RXADVANCE
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Clinical Policy Title:	mecasermin
Policy Number:	RxA.171
Drug(s) Applied:	Increlex®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

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

Increlex is indicated for the treatment of growth failure in pediatric patients 2 years of age and older with severe primary IGF-1 deficiency (IGFD) or with 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Mecasermin (Increlex)	Growth failure in children with severe primary IGF-1 deficiencyor with GH gene deletion who have developed neutralizing antibodies to GH	Initial dose: 40 mcg/kg to 80 mcg/kg SC BID. Dose may be increased by 40 mcg/kg per dose up to 120 mcg/kg SC BID	0.12 mg/kg per dose

Dosage Forms

- Multi-dose vial: 10 mg per mL (40 mg per vial).

Clinical Policy

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

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) and associated growth failure as evidenced by all of the following (a, b, and c):
    a. Basal IGF-1 is ≥ 3 standard deviations (SD) below the mean;
    b. Normal or elevated GH level;
    c. Height is ≥ 3 SD below the mean;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 2 and < 18 years;
4. Documentation of baseline height is provided at the time of request;
5. Somatropin (recombinant human GH)) is not prescribed concurrently with Increlex;
6. Dose does not exceed 0.12 mg per kg twice daily.

Approval Duration
Commercial: 6 months
Medicaid: 12 months
HIM: 6 months

B. **Growth Hormone Insensitivity** (must meet all)**:**
1. Diagnosis of acquired GH insensitivity as evidenced by both of the following (a and b):
    1. Documentation of genetic GH deficiency due to a GH gene deletion;
    2. Documentation of presence of neutralizing GH antibodies;
2. Age ≥ 2 and < 18 years;
3. Prescribed by or in consultation with an endocrinologist;
4. Documentation of growth failure as indicated by any of the following (a, b, c, d, or e):
    1. Height > 3 SD below the mean;
    2. Height > 2 SD below the mean and one of the following (i or ii):
        a. Height velocity > 1 SD below the mean over 1 year;
        b. Decrease in height SD > 0.5 over 1 year in children > 2 years of age;
    3. Height > 1.5 SD below midparental height;
    4. Height velocity > 2 SD below the mean over 1 year;
    5. Height velocity > 1.5 SD below the mean over 2 years;
5. Documentation of baseline height is provided at the time of request;
6. Somatropin (recombinant human GH) is not prescribed concurrently with Increlex;
7. Dose does not exceed 0.12 mg per kg twice daily.

Approval Duration
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If member has received treatment for ≥ 1 year, height velocity is currently > 2 cm per year;
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
Commercial: 12 months
Medicaid: 6 months
HIM: 12 months

III. Appendices

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
None

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

APPENDIX D: General Information
Primary IGF-1 Deficiency (i.e., Inherited Growth Hormone Insensitivity) *

- 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.
- Definition:
  - Height standard deviation score less than or equal to –3.0 and
  - Basal IGF-1 standard deviation score less than or equal to –3.0 and
  - Normal or elevated growth hormone (GH).

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

- 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.
- Clinical growth charts with 5th & 95th percentiles and 3rd & 97th percentiles are published by the Centers for Disease Control and Prevention (CDC) website:

https://www.cdc.gov/growthcharts/clinical_charts.htm.

References

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3. Grimberg A, DiVall SA, Polychronakos C, et al. Growth Hormone Treatment for Growth Hormone Deficiency and Idiopathic Short Stature: New Guidelines Shaped by the Presence and Absence of Evidence. Curr Opin Pediatr. 2017 Aug; 29(4): 466–471. doi: 10.1097/MOP.0000000000000505
4. 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.
5. 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.
6. 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.
7. 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. Accessed July 9,2020.
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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: **1.** Policy description table was updated	07/09/2020	09/14/2020

2. Background indication updated to include “pediatric patients 2 years of age and older” 3. Dosage form updated 4. Initial therapy and continued therapy approval duration for HIM was added 5. Continuation therapy criteria II.A.1. was repharsed to” criteriaMember is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy”Appendix C was updated to include malignant neoplasm 6. References were updated		