrine-Metabolic Agent; Somatotropin Agonists

FDA-APPROVED USES:
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).a-f Correct thyroid and nutritional deficiencies prior to initiation of mecasermin therapy.a-f 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.

Other labeled contraindications included: Known hypersensitivity to mecasermin or any ingredient (e.g., benzyl alcohol) in the formulation, Closed epiphyses (bone growth plates), Active or suspected neoplasia (therapy should be discontinued if evidence of neoplasia develops), Chronic illness (e.g., cystic fibrosis, diabetes, etc.), Intravenous (IV) administration OR Growth failure associated with other

OTHER SPECIAL CONSIDERATIONS:

Increlex should be administered shortly before or after (± 20 minutes) a meal or snack, because it has insulin-like hypoglycemic effects. Patient should avoid engaging in any high-risk activities within2 – 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. Increlex should be initiated at a low dose and the dose should be increased only if no hypoglycemic episodes have occurred after at least 7 days of dosing. If severe hypoglycemia or persistent hypoglycemia occurs on treatment despite adequate food intake, Increlex dose reduction should be considered. Patients and caregivers should be educated on how to recognize and treat the signs and symptoms of hypoglycemia.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:

Increlex SOLN 10mg/ml multi-dose vial (40mg/vial)

REFERENCES

1. Increlex (mecasermin [rDNA origin]) [prescribing information]. Cambridge, MA: Ipsen Biopharmaceuticals Inc; December 2019.
2. Rosenfeld RG. The IGF system: new developments relevant to pediatric practice. EndocrineDevelopment 2005;9:1-10
3. Clark RG. Recombinant human insulin-like growth factor I (IGF-I): risks and benefits of normalizing blood IGF-I concentrations. Frontiers of Hormone Research 2004; 62 Suppl 1:93-100

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 withSevere 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.
6. Keating GM. Mecasermin. Biodrugs. 2008; 22:177-88. [PubMed 18481900]
7. Backeljauw PF, Underwood LE, GHIS Collaborative Group. Therapy for 6.5–7.5 years withrecombinant 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]
9. Collett-Solberg PF, Misra M, Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. The role of recombinant human insulin-like growth factor-I in treating children with short stature. J Clin Endocrinol Metab. 2008;93(1):10-8.
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.