

Clinical Policy Title:	mecasermin
Policy Number:	RxA.171
Drug(s) Applied:	Increlex®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
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 deficiency or with GH gene deletion who have developed neutralizing antibodies to GH	Initial dose: 40 mcg/kg to 80 mcg/kg SC twice daily Dose may be increased by 40 mcg/kg per dose up to 120 mcg/kg SC twice daily	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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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;

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

- 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

B. Growth Hormone Insensitivity (must meet all):

1. Diagnosis of acquired GH insensitivity as evidenced by both of the following (a and b):
 - a. Documentation of genetic GH deficiency due to a GH gene deletion;
 - b. 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):
 - a. Height > 3 SD below the mean;
 - b. Height > 2 SD below the mean and one of the following (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;
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

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

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.
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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: <ol style="list-style-type: none"> 1. Policy description table was updated. 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 rephrased to “criteriaMember is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval 	07/09/2020	09/14/2020

<p>criteria listed in this policy”Appendix C was updated to include malignant neoplasm.</p> <p>6. References were updated.</p>		
<p>Policy was reviewed:</p> <ol style="list-style-type: none"> 1. Dosing frequency abbreviations were expanded. 2. Clinical policy section standard verbiage was updated to include “The provision of prescriber samples...”. 3. References reviewed and updated. 	<p>03/31/2021</p>	<p>06/10/2021</p>