Pharmacy Medical Necessity Guidelines: Increlex® (mecasermin)

Effective: August 7, 2018

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<th>Prior Authorization Required</th>
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Pharmacy (RX) or Medical (MED) Benefit

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This Pharmacy Medical Necessity Guideline applies to the following:

- Tufts Health Plan Commercial Plans
  - Tufts Health Plan Commercial Plans – large group plans
  - Tufts Health Plan Commercial Plans – small group and individual plans
- Tufts Health Public Plans
  - Tufts Health Direct – Health Connector
  - Tufts Health Together – A MassHealth Plan
  - Tufts Health RITogether – A Rite Care + Rhody Health Partners Plan
- Tufts Health Freedom Plan products
  - Tufts Health Freedom Plan – large group plans
  - Tufts Health Freedom Plan – small group plans

Fax Numbers:

- RXUM: 617.673.0988

Note: For Tufts Health Plan Medicare Preferred Members, please refer to the Tufts Health Plan Medicare Preferred Prior Authorization Criteria. Background, applicable product and disclaimer information can be found on the last page.

OVERVIEW

FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS

Increlex (mecasermin) is indicated for the long-term 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, basal IGF-1 standard deviation score ≤ -3.0, and normal or elevated GH.

Severe Primary IGFD includes classical and other forms of GH insensitivity. Patients with Primary IGFD may have mutations in the GH receptor (GHR), post-GHR signaling pathway including IGF-1 gene. They are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment. Increlex (mecasermin) 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 (mecasermin) treatment.

Increlex (mecasermin) is not a substitute to GH for approved GH indications.

Insulin like growth factors (IGF) are low molecular weight peptides produced by hepatocytes under the influence of growth hormone (GH). IGF are GH-dependent with IGF1 being more influenced by GH than IGF2. Factors other than GH (age, pubertal status, nutritional status and liver functions) also affect IGF production. IGF1 levels are 50% of adult levels at birth and increase gradually to adult levels at the onset of puberty. There is an exponential increase in IGF1 levels during puberty (up to two-to-three times the adult levels) followed by a gradual decline.

Most growth-promoting effects of IGF are mediated by the type 1 IGF receptor. The type 1 IGF receptor has been identified in most body systems including brain, testes, liver, and bones suggesting important paracrine and endocrine roles of IGF. Insulin binds to the type 1 IGF receptor (although with lower potency compared to IGF1 and 2), a fact that explains growth-promoting effect of the hormone. IGF, on the other hand, binds the insulin receptor and shares its hypoglycemic effect. IGF differs from insulin in having large circulatory binding proteins. These proteins are involved in regulation of delivery and metabolism of IGF. The insulin-like growth factor binding protein (IGFBP) system is widely distributed in the body and controls paracrine actions of IGF.

Children with growth hormone insensitivity syndrome GHIS have phenotypic features of growth hormone deficiency (GHD) in the wake of elevated GH levels. GH provocation tests are of no value in these settings, and IGF-based tests are clearly the investigations of choice. GHIS is diagnosed in the presence of growth retardation (height < -3 SDS for age), low IGFI and IGFBP3 (< -3 SDS for age), elevated basal GH (> 5 ng/mL), and lack of increase in IGF1 following administration of GH (peak levels < 15 ng/mL). IGF generation test, the assessment of increase in IGF 1 following administration of GH, is considered the gold standard for the diagnosis of GHIS.
Elevated GH levels in the presence of hyperglycemia have been traditionally used for the diagnosis of GH excess. IGF1 and IGFBP3 levels are good indicators of GH excess, and should be employed as screening tests for the diagnosis of the condition. High IGF1 levels and IGFBP3 should be followed up with glucose suppression test.

IGF1 is the only treatment option in GHIS where GH is ineffective. Successful induction of hypoglycemia with IGF1 in individuals with GHIS not only demonstrated preserved responsiveness to the peptide in GHIS but also provided an option for treatment of the condition. The benefits of IGF1 therapy in GHIS are not restricted to growth, but also include improvement in bone mineral density, body composition and insulin resistance. Growth response to IGF1 in GHIS is, however, lower than that following GH treatment in GHD. This relative 'IGF1 insensitivity' may be caused by low IGFBP3 levels in GHIS resulting in faster metabolism of IGF1.

**COVERAGE GUIDELINES**
The plan may authorize coverage of Increlex (mecasermin) for Members age 2 to 18 years if all of the following criteria are met:

1. Documented diagnosis of one of the following:
   a. Severe primary insulin-like growth factor-1 (IGF-1) deficiency (primary IGFD) as defined by all of the following:
      • A height standard deviation score less than or equal to -3.0
      • A basal IGF-1 standard deviation score less than or equal to -3.0
      • Normal or elevated growth hormone level
      OR
   b. Growth hormone (GH) gene deletion and has developed neutralizing antibodies to GH
   AND
2. Member must be evaluated, and therapy must be prescribed and monitored by a pediatric endocrinologist
   AND
3. Radiographs documenting open epiphyses are required for Members who are Tanner stage III or greater

**LIMITATIONS**
1. Initial authorization will be provided for a six-month period. Subsequent authorization will require at least a doubling of the pretreatment annualized growth rate. Annual authorization, thereafter, will require evidence that the epiphyses remain open, and that the Member has grown at least three centimeters over the previous year.
2. The plan does not provide coverage of Increlex (mecasermin) for conditions resulting in secondary forms of IGF-1 deficiency that include, but are not limited to, the following:
   • Growth hormone deficiency
   • Malnutrition
   • Hypothyroidism
   • Chronic steroid therapy

**CODES**
Medical billing codes may not be used for these medications. These medications must be obtained via the Member’s pharmacy benefit.

**REFERENCES**
APPRAISAL HISTORY
August 8, 2006: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:
- December 12, 2006: Removed IPLEX® (mecasermin rinfabate) from title and pharmacy coverage guidelines. Added, “Tufts Health Plan does not cover IPLEX® (mecasermin rinfabate)” to the limitations section.
- November 13, 2007: No changes
- November 11, 2008: No changes
- November 10, 2009: Removed non-covered IPLEX® (mecasermin rinfabate) from limitations section of medical necessity guidelines as product has been discontinued.
- September 14, 2010: No changes
- September 13, 2011: No changes
- September 11, 2012: No changes
- August 6, 2013: No changes
- August 12, 2014: No changes
- August 11, 2015: No changes
- January 1, 2016: Administrative change to rebranded template.
- August 9, 2016: No changes
- August 8, 2017: No changes
- August 7, 2018: No changes. Administrative update to move information about initial and subsequent approval requirements to the Limitations section.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION
Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. They are used in conjunction with a Member’s benefit document and in coordination with the Member’s physician(s). The plan makes coverage decisions on a case-by-case basis considering the individual Member’s health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

This Pharmacy Medical Necessity Guideline does not apply to Uniformed Services Family Health Plan Members or to certain delegated service arrangements. Unless otherwise noted in the Member’s benefit document or applicable Pharmacy Medical Necessity Guideline, Pharmacy Medical Necessity Guidelines do not apply to CareLinkSM Members. For self-insured plans, drug coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a coverage guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern. Applicable state or federal mandates will take precedence.

For Tufts Health Plan Medicare Preferred, please refer to Tufts Health Plan Medicare Preferred Prior Authorization Criteria.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to Member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.

Provider Services