

## Clinical Policy: Mecasermin (Increlex)

Reference Number: PA.CP.PHAR.150

Effective Date: 01/2018

Last Review Date: 07/2024

### Description

Mecasermin (Increlex<sup>®</sup>) 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  $\leq -3.0$  and basal IGF-1 standard deviation score  $\leq -3.0$  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  $\geq 2$  and  $< 18$  years;
4. If age  $> 10$  years, open epiphysis on x-ray;
5. IGF-1 serum level is  $\geq 3$  standard deviations (SD) below the mean;
6. GH serum level is normal or elevated;
7. Height is  $\geq 3$  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. Increlex is not prescribed concurrently with growth hormone(e.g., Somatropin and Skytrofa<sup>®</sup> [recombinant human GH], Sogroya<sup>®</sup> and Ngenla<sup>™</sup> [human GH]);
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  $\geq 2$  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. Increlex is not prescribed concurrently with growth hormone (e.g., Somatropin and Skytrofa [recombinant human GH], Sogroya and Ngenla [human GH]);
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  $\geq 1$  year, height has increased  $\geq 2$  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. Increlex is not prescribed concurrently with growth hormone (e.g., Somatropin and Skytrofa [recombinant human GH], Sogroya and Ngenla [human GH]);
- 5.
6. 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](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:<br>0.04 mg/kg to 0.08 mg/kg (40 mcg/kg to 80 mcg/kg) SC BID.<br><br>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.; March 2024. Available at: <http://www.increlex.com/pdf/patient-full-prescribing-information.pdf>. Accessed May 10, 2024.
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 January 13, 2022. Available at [https://www.cdc.gov/nccdphp/dnpao/growthcharts/who/using/assessing\\_growth.htm](https://www.cdc.gov/nccdphp/dnpao/growthcharts/who/using/assessing_growth.htm). Accessed May 23, 2024.
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. Available at: <http://www.cdc.gov/growthcharts/>. Accessed May 23, 2024.

**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    |
|---|---------|
| 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 |

**CLINICAL POLICY**

**Mecasermin**



| <b>Reviews, Revisions, and Approvals</b>   | <b>Date</b> |
|--|-------------|
| 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     |
| 3Q 2024 annual review: revised verbiage that Increlex is not prescribed concurrently with growth hormone (previously only Somatropin was included); references reviewed and updated. | 07/2024     |