Clinical Policy: Mecasermin (Increlex)

Reference Number: PA.CP.PHAR.150
Effective Date: 01/2018
Last Review Date: 07/2023

Coding Implications
Revision Log

Description
Mecasermin (Increlex®) is a human insulin-like growth factor-1 (IGF-1).

FDA Approved Indication(s)
Increlex is indicated for the treatment of growth failure (GF) in pediatric patients 2 years of age and older with:

- Severe primary IGF-1 deficiency (IGFD)
  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 (GH).
- Growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH

Limitation(s) of use:

- Increlex is not a substitute to GH for approved GH indications.
- Increlex is not indicated for use in patients with secondary forms of IGFD, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory corticosteroids.

Policy/Criteria
It is the policy of PA Health & 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. Diagnosis of severe primary IGF-1 deficiency (IGFD) (i.e., inherited growth hormone insensitivity [GHI])
2. Prescribed by in consultation with a pediatric endocrinologist;
3. Age ≥ 2 and < 18 years;
4. If age > 10 years, open epiphysis on x-ray;
5. IGF-1 serum level is ≥ 3 standard deviations (SD) below the mean;
6. GH serum level is normal or elevated;
7. Height is ≥ 3 SD below the mean for age and sex (SD, height, date, and age in months within the last 90 days are required);
8. Member does not have malignant neoplasia or a history of malignancy;
9. Somatropin (recombinant human GH) is not prescribed concurrently with Increlex;
10. Dose does not exceed 0.12 mg/kg twice daily.

Approval duration: 12 months or up to age 18, whichever is shorter

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

1. Diagnosis of acquired GH insensitivity;
2. Prescribed by or in consultation with a pediatric endocrinologist;
3. Age ≥ 2 and < 18 years;
4. If age > 10 years, open epiphysis on x-ray;

5. Documentation of genetic GH deficiency due to a GH gene deletion;
6. Documentation of neutralizing GH antibodies;
7. Member meets (a or b):
   a. Short stature (SS): height is > 2 SD below the mean for age and sex (SD, height, date, and age in months within the last 90 days are required);
   b. GF: one of the following (i, ii, or iii):
      i. Height deceleration across two growth chart percentiles representing > 1 SD below the mean for age and sex (SD and 2 heights, dates, and ages in months at least 6 months apart within the last year are required);
      ii. Growth velocity > 2 SD below the mean for age and sex over 1 year (SD and 2 heights, dates, and ages in months at least 1 year apart within the last year are required);
      iii. Growth velocity > 1.5 SD below the mean for age and sex sustained over 2 years (SD and 2 heights, dates, and ages in months at least 2 years apart within the last two years are required);
8. Member does not have malignant neoplasia or a history of malignancy;
9. Somatropin (recombinant human GH) is not prescribed concurrently with Increlex;
10. Dose does not exceed 0.12 mg per kg twice daily.

Approval duration: 6 months or up to age 18, whichever is shorter

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. If member has received treatment for ≥ 1 year, height has increased ≥ 2 cm in the last year as documented by 2 height measurements taken no more than 1 year apart (dates and height measurements are required);
3. Member does not have malignant neoplasia or a history of malignancy;
4. Somatropin (recombinant human GH) is not prescribed concurrently with Increlex;
5. If request is for a dose increase, new dose does not exceed 0.12 mg per kg twice daily.

Approval duration: 12 months or up to age 18, whichever is shorter

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

1. Currently receiving medication via PA Health & 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.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53 or evidence of coverage documents;

B. Secondary forms of IGF-1 deficiency, such as:
1. GH deficiency;
2. Malnutrition;
3. Hypothyroidism;
4. Chronic treatment with pharmacologic doses of anti-inflammatory steroids.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
GH: growth hormone
IGF-1: insulin-like growth factor -1
IGFD: insulin-like growth factor deficiency
SD: standard deviation

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - In pediatric patients with malignant neoplasia or a history of malignancy. Therapy should be discontinued if evidence of malignancy develops
  - Known hypersensitivity to mecasermin
  - Intravenous administration
  - In patients with closed epiphyses for growth promotion
- Boxed warning(s): none reported

*Appendix D: Primary IGF-1 Deficiency**

- Causes:
  - 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, IGF-1 levels are normal or elevated in the case of IGF-1 receptor mutations 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.*

Appendix E: General Information

- Severe Primary IGFD includes patients with mutations in the growth hormone receptor (GHR), post-GHR signaling pathway, and IGF-1 gene defects; they are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment.
- 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 treatment.

- Increlex is not a substitute for GH treatment.
- Failure to increase height velocity during the first year of therapy by at least 2 cm/year suggests the need for assessment of compliance and evaluation of other causes of growth failure, such as hypothyroidism, under-nutrition, and advanced bone age.
- CDC recommended growth charts, data tables, and related information that may be helpful in assessing length, height and growth are available at the following link: https://www.cdc.gov/growthcharts/clinical_charts.htm.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Growth failure in children with severe primary IGFD or with GH gene deletion who have developed neutralizing antibodies to GH	Initial dose: 0.04 mg/kg to 0.08 mg/kg (40 mcg/kg to 80 mcg/kg) SC BID. Dose may be increased by 0.04 mg/kg (40 mcg/kg) per dose up to 0.12 mg/kg (120 mcg/kg) SC BID	0.12 mg/kg per dose

VI. Product Availability

Multi-dose vial: 40 mg/4 mL (10mg/mL)

VII. References

1. Increlex Prescribing Information. Cambridge, MA: Ipsen Bipharmaceuticals, Inc.; December 2019. Available at: http://www.increlex.com/pdf/patient-full-prescribing-information.pdf. Accessed April 7, 2023.
2. Grimberg A, DiVall SA, Polychronakos C, et al. Guidelines for growth hormone and insulin-like growth factor-1 treatment in children and adolescents: growth hormone deficiency, idiopathic short stature, and primary insulin-like growth factor-1 deficiency. Horm Res Paediatr 2016;361-397. DOI: 10.1159/000452150.
3. 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.
4. 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.

Auxology for acquired GH insensitivity

5. WHO Child Growth Standards: Length/Height-for-Age, Weight-for-Age, Weight-for-Length, Weight-for-Height and Body Mass Index-for-Age: Methods and Development. Geneva, Switzerland: World Health Organization; 2006. As cited in CDC. Division of Nutrition, Physical Activity, and Obesity. Growth Chart Training: Using the WHO Growth Charts. Page last reviewed April 15, 2015. Available at https://www.cdc.gov/nccdphp/dnpao/growthcharts/who/using/assessing_growth.htm. Accessed April 7, 2023.

6. Haymond M, Kappelgaard AM, Czernichow P, et al. Early recognition of growth abnormalities permitting early intervention. Acta Pædiatrica ISSN 0803-5253. April 2013. DOI:10.1111/apa.12266.
7. Rogol AD, Hayden GF. Etiologies ad early diagnosis of short stature and growth failure in children and adolescents. J Pediatr. 2014 May;164(5 Suppl):S1-14.e6. doi: 10.1016/j.jpeds.2014.02.027.
8. 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.
9. Centers for Disease Control and Prevention, National Center for Health Statistics. CDC growth charts: United States. http://www.cdc.gov/growthcharts/. Accessed April 7, 2023.

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
revised positive response to therapy and increased initial approval duration from 6 months to 12 months and added requirement for baseline height. Removed requirements to correct nutritional or thyroid deficiencies if present; references reviewed and updated.	05/2018	
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/2019	
3Q 2020 annual review: open epiphyses added; auxology updated for acquired GH insensitivity to reconcile with somatropin policy; malignancy contraindication added; positive response removed in deference to growth criteria; references reviewed and updated.	07/2020	
3Q 2021 annual review: no significant changes; references reviewed and updated.	07/2021	
3Q 2022 annual review: no significant changes; references reviewed and updated.	07/2022	
3Q 2023 annual review: added Diagnoses/Indications for which coverage is NOT authorized: Secondary forms of IGF-1 deficiency; references reviewed and updated.	07/2023	