Medication Policy Manual | **Policy No:** dru126

Topic: Increlex®, mecasermin | **Date of Origin:** January 3, 2006

Committee Approval Date: October 13, 2017 | **Next Review Date:** October 2018

Effective Date: November 1, 2017

IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Mecasermin (Increlex®) is a man-made insulin growth factor (IGF-1), a protein necessary for linear growth in children. It is administered as a subcutaneous injection and indicated for growth failure in children with extreme short stature and severe primary IGF-1 deficiency or with growth hormone gene deletion who have developed antibodies to growth hormone.

Policy/Criteria

I. Most contracts require prior authorization approval of mecasermin prior to coverage. Mecasermin may be considered medically necessary in children when all the following criteria are met:

A. Mecasermin is prescribed by a pediatric endocrinologist.

AND

B. Diagnosis of one of the following conditions:

1. Severe primary IGF-1 deficiency.

OR

2. Growth hormone gene deletion.

OR

3. Genetic mutation of growth hormone receptor (i.e., Laron Syndrome).

AND

C. Current height measurement at less than the 3rd percentile for age and sex.

AND

D. IGF-1 level greater than or equal to 3 standard deviations below normal (based on lab reference range for age and sex).

AND

E. Normal or elevated growth hormone levels based on at least one growth hormone stimulation test.

AND

F. Open growth plates.

II. Administration, Limitations, and Authorization Period

A. OmedaRx considers mecasermin to be a self-administered medication.

B. Initial authorization: Mecasermin may be authorized for a period of up to 12 months when all criteria in IA through IF are met.

C. Authorization shall be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective. Continued authorization in children may be given for up to 12 months until any one of the following conditions occurs:

1. Growth velocity is less than 2.5 cm/year.

OR

2. Bone age in males exceeds $16^{0/12}$ years of age.

OR

3. Bone age in females exceeds $14^{0/12}$ years of age.

III. Mecasermin is considered investigational for all other indications, including, but not limited to:

A. Amyotrophic lateral sclerosis (ALS).

B. Children less than two years of age.

C. Combination treatment with growth hormone.

D. Diabetes.

E. Individuals with closed growth plates.

F. Secondary forms of IGF-1 deficiency, such as growth hormone deficiency, malnutrition, hypothyroidism, or chronic treatment with steroids.

G. Idiopathic short stature.

H. Growth failure due to other identifiable causes (including, but not limited to, Prader-Willi syndrome, Russell-Silver syndrome, Turner syndrome, Noonan syndrome).

I. Less severe forms of IGF-1 deficiency.

J. Rett Syndrome (RTT)

K. HIV lipodystrophy

Position Statement

- The U. S. Food and Drug Administration (FDA) has approved mecasermin for the indication of long-term treatment of growth failure in children with either severe primary IGF-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone. The published indication defines severe primary IGF-1 deficiency as[1]:
  * height standard deviation score ≤ -3.0 **and**
  * basal IGF-1 standard deviation score ≤ -3.0 **and**
  * normal or elevated growth hormone (GH)[1]
- Mecasermin has received orphan drug status because of the rarity of this condition and lack of existing options to treat severe primary IGF-1 deficiency.
  * There are fewer than 60,000 patients world-wide with primary IGF-1 deficiency.
  * Fewer than 10,000 patients world-wide are diagnosed with severe primary IGF-1 deficiency.
- The goal of treatment with mecasermin is to promote normal linear growth in children and achieve their predicted adult height.
- There are phase III trials currently in progress evaluating mecasermin in children with less severe forms of primary IGF-1 deficiency.
- Although mecasermin is reported to increase height in children with IGF-1 deficiency, there is no proven benefit of height gain with mecasermin on functional disability or psychosocial performance in children with extreme or mild degrees of short stature from primary IGF-1 deficiency.

Efficacy/Safety in Primary IGF-1 Deficiency

- FDA approval for mecasermin is based on a pooled data analysis from five smaller (four open-label and one-double-blind, placebo controlled) clinical studies in 71 children with extreme short stature caused by severe primary IGF-1 deficiency. [1,2]
    * Children were treated for an average of 3.9 years, with some patients being treated up to 11.5 years. [1,2]
    * Compared to baseline, children were observed to gain on average an additional inch per year for each year of therapy over a course of 8 years with mecasermin 60-120 mcg/kg twice daily administration.[1,2]
    * Adverse events reported in the study included hypoglycemia (42%), injection site lipohypertrophy, and tonsillar hypertrophy (15%). [1,2]
    * Adverse events are avoided with rotation of injection sites to prevent lipohypertrophy and eating a meal or snack 20 minutes after mecasermin to avoid symptomatic hypoglycemia.[1, 2]
- Allergic reactions to mecasermin (Increlex) have been reported post-marketing. They range in severity from localized (injection site) reactions to systemic reactions, including rare cases of anaphylaxis requiring hospitalization.

Other Conditions

- Mecasermin is not a substitute for growth hormone treatment.[1,2]
- FDA labeling specifies that mecasermin is not intended for use in individuals with secondary forms of IGF-1 deficiency, such as growth hormone deficiency, malnutrition, hypothyroidism, or chronic treatment with steroids.[1]
- Mecasermin is contraindicated in patients with closed epiphyses (bone growth plates are closed) or active or suspected neoplasia. [1]
- The long-term clinical benefits and safety of mecasermin in other conditions, such as diabetes,[6-7,9] amyotrophic lateral sclerosis,[3] acquired immune deficiency syndrome (AIDS) [4, 8], cystic fibrosis,[5] or in growth failure associated with other identifiable causes (i.e., Prader-Willi, Russell-Silver Syndrome, Turner Syndrome or Noonan Syndrome) remain unproven.

Cross Reference
Gattex, teduglutide, dru304
Growth Hormone, dru015
Self-Administered Injectables, dru110

Codes	Number	Description
		Retail Prescription Drug
HCPCS	**J2170**	mecasermin (Increlex®) 1mg
	NOTE:	Mecasermin is a self-administered injectable medication and is covered according to the member's benefit for self-administered injectables.

References

1. Increlex® (mecasermin) prescribing information. Tercica; Brisbane, CA. September 2012.
2. FDA web site: Drugs@FDA.gov. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search. Overview&DrugName=INCRELEX. Accessed December 13, 2005.
3. Mitchell JD, Wokke JHJ, Borasio GD. Recombinant human insulin-like growth factor (rhIGF-I) for amyotrophic lateral sclerosis/motor neuron disease. *The Cochrane Database of Systematic Reviews* 2002, Issue 3. Art No.: CD002064. DOI:10.1002/14651858.CD002064.
4. Lee PDK, Pivarnik JM, Bukar JG, Muurahainen N, Berry PS, Skolnik PR et al A randomized, placebo-controlled trial insulin-like growth factor I and low dose growth therapy for wasting associated with human immunodeficiency virus infection. *J Clin Endocrinol Metab* 1996;81:2968-75.
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6. Moses AC, Young SC, Morrow LA, O'Brien M, Clemmons DR. Recombinant human insulin-like growth factor I increases insulin sensitivity and improves glycemic control in type II diabetes. *Diabetes* 1996;45:91-100.
7. Acerini CL, Patton CM, Savage MO, Kernell A, Westphal O, Dunger DB. Randomized placebo-controlled trial of human recombinant insulin-like growth factor I plus intensive insulin therapy in adolescents with insulin-dependent diabetes mellitus. *Lancet* 1997;350:1199-204.
8. Waters D, Danska J, Hardy K, Koster F, Oualls C, Nickell D, et al. Recombinant human growth hormone, insulin-like growth factor 1, and combination therapy in AIDS-associated wasting. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1996;125:865-72.
9. Thrailkill KM, Quattrin T, Baker L, Kuntze Je, Compton PG, Martha PM. Cotherapy with recombinant human insulin-like growth factor I and insulin improves glycemic control in type 1 diabetes. RhIGF-I in IDDM Study Group. *Diabetes Care* 1999;22:585-92.
10. FDA Center for Drug Evaluation and Research. Approval package for application number NDA 21-884. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm (assessed September 6, 2006).

Revision History

Revision Date	Revision Summary
10/13/2017	No changes to coverage criteria with this annual update.
12/16/2016	No changes to coverage criteria with this annual update.
01/08/2016	No changes to coverage criteria with this annual update.