



Prior Authorization Approval Criteria
Department of Pharmacy Services

Generic Name: mecasermin

Brand Name: Increlex

Medication Class: insulin-like growth factor (IGF-1)

FDA Approved Uses: 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.

Available Dosage Forms: 10mg/ml multi-dose vial (40mg/vial)

Usual Dose: starting dose: 0.04 to 0.08mg/kg SC twice daily; maximum dose: 0.12mg/kg twice daily.

NOTE: Increlex should be administered shortly before or after (\pm 20 minutes) a meal or snack, because it has insulin-like hypoglycemic effects. Patient should avoid engaging in any high-risk activities within 2 – 3 hours after dosing, particularly at the initiation of treatment, until a well-tolerated dose has been established. Increlex should not be administered when the meal or snack is omitted. The dose of Increlex should never be increased to make up for one or more omitted doses. Increlex should be initiated at a low dose and the dose should be increased only if no hypoglycemic episodes have occurred after at least 7 days of dosing. If severe hypoglycemia or persistent hypoglycemia occurs on treatment despite adequate food intake, Increlex dose reduction should be considered. Patients and caregivers should be educated on how to recognize and treat the signs and symptoms of hypoglycemia.

Storage: Before opening: store refrigerated (2° to 8°C or 35° to 46°F)
After opening: stable for 30 days when refrigerated (2° to 8°C or 35° to 46°F). Discard after 30 days.

Duration of Therapy: until epiphyses close or patient no longer responds to treatment

Criteria for Use: (bullet points below are all inclusive unless otherwise noted)

- Prescribed by endocrinologist only
- Other reasons for short stature have been ruled out, such as hypothyroidism, chronic system disease, chronic illnesses, skeletal disorders, and medications.
- Must be child 2 years of age or older
- Must have documented severe primary IGF-1 deficiency or GH gene deletion with neutralizing antibodies to GH.



- Must have short stature with a height less than or equal to 3 standard deviations below the mean for age and gender.
- Must have an IGF-1 less than or equal to 3 standard deviations below the mean for age and gender.
- Must have normal or elevated growth hormone levels (for Primary IGFD):
 - normal response to at least one provocative stimuli of GH release.
- Must have IGFBP-3 levels below the normal for age and gender, based on specific lab reference values
- Predicted adult height more than 1.5 standard deviations below the mid-parental height.
- Documentation of bone age (radiograph).
- Clinically determined growth failure as defined by a growth rate velocity $< 2.5\text{cm/year}$
Note: During puberty normal growth is about 7-10 cm/year and after puberty about 1-3 cm/year.
- Patient and caregivers must be able to understand and comply with dosing and the possibility of hypoglycemia (signs, symptoms and treatment)

Criteria for Continuation of Therapy:

- Epiphysis must not be closed.
- Growth rate velocity must be equal to or greater than 2.5cm/year
Note: Should see a doubling of pretreatment growth rate or an increase of 3cm/yr or more in the first year and 2.5 cm/yr thereafter.

Monitoring:

- Patients and caregivers should be aware of the signs and symptoms of hypoglycemia. Hypoglycemia frequency was highest in the first month of therapy, and episodes were more frequent in younger children. Symptomatic hypoglycemia was generally avoided when a meal or snack was consumed ± 20 minutes from time of administration. If patient is unable to eat for any reason, that Increlex dose should be withheld. Subsequent doses should never be increased to make up for an omitted dose.
- Pre-prandial glucose monitoring should be considered 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.
- Treatment of acute overdose should be directed at reversing hypoglycemia. Oral glucose or food should be consumed. If the overdose results in loss of consciousness, IV glucose or parenteral glucagon may be required.
- If patient is on insulin or anti-diabetes medications, dose adjustments for these medications may be necessary.
- Thyroid function tests about every 6 months
- Glucose tolerance / diabetes testing
- Periodic monitoring for intracranial hypertension
- Periodic examinations to rule out lymphoid tissue (e.g., tonsillar) hypertrophy
- If patient has history of scoliosis, then monitor for progression of scoliosis
- Monitor for malignant transformation of skin lesion
- Monitor for slipped capital femoral epiphysis
- Monitor for thickening of the soft tissues of the face

Contraindications:

- sensitivity to product
- active or suspected neoplasia



- Intravenous administration
- closed epiphysis

Not approved if:

- Patient is not a child
- Patient has secondary forms of IGF-1 deficiency, such as GH deficiency, malnutrition, hypothyroidism, or chronic treatment with pharmacologic doses of anti-inflammatory steroids. Increlex is not a substitute for GH treatment.
- Being used for antiaging
- Being used for performance-enhancement for athletes
- Patient has any contraindications to the use of Increlex.
- Patient has delayed puberty, growth hormone insufficiency-associated dwarfism, renal failure associated IGF-1 deficiency, adult IGF-1 deficiency, type 2 diabetes with severe insulin resistance.
- Patient does not meet above criteria

Notes:

Provocative tests of growth hormone stimulation include arginine, clonidine, glucagon, insulin, and levodopa. Peak GH level must be adjusted if monoclonal-based assay or recombinant human GH reference preparations are used, based upon specific lab reference values.

Note: IGF-1 can be low due to other conditions such as psychosocial deprivation, malnutrition, or hypothyroidism. IGF may be normally low in infants and young children. IGFBP-3 is less nutrition dependent than IGF.

ng/ml = mcg/L

P&T Approval: _____ Date: _____