Clinical Policy: Mecasermin (Increlex)

Reference Number: CP.PHAR.150
Effective Date: 03.01.11
Last Review Date: 08.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® 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 IGFD;
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. 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:
Medicaid/HIM – 12 months or up to age 18 years, whichever is shorter
Commercial – 6 months or to the member's renewal date, whichever is longer

B. 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:
Medicaid/HIM – 6 months or up to age 18 years, whichever is shorter
Commercial – 6 months or to the member's renewal date, whichever is longer

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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:
Medicaid/HIM – 12 months or up to age 18 years, whichever is shorter
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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
  - 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.

**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/index.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 (10 mg/mL)

VII. References

1. Increlex Prescribing Information. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; December 2019. Available at: http://www.increlex.com/pdf/patient-full-prescribing-information.pdf. Accessed April 12, 2022.
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 12, 2022.

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 12, 2022.

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	P&T Approval Date
3Q 2018 annual review: policies combined Centene Commercial and Medicaid lines of business; added HIM line of business; added contraindicated states to section III; revised positive response to therapy and increased initial approval duration from 6 months to 12 months to align with somatropin policy and added requirement for baseline height; Medicaid: removed requirements to correct nutritional or thyroid deficiencies if present; Commercial: added prescriber requirement, age requirement, and evidence for diagnosis; removed documentation of compliance with therapy for continued approval; added requirement that rhGH is not concomitantly used; references reviewed and updated.	05.15.18	08.18
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.21.19	08.19
3Q 2020 annual review: HIM non-formulary language removed; 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.	06.02.20	08.20
3Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	03.23.21	08.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2022 annual review: no significant changes; references reviewed and updated.	04.12.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.30.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.