



MEDICAL COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 08/29/08
LAST REVIEW DATE: 03/04/14
LAST CRITERIA REVISION DATE: 03/04/14
ARCHIVE DATE:

INCRELEX® (mecasermin)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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Description:

Increlex (mecasermin) is an injectable solution of human insulin-like growth factor-1 produced by recombinant DNA technology. Increlex is used for the treatment of growth failure in children with severe primary insulin-like growth factor (IGF-1) deficiency, also referred to as primary IGFD. These children have normal or elevated levels of growth hormone but due a deficiency of IGF-1, are unable to utilize the growth hormone resulting in extremely short stature.

Severe primary IGF-1 deficiency is defined by:

- Height standard deviation score less than or equal to -3.0 for age and sex of the individual
- Basal IGF-1 standard deviation score less than or equal to -3.0 for age and sex of the individual
- Normal or elevated growth hormone

Increlex is also used in children with a growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH.

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INCRELEX (mecasermin) (cont.)

Criteria:

- Increlex in individuals 2 through 17 years of age* with the growth hormone gene deletion who have developed neutralizing antibodies to growth hormone is considered **medically necessary** with documentation of **ALL** of the following:
 1. Growth hormone levels are normal or low
 2. IGF-1 levels are on the lowest 25% of reference laboratory's range**
 - Increlex for the long-term treatment of growth failure in individuals 2 through 17 years of age* with severe primary IGF-1 deficiency is considered **medically necessary** with documentation of **ALL** of the following:
 1. Normal or elevated growth hormone level
 2. Height standard deviation score equal to or less than -3.0 for age and sex of the individual
 3. Basal IGF-1 standard deviation score equal to or less than -3.0 for age and sex of the individual**
 4. No evidence of **ANY** of the following:
 - Closed epiphyses (growth plates)
 - Active or suspected neoplasia
 - Chromosome aberrations
 - Chronic disease
 - Malnutrition
 - Pituitary tumors
 - Secondary forms of IGF deficiency (e.g., growth hormone deficiency, hypothyroidism, chronic treatment with systemic anti-inflammatory steroids)
 5. Dosage is not greater than 0.04 to 0.08 mg/kg (40 to 80 µ/kg) twice daily given subcutaneously for at least one week and, if well tolerated, increased by 0.04 mg/kg per dose to the maximum dose of 0.12 mg/kg given subcutaneously twice daily
- * Increlex has not been studied in children less than 2 years of age or in adults.
- ** The laboratory performing the test should include their specific reference range for age and sex of the individual to determine the basal serum IGF-1 level deviation.
- *** Review by the clinical pharmacist and/or medical director(s) and/or clinical advisor(s) is required if medication dosages differ from those listed above.



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INCRELEX (mecasermin) (cont.)

Criteria: (cont.)

- Increlex for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:
1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
 2. Insufficient evidence to support improvement of the net health outcome, and
 3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives.

Resources:

1. CenterWatch. Drugs Approved by the FDA Drug Name: Increlex (mecasermin). Updated 06/20/2008
2. Lewis ME, Neff NT, Contreras PC, et al. Insulin-like growth factor-I: potential for treatment of motor neuronal disorders. *Exp Neurol*. 1993 Nov;124(1):73-88
3. Mohamed-Ali V, Pinkney J. Therapeutic potential of insulin-like growth factor-1 in patients with diabetes mellitus. *Treat Endocrinol*. 2002;1(6):399-410
4. Tercica, Inc. Increlex Efficacy. Accessed 08/25/2008
5. Williams RM, McDonald A, O'Savage M, Dunger DB. Mecasermin rinfabate: rhIGF-I/rhIGFBP-3 complex: iPLEX. *Expert Opin Drug Metab Toxicol*. 2008 Mar;4(3):311-324
FDA Product Approval Information for Increlex:

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INCRELEX (mecasermin) (cont.)

Resources: (cont.)

FDA Product Approval Information for Increlex:–

- FDA-approved indication: INCRELEX (mecasermin [rDNA origin] injection) is indicated for the treatment of growth failure in children with severe primary IGF-1 deficiency (Primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH. Severe Primary 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). 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. INCRELEX is not a substitute for GH treatment.

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INCRELEX (mecasermin) (cont.)

Resources: (cont.)

FDA Product Approval Information for Increlex: (cont.)

- FDA-approved dosage: Preprandial glucose monitoring is recommended at treatment initiation and until a well tolerated dose is established. If frequent symptoms of hypoglycemia or severe hypoglycemia occur, preprandial glucose monitoring should continue. 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 µg/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. Doses greater than 0.12 mg/kg given twice daily have not been evaluated in children with Primary IGFD and, due to potential hypoglycemic effects, should not be used. 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. Subsequent doses of INCRELEX should never be increased to make up for one or more omitted dose.