Clinical Policy: Mecasermin (Increlex)

Reference Number: PA.CP.PHAR.150
Effective Date: 01/18
Last Review Date: 11/16

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for mecasermin (Increlex®).

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Increlex is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Severe Primary IGF-1 Deficiency (must meet all):

1. Prescribed by an endocrinologist;
2. Diagnosis of severe primary IGF-1 deficiency (IGFD) (i.e., inherited growth hormone insensitivity [GHI]) and associated growth failure as evidenced by all of the following:
   a. Basal IGF-1 is ≥ 3 standard deviations (SD) below the mean;
   b. Normal or elevated growth hormone (GH) level;
   c. Height is ≥ 3 SD below the mean;
3. The following secondary forms of IGFD have been ruled out:
   a. GH deficiency;
   b. Malnutrition;
   c. Hypothyroidism;
   d. Chronic treatment with pharmacologic doses of anti-inflammatory steroids;
4. If member has hypothyroidism or nutritional deficiencies, they have been corrected;
5. Somatropin (i.e., recombinant human growth hormone [rhGH]) is not prescribed concurrently with Increlex;
6. Member has none of the following contraindications:
   a. Known hypersensitivity to mecasermin (rhIGF-1) or any of the inactive ingredients in Increlex;
   b. Presence of active or suspected malignancy;
   c. Closed epiphyses.

Approval duration: 6 months

B. Acquired Growth Hormone Insensitivity (must meet all):

1. Prescribed by an endocrinologist;
2. Diagnosis of acquired growth hormone insensitivity (GHI) due to development of neutralizing GH antibodies (documentation confirming the presence of GH antibodies required) after treatment for GH deficiency;
3. GH deficiency is due to a GH gene deletion (documentation confirming GH gene deletion required) with associated growth failure as indicated by any of the following:
   a. Height > 3 SD below the mean;
   b. Height > 2 SD below the mean and (i or ii);

i. Height velocity > 1 SD below the mean over 1 year;
ii. Decrease in height SD > 0.5 over 1 year in children > 2 years of age;

c. Height > 1.5 SD below midparental height;
d. Height velocity > 2 SD below the mean over 1 year;
e. Height velocity > 1.5 SD below the mean over 2 years;

4. If member has thyroid or nutritional deficiencies, they have been corrected;
5. Somatropin is not prescribed concurrently with Increlex;
6. Member has none of the following contraindications:
   a. Known hypersensitivity to mecasermin (rhIGF-1) or any of the inactive ingredients in Increlex;
   b. Presence of active or suspected malignancy;
   c. Closed epiphyses.

Approval duration: 6 months

C. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. All Indications (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If member has received treatment for ≥ 1 years, height velocity is currently > 2 cm/year;
4. Somatropin is not prescribed concurrently with Increlex;
5. Member has none of the following reasons to discontinue:
   a. Known hypersensitivity to mecasermin (rhIGF-1) or any of the inactive ingredients in Increlex;
   b. Presence of active or suspected malignancy;
   c. Closed epiphyses.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy**.**

Background

Description/Mechanism of Action:

Increlex (mecasermin [rDNA origin] injection) contains human insulin-like growth factor-1 (rhIGF-1) produced by recombinant DNA technology. The amino acid sequence of the product is identical to that of endogenous human IGF-1. The rhIGF-1 protein is synthesized in bacteria (E. coli) that have been modified by the addition of the gene for human IGF-1.

Formulations:
Increlex is a sterile solution intended for subcutaneous injection. Each multi-dose vial of Increlex contains 10 mg per mL mecasermin (40 mg per vial). Contains benzyl alcohol.

FDA Approved Indications:
Increlex (mecasermin [rDNA origin] injection) is indicated for the treatment of growth failure in children with

- Severe primary IGFD is defined by:
  - Height standard deviation score ≤ –3.0 and
  - Basal IGF-1 standard deviation score ≤ –3.0 and
  - Normal or elevated growth hormone.
    Severe primary IGFD includes classical and other forms of growth hormone insensitivity. Patients with primary IGFD may have mutations in the GHR, post-GHR signaling pathway including the IGF-1 gene. They are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment.
- GH gene deletion who have developed neutralizing antibodies to GH.

Limitations of use:

- Increlex is not a substitute to GH for approved GH indications.
- 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.

Appendices
Appendix A: Abbreviation Key

GH: growth hormone
GHI: growth hormone insensitivity
GHR: growth hormone receptor
IGF-1: insulin-like growth factor -1
IGFD: insulin-like growth factor deficiency
rhGH: recombinant human growth hormone (somatropin)
rhIGF-1: recombinant human IGF-1 (mecasermin)
SD: standard deviation
SDS: standard deviation score

Appendix B: Causes of Primary IGF-1 Deficiency (i.e., Inherited Growth Hormone Insensitivity)*

- GH receptor mutations (known as Laron syndrome or the classical model of GH insufficiency)
- Post-GH receptor mechanisms
  - GH receptor signal transduction
  - IGF-I gene mutations
  - Impaired IGF-1 promoter function
  - Defective stabilization of circulating IGF-I
- IGF-1 receptor mutations

Unlike the causes above, in the case of IGF-1 receptor mutations, IGF-1 levels are normal or elevated which would render mecasermin therapy ineffective.

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**GH production and secretion is normal or above normal; therefore, exogenous GH treatment would be ineffective.*

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2170	Injection, mecasermin, 1 mg

Reviews, Revisions, and Approvals	Date	Approval Date

References

1. Increlex Prescribing Information. Basking Ridge, NJ: Ipsen Bipharmaceuticals, Inc.; March 2016. Available at http://www.increlex.com/pdf/patient-full-prescribing-information.pdf. Accessed September 19, 2016.
2. Collett-Solberg PF, Misra M. The role of recombinant human insulin-like growth factor-1 in treating children with short stature. *J Clin Endocrinol Metab*. January 2008; 93(1): 10-18.
3. Rogol AD. Growth hormone insensitivity syndromes. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at UpToDate.com. Accessed January 20, 2016.
4. GH Research Society. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. *JCEM*. 2000; 85(11): 3990-3993.
5. Wilson TA, Rose SR, Cohen P, et al. Update of guidelines for the use of growth hormone in children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. *J Pediatr*. 2003; 143: 415-421.
6. Chernausek SD, Backeljauw PF, Frane J, et al. 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. J Clin Endocrinol Metab. March 2007; 92(3): 902-10.