09-J0000-57

Original Effective Date: 06/15/06

Reviewed: 02/12/14

Revised: 10/01/16

Subject: Mecasermin (Increlex®) Injection

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DESCRIPTION:

Mecasermin (Increlex®) is a biosynthetic (recombinant DNA origin) form of insulin-like growth factor 1 (IGF-1) and is used for the long-term treatment of growth failure in children with severe primary IGF-1 deficiency or those with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH following exposure to exogenous GH preparations. Severe IGF-1 deficiency is rare; individuals with severe primary IGF-1 have extremely short stature, low serum concentrations of IGF-1, and normal or elevated GH secretion. Individuals with severe IGF-1 deficiency may have abnormalities of the GH receptor, abnormalities of the post-GH-receptor signaling pathway, or defects in the IGF-1 gene, any of which may result in insensitivity to GH. IGF-1 peptides, such as mecasermin, may bypass the blockade of GH action and improve growth. Pooled results from several open-label studies and one placebo-controlled trial in pediatric individuals demonstrated a rapid catch-up growth during the first year of mecasermin therapy.

Of note, mecasermin has not demonstrated efficacy in the treatment of secondary forms of IGF-1 deficiency, including malnutrition and hypothyroidism. Hypothyroidism and malnutrition should be corrected prior to mecasermin therapy initiation. Additionally, mecasermin is not a substitute for GH treatment.

POSITION STATEMENT:

Mecasermin (rDNA origin) (Increlex®) **meets the definition of medical necessity** for the treatment of growth failure in members between the ages of 2 to 18 with **EITHER** of the following conditions:

1. Severe primary insulin-like growth factor-1 deficiency (IGFD) when **ALL** of the following criteria are met:
    a. Height is three standard deviations (SDs) or more below normal for age and gender
    b. Basal IGF-1 level is three SDs or more below normal for age and gender
    c. Growth hormone level is normal or elevated (defined as stimulated serum GH level [peak level] of greater than 10 nanograms/mL [ng/mL] or basal [unstimulated] serum GH level greater than 5 ng/mL).
    d. Member's bone epiphyses are not closed.
2. Growth hormone gene deletion who have developed neutralizing antibodies to growth hormone and bone epiphyses are not closed.

Approval duration: 1 year

Mecasermin is considered **experimental or investigational** for all other indications since there is insufficient clinical evidence to support their use.

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-Approved: Mecasermin is approved for the long-term treatment of growth failure in children with severe primary IGFD or with GH gene deletion who have developed neutralizing antibodies to GH.

- Initially, mecasermin is dosed at 0.04-0.08 mg/kg (40-80 mcg/kg) and is injected subcutaneously (to abdomen, buttock, thigh, or upper arm) twice daily, within 20 minutes of a meal or snack.
- After the dose has is well-tolerated for at least one week, the dose may be increased by 0.04 mg/kg (40 mcg/kg) per dose, to a maximum of 0.12 mg/kg (120 mcg/kg) twice daily by subcutaneous injection.
- Preprandial glucose monitoring is recommended until a well-tolerated dose is established; if persistent or severe hypoglycemia occurs at recommended doses (despite adequate food intake) the dose should be reduced. Members should avoid rigorous activity (e.g., swimming) within 2-3 hours after administration until a well-tolerated dose is established. To prevent lipohypertrophy, injection sites should be rotated.

Missed doses: If a dose is missed, subsequent doses should never be increased to make up for omitted doses.

Drug Availability: mecasermin is available as a 10 mg/mL solution for injection

PRECAUTIONS:

CONTRAINDICATIONS:

Mecasermin is contraindicated in members with an active or suspected malignancy. If evidence of a malignancy develops, mecasermin should be discontinued. Additionally, mecasermin is contraindicated in members with closed epiphyses or those with a known hypersensitivity to the active or inactive ingredients.

Mecasermin is injected subcutaneously; intravenous administration is contraindicated.

WARNINGS:

Hypoglycemia: Mecasermin has insulin-like hypoglycemic effects; as such, it should be administered shortly before or after (within 20 minutes) a meal or snack. Glucose monitoring is indicated during initiation and titration.

Hypersensitivity: Injection site reactions and systemic reactions, including hospitalization have been reported during post-marketing surveillance. Members experiencing hypersensitivity reactions should seek medical attention.

Intracranial hypertension: intracranial hypertension may occur in members receiving mecasermin; signs and symptoms typically resolve following product discontinuation. Funduscopic examination is recommended at baseline and periodically during treatment with mecasermin.

Slipped Capital Femoral Epiphysis (SCFE): Any pediatric member with the onset of a limp or complaints of hip/knee pain during mecasermin therapy should be carefully evaluated.

Progression of pre-existing scoliosis: Members with a history of scoliosis who are treated with mecasermin should be monitored for the progression of scoliosis.

Pregnancy/Lactation: Mecasermin is not indicated for use in adults, including pregnant women and nursing women. Mecasermin is classified as pregnancy category C and it is unknown whether mecasermin is distributed into breast milk.

BILLING/CODING INFORMATION:

The following codes may be used to report mecasermin:

HCPCS Coding:

J2170	Injection, mecasermin, 1mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

E23.0	Hypopituitarism
E23.1	Drug-induced hypopituitarism
E23.3	Hypothalamic dysfunction, not elsewhere classified
E23.6	Other disorders of pituitary gland

E23.7	Disorder of pituitary gland, unspecified
E89.3	Post-procedural hypopituitarism
E34.3	Short stature due to endocrine disorder
E34.8	Other specified endocrine disorder
E34.9	Endocrine disorder, unspecified
Q87.1	Congenital malformation syndromes predominantly associated with short stature
Q89.2	Congenital malformations of other endocrine glands
R62.50	Unspecified lack of expected normal physiological development in childhood
R62.51	Failure to thrive (child)
R62.52	Short stature (child) [covered for SHOX deficiency in children whose epiphyses are not closed]

REIMBURSEMENT INFORMATION:

Please see section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

DEFINITIONS:

Insulin-like growth factor (IGF-1): basal serum IGF-I reference ranges vary by age, gender and pubertal status. Reference ranges for serum IGF-I vary among laboratories and the reference range for the laboratory performing the test should be used to determine whether the member's basal serum IGF-I level meets criteria.

Lipohypertrophy: hypertrophy of subcutaneous fat.

RELATED GUIDELINES:

Growth Hormone Therapy, 09-J0000-27

OTHER:

None applicable.

REFERENCES:

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6. Mecasermin. In: McEvoy GK, editor. AHFS drug information 2013 [monograph on the Internet]. Bethesda (MD): American Society of Health-System Pharmacists; 2013 [cited 2013 Dec 30]. Available from: http://online.statref.com. Subscription required to view.
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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 02/12/14.

GUIDELINE UPDATE INFORMATION:

06/15/06	New Medical Coverage Guidelines.
01/01/07	HCPCS update, added J2170.
08/15/07	Reviewed guideline: Reformatted guideline, maintain current coverage and limitations, changed name to include both products available, updated reference range for both LabCorp and Quest, updated dosage and administration, updated precautions, updated program exceptions to include Medicare Part D, updated definitions, and updated references.
07/15/08	Reviewed guideline with no coverage changes. Updated IGF-1 reference range tables.
08/15/09	Review and revision to guideline; consisting of the addition of open epiphyses requirement under the position statement, added the definition of severe primary IGFD and updated references.
11/15/10	Review and revision to guideline; consisting of adding an age limit and closed epiphyses to the position statement, reformatting, updating codes and references.
11/15/11	Review and revision to guideline; consisting of updating references.

11/15/12	Review and revision to guideline; consisting of revising the position statement, dosage administration section and precaution/warning sections; adding contraindication section; updating references.
03/15/13	Review and revision to guideline; consisting of updating references and reformatting precautions/warnings section.
03/15/14	Review and revision to guideline; consisting of updating program exceptions and references.
11/01/15	Revision: ICD-9 Codes deleted.
10/01/16	Revision to guideline; consisting of updating ICD10 codes.