

Drug and Biologic Coverage Policy



Effective Date..... 8/1/2020

Next Review Date..... 8/1/2021

Coverage Policy Number 6107

Mecasermin

Table of Contents

Coverage Policy.....	1
FDA Approved Indications	2
Recommended Dosing	3
General Background	3
Coding/Billing Information	4
References	4

Related Coverage Resources

[Somatropin](#)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

Mecasermin (Increlex®) is considered medically necessary for EITHER of the following:

- For the treatment of growth failure in children with **Severe Primary Insulin-like Growth Factor-1 (IGF-1) Deficiency** and **ALL** of the following criteria are met:
 - Child is 2 years of age or older
 - Height score less than or equal to 3.0 standard deviations below the mean
 - Basal IGF-1 score less than or equal to 3.0 standard deviations below the mean
 - Normal or elevated growth hormone (GH)
 - No concurrent treatment with growth hormone for Growth Hormone Deficiency (GHD)
 - Bony epiphyses are open

Note: Severe-primary IGF-1 deficiency includes patients with mutations in the GH receptor (GHR), post-GHR signaling pathway including the IGF-1 genes.

- For the treatment of growth failure in children with **Growth Hormone (GH) Gene Deletion with Development of Neutralizing Antibodies to GH** and **ALL** of the following criteria are met:
 - Child is 2 years of age or older
 - Individual has a diagnosis of growth hormone (GH) gene deletion and has developed neutralizing antibodies to GH

- No concurrent treatment with growth hormone for Growth Hormone Deficiency (GHD)
- Bony epiphyses are open

Mecasermin (Increlex®) is considered NOT medically necessary for the following use:

- Idiopathic (unknown origin) Short Stature, also called non-growth hormone deficient short stature in children

Initial authorization is up to 12 months.

Mecasermin (Increlex®) is considered medically necessary for continued use when the following criteria are met:

- Initial criteria have been met
- Documented beneficial clinical response as evidenced by growth curve chart
- Bony epiphyses remain open in order to continue coverage for growth promotion
- No concurrent treatment with growth hormone for Growth Hormone Deficiency (GHD)

Reauthorization is up to 12 months.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Mecasermin (Increlex®) is considered experimental, investigational or unproven for ANY other use including the following:

- Amyotrophic Lateral Sclerosis (ALS)
- Autism Spectrum Disorder
- Bone loss associated with Anorexia
- Phelan- McDermid Syndrome
- Prevention of Retinopathy of Prematurity
- Rett Syndrome
- Treatment of secondary forms of IGF-1 deficiency such as chronic treatment with pharmacologic doses of anti-inflammatory drugs, GH deficiency, hypothyroidism, or malnutrition

Note: Receipt of sample product does not satisfy any criteria requirements for coverage

FDA Approved Indications

FDA Approved Indication

Increlex® is indicated for the treatment of growth failure in pediatric patients 2 years of age and older with:

- severe primary IGF-1 deficiency or
- growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH.

Severe Primary IGF-1 deficiency (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).

Limitations 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 IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory corticosteroids.

Severe primary IGFD includes classical and other forms of growth hormone insensitivity. Patients with primary IGFD may have mutations in the GH receptor (GHR), post-GHR signaling pathway including the IGF-1 gene. 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 Increlex treatment.

Recommended Dosing

FDA Recommended Dosing

- Treatment with Increlex® should be supervised by a physician who is experienced in the diagnosis and management of pediatric patients with short stature associated with severe primary IGF-1 deficiency or with growth hormone gene deletion and who have developed neutralizing antibodies to growth hormone.
- The dosage of Increlex® should be individualized for each patient. The recommended starting dose of Increlex® is 0.04 to 0.08 mg/kg (40 to 80 micrograms/kg) twice daily by subcutaneous injection. If well-tolerated for at least one week, the dose may be increased by 0.04 mg/kg per dose, to the maximum dose of 0.12 mg/kg given twice daily [see *Warnings and Precautions* (5.1 and 5.7)]
- Pre-prandial glucose monitoring is recommended at treatment initiation and until a well-tolerated dose is established. If frequent symptoms of hypoglycemia or severe hypoglycemia occur, pre-prandial glucose monitoring should continue. If hypoglycemia occurs with recommended doses despite adequate food intake, the dose should be reduced. Increlex® should be administered shortly before or after (\pm 20 minutes) a meal or snack. If the patient is unable to eat shortly before or after a dose for any reason, that dose of Increlex® should be withheld.
- If one or more doses of Increlex® is missed, do not increase the subsequent doses to make up for omitted doses.

General Background

Disease Overview

IGF-1 (insulin-like growth factor-1) is the principal hormonal mediator of growth hormone action. Under normal circumstances, GH binds to its receptor in the liver and other tissues and stimulates the synthesis/secretion of IGF-1. In target tissues, the Type 1 IGF-1 receptor, which is homologous to the insulin receptor, is activated by IGF-1, leading to intracellular signaling which stimulates multiple processes leading to stature growth. The metabolic actions of IGF-1 are in part directed at stimulating the uptake of glucose, fatty acids, and amino acids so that metabolism supports growing tissues. Primary IGFD is a group of disorders characterized by decreased IGF production with normal or increased GH secretion. Three distinct molecular abnormalities have been identified as causes of primary IGFD: 1) mutations or gene deletions of the GH receptor gene; 2) mutations affecting the post- GH receptor (GHR) signaling cascade, as observed in a patient homozygous for a point mutation of the gene for signal transducer and activator of transcription (STAT)-5b; and 3) mutations or deletions of the gene for IGF-1. These patients are not GH deficient, and do not respond adequately to exogenous GH treatment. Once a diagnosis of severe primary IGFD is made, treatment is recommended as soon as possible. Growth rates are highest during the first year of treatment and both first year catch-up growth and long-term outcomes are improved when initiated in younger children. (Cohen, 2014; Rosenfeld, 2005)

Professional Societies/Organizations

Pediatric Endocrine Society

The Pediatric Endocrine Society provides guidance regarding the use of IGF-1 therapy to increase height in patients with severe Primary Insulin-like Growth Factor Deficiency and administering IGF-1 20 minutes after a carbohydrate-containing meal or snack. In addition, the guideline recommends a trial of GH therapy before initiating IGF-1 for patients with unexplained IGF-1 deficiency. This recommendation, however, is not supported by clinical trial evidence. Patients with hormone signaling defects known to be unresponsive to GH treatment can start directly on IGFI replacement; these include patients with very low or undetectable levels of GHBP and/or

proven GHR gene mutations known to be associated with Laron syndrome/ GHIS, GH-neutralizing antibodies, STAT5b gene mutations, and IGF1 gene deletion or mutation. (Grimberg, 2016)

The American Board of Internal Medicine's (ABIM) Foundation Choosing Wisely® Initiative:
No recommendations are available for mecasermin (Increlex®).

Other Uses with Supportive Evidence

AHFS Drug Information 2020 Edition does not support any off-label uses of mecasermin (Increlex®).

Experimental, Investigational, Unproven Uses

Mecasermin (Increlex®) has also been studied in a limited number of patients for treating: Autism Spectrum Disorder, bone loss associated with anorexia, Phelan-McDermid Syndrome, prevention of retinopathy of prematurity, Rett Syndrome, and Amyotrophic Lateral Sclerosis. (Borasio, 1998; Kolevzon, 2014; Ley D, 2019; Misra, 2009; Mitchell, 2007; O'leary, 2018) At this time there is insufficient or no published evidence to support use of mecasermin (Increlex®) in these conditions.

Compendia and other published clinical studies do not currently support any uses other than the FDA indication. Criteria will be updated as new published data are available.

Coding/Billing Information

Note: Mecasermin (Increlex®) is typically covered under pharmacy benefit plans. Certain prescription drugs require an authorization for coverage to ensure that appropriate treatment regimens are followed. Medical drug coding and diagnosis codes, however, are generally not required for pharmacy claims submissions, therefore, this section is not in use.

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