BlueCross BlueShield of Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

Increlex® (mecasermin)

Policy Number: 5.02.507
Origination: 12/2006
Last Review: 12/2013
Next Review: 12/2014

Policy

BCBSKC will provide coverage for Increlex® (mecasermin) when it is determined to be medically necessary because the criteria shown below have been met.

When Policy Topic is covered

Increlex® therapy may be considered medically necessary for the treatment of growth failure in children with severe primary insulin-like growth factor-1 deficiency (IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH. These medications will be considered for coverage for children when all of the following criteria have been met:

- Basal IGF-1 and insulin-like growth factor binding protein-3 (IGFBP-3) standard deviation score less than or equal to -3.0 for age and gender,
- Normal or elevated GH,
- Height less than the 3rd percentile for normal or 2 standard deviations below the 50th percentile for age and gender [1],
- Growth velocity less than the 10th percentile of normal as tracked over at least one year,
- Evidence that the patient does not have other reasons for short stature.

Increlex® is administered by twice-daily subcutaneous injections. The recommended dosage is 60 mcg/kg to 120 mcg/kg. Doses beyond this have not been proven to be clinically effective and, therefore, are not considered to be medically necessary.

Recommended starting dose is 40 mcg/kg to 80mcg/kg. If the dose is well tolerated for at least one week, the dose may be increased by 40mcg/kg per dose to the maximum dose of 120 mcg, twice daily. The dosage of Increlex® should be individualized for each patient.

Treatment may continue until target height is obtained or until epiphyses are closed.

Failure to increase height velocity during the first year of therapy by at least 2 cm/year suggests the need for evaluation of other causes of growth failure.

When Policy Topic is not covered

Increlex is considered investigational in the following situations [2]:

- Children who do not have proven severe primary IGF-1 deficiency,
- Children less than two years of age,
- As an additive treatment to Growth Hormone Therapy,
- As a substitute for Growth Hormone treatment, and
- For treatment of growth failure secondary to:
    - Growth hormone deficiency
    - Malnutrition

- o Hypothyroidism
- o Chronic treatment with pharmacologic doses of anti-inflammatory steroids

Considerations

Prior authorization through the pharmacy services area is required.

(1) This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Hayes Medical Technology Directory, Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service

Increlex® is indicated for the treatment of growth failure in children with severe primary IGFD or with GH gene deletion who have developed neutralizing antibodies to GH. Both drugs contain recombinant human insulin-like growth factor-1 (rhIGF-1), which is identical to the natural hormone, IGF-1. In humans, IGF-1 is released in response to stimulation by growth hormone, and has a broad range of activity with regard to growth and metabolism (i.e. statural growth, glucose and amino acid uptake, and tissue and organ growth). Increlex® seeks to replicate the naturally occurring form of IGF-1, providing patients who are IGF-1 deficient with a viable replacement source for the protein.

Rationale

Primary insulin growth factor deficiency (IGFD) afflicts an estimated 30,000 children evaluated for short stature in the United States. Primary IGFD is a growth hormone-resistant state characterized by lack of insulin-like growth factor-1 (IGF-1) production in the presence of normal or elevated levels of endogenous growth hormone. Approximately 6,000 children suffer from a more severe form of this condition, called severe primary IGFD. Severe primary IGFD includes persons with mutations in the GH receptor (GHR), post-GHR signaling pathway, and IGF-1 gene defects; these persons are not GH deficient, and therefore, they cannot be expected to respond adequately to exogenous GH treatment.

The FDA's approval of Increlex® was based upon the results of five Phase III clinical studies (four open-label and one double-blind, placebo-controlled), with subcutaneous doses of Increlex® generally ranging from 0.06 to 0.12 mg/kg administered twice daily for the treatment of short stature caused by severe primary IGFD (n=71). Patients were enrolled in the trials on the basis of extreme short stature, slow growth rates, low IGF-1 serum concentrations, and normal GH secretion. In clinical studies, normal growth hormone was defined as serum GH level (peak level) of greater than 10 nanograms per milliliter (ng/ml) (20 mU/liter), after stimulation with insulin, levodopa, arginine, propranolol, clonidine, or glucagons, or an unstimulated (basal) serum GH level of greater than 5 ng/ml. Data from these five clinical studies were pooled for global efficacy and safety analysis. Of these children, 61 completed at least one year of rhIGF-1 replacement therapy, which is the generally accepted minimum length of time required to adequately measure growth responses to drug therapy. Fifty-three (87%) had Laron Syndrome; 7 (11%) had GH gene deletion, and 1 (2%) had neutralizing antibodies to GH. Data from the study, presented during the 86th Annual Meeting of The Endocrine Society (June 2004), demonstrated a statistically significant increase ($p<0.001$) in growth rate over an eight-year period in response to therapy. Compared to pre-treatment growth patterns, on average, children gained an additional inch per year for each year of therapy over the course of eight years. Patients were treated for an average of 3.9 years, with some patients being treated up to 11.5 years. An analysis of safety in the study concluded that long-term treatment with rhIGF-1 appears to be well tolerated. Side effects were mild to moderate in nature and included hypoglycemia (42%), injection site lipohypertrophy, and tonsillar hypertrophy (15%). Intracranial hypertension occurred in three subjects. Funduscopic examination is recommended at the initiation and periodically during the course of Increlex® therapy. Symptomatic hypoglycemia was generally avoided when a meal or snack was consumed either shortly before (i.e., 20 minutes) or after the administration of Increlex® [3].

Increlex® is indicated for the long-term treatment of growth failure in children with severe primary IGF-1 deficiency (primary IGFD) or with GH gene deletion who have developed neutralizing antibodies to GH. Increlex® is not intended for use in individuals 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[3].

Contraindications to Increlex® include the following[3]:

Patients with closed epiphyses (bone growth plates are closed)

Active or suspected neoplasia

Allergy to mecasermin (IGF-1) or any of the inactive ingredients in Increlex®

Growth failure associated with other identifiable causes (e.g., Prader-Willi syndrome, Russell-Silver syndrome, Turner syndrome, Noonan syndrome or chromosomal abnormality)

Chronic illness (e.g., diabetes, cystic fibrosis, etc.).

The use of mecasermin has not been studied in adults or in children less than 2 years of age and is not proven to be clinically effective and, therefore, is not considered to be medically necessary in those age groups[3].

References

1. DiPiro J, et al. Pharmacotherapy A Pathophysiologic Approach. 6th ed. In: *Pituitary Gland Disorders.* New York, NY: McGraw-Hill Companies Inc.; 2005: 1414.
2. Increlex® for Healthcare Professionals. Available at http://www.Increlex.com/wt/page/pro
3. Increlex® Package Insert. Tercica Incorporated. 2006.

Billing Coding/Physician Documentation Information

J2170 Injection, mecasermin, 1mg

Additional Policy Key Words

N/A

Related Topics

Growth Hormone Therapy

Policy Implementation/Update Information

12/2006	New policy titled Increlex® (mecasermin) and Iplex® (mecasermin rinfabate)
12/2007	Reviewed – no changes made
12/2008	Reviewed – Changed title to Increlex® (mecasermin). Statements regarding Iplex removed due to Iplex being taken off market.
12/2009	Reviewed – no changes made
12/2010	Reviewed – no changes made
12/2011	Reviewed – no changes made
12/2012	Reviewed – no changes made
12/2013	Reviewed – no changes made