

## Corporate Medical Policy

### Treatment for Severe Primary IGF-1 Deficiency

**File Name:** treatment\_for\_severe\_IGF-1\_deficiency  
**Origination:** 2/2006  
**Last CAP Review:** 7/2011  
**Next CAP Review:** 7/2012  
**Last Review:** 7/2011

#### Description of Procedure or Service

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There are approximately thirty thousand children in the US with short stature due to primary insulin-like growth factor-1 deficiency (IGFD). These children have normal or elevated levels of growth hormone but due to a deficiency in insulin-like growth factor, they are unable to utilize the growth hormone resulting in short stature. Six thousand of these children have growth failure due to severe primary IGF-1 deficiency. Children with untreated severe primary IGFD have extremely short stature and may have an increased risk of other metabolic disorders such as lipid abnormalities, decreased bone density, insulin resistance and obesity.

This rare condition is diagnosed in children having normal or elevated growth hormone but have height and serum IGF-1 levels less than 3 standard deviations below normal.

Recently the FDA has approved two protein replacements for the IGF-1 deficiency to be used only in children with severe primary insulin-like growth factor deficiency or in children who have growth hormone gene deletion and have developed neutralizing antibodies to growth hormone. These children must have had all secondary causes of insulin-like growth factor deficiency ruled out. Secondary insulin-like growth factor deficiency may be caused by various other conditions such as malnutrition, hypothyroidism or chronic treatment with anti-inflammatory steroids.

Increlex™ (mecasermin, rDNA origin) a twice a day non-glycosylated human IGF-1 replacement injection, was developed by Tercica Inc, of Brisbane, CA. It was approved under the 505b requirements of the FDA in August 2005 for the treatment of severe primary IGF-1 deficiency or growth hormone gene deletion who have developed neutralizing antibodies to growth hormone.

IPLEX™ developed by Insmad Inc., Glen Allen VA (formerly called SomatoKine) was approved as the first once a day treatment for severe primary IGF-1 deficiency or growth hormone gene deletion who have developed neutralizing antibodies to growth hormone in December 2005. The generic name for this drug is mecasermin rinfabate and is made of recombinant insulin-like growth factor I (rhIGF-1) and insulin-like growth factor binding protein-3 (rhIGFBP-3).

**\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

#### Policy

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**BCBSNC will provide coverage for treatment of Severe Primary IGF-1 Deficiency when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.**

# Treatment for Severe Primary IGF-1 Deficiency

**BCBSNC will provide coverage for treatment of growth hormone gene deletion in children who have developed neutralizing antibodies to growth hormone when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.**

## Benefits Application

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## When Treatment of Severe Primary IGF-1 Deficiency is covered

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Treatment in children with severe primary insulin-like growth factor-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone may be considered medically necessary when all the following criteria are met:

- The child's height standard deviation is less than or equal to -3.0 for the child's age and sex (documentation should include sequential growth chart data utilizing clinical growth charts which are consistent with those available through the CDC at [http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/clinical\\_charts.htm](http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/clinical_charts.htm) ); and
- The child's basal IGF-1 standard deviation is less than or equal to -3.0; and
- The child has normal or elevated growth hormone (GH) except for children with growth hormone gene deletion; and
- All indications of secondary IGF-1 deficiency have been ruled out such as growth hormone deficiency, malnutrition, and hypothyroidism; and
- The diagnosis has been made by an endocrinologist; and
- The child is not currently taking growth hormone or corticosteroids.

## When Treatment of Severe Primary IGF-1 Deficiency is not covered

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Treatment of severe primary IGF-1 deficiency is not covered when the criteria stated above are not met; or

- The child's epiphyses (bone growth plates are closed); or
- The child has an active or suspected neoplasia; or
- The child has an allergy to mecasermin (IGF-1) or any of the other ingredients in the medication; or
- The child has growth failure due to other causes; or
- The child has a chronic illness such as diabetes, cystic fibrosis, etc.; or
- The child is less than 2 years old.

# Treatment for Severe Primary IGF-1 Deficiency

## Policy Guidelines

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Treatment for insulin-like growth factor-1 deficiency should be administered at approximately the same time every day. It should be scheduled for administration either just before a meal or just after a meal due to its hypoglycemic (low blood sugar) effects.

Dosing should be initiated gradually until the tolerance level can be established. The child's endocrinologist will monitor the child's growth and dosage at least 4 times a year. Swelling of the tonsils and adenoids has been associated with this treatment and should be reported to the physician as soon as possible.

Patients and caregivers should be instructed in the proper technique of administration, disposal of needles and understand how to recognize the signs and symptoms of any adverse reaction to the therapy

Treatment should be discontinued once fusion of the epiphysis has occurred. If growth in height velocity does not increase by 2cm in the first year the physician should re-evaluate the cause of growth failure. Response in growth velocity will decrease with time.

Neither Increlex nor IPLEX are intended for use in patients with secondary forms of Insulin Growth-Like Factor 1 Deficiency per FDA.

This drug may require prior approval.

## Billing/Coding/Physician Documentation Information

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: J2170*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

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FDA Approval Letter for Increlex. Retrieved 1/9/06 from <http://www.fda.gov/cder/foi/appletter/2005/021839ltr.pdf>

FDA Approved Package Insert for Increlex. Retrieved 1/9/06 from <http://www.fda.gov/cder/foi/label/2005/021839lbl.pdf>

FDA Approval Letter for IPLEX. Retrieved 1/9/06 from <http://www.fda.gov/cder/foi/appletter/2005/021884ltr.pdf>

FDA Approved Package Insert for IPLEX. Retrieved 1/9/06 from <http://www.fda.gov/cder/foi/label/2005/021884lbl.pdf>

Specialty Matched Consultant Advisory Panel - 5/2006

# Treatment for Severe Primary IGF-1 Deficiency

CDC. National Center for Health Statistics. Clinical growth charts. Retrieved 5/18/2006 from [http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/clinical\\_charts.htm](http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/clinical_charts.htm)

Specialty Matched Consultant Advisory Panel - 5/2008.

Fintini D, Brufani C, Cappa M. Profile of mecasermin for the long-term treatment of growth failure in children and adolescents with severe primary IGF-1 deficiency. *Ther Clin Risk Manag.* 2009; 5: 553–559. Retrieved July 27, 2010 from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2724186/?tool=pubmed>

Specialty Matched Consultant Advisory Panel 8/2010

Midyett LK, Rogol AD, Van Meter QL, Frane J, Bright GM, on behalf of the MS301 Study Group 2010 Recombinant insulin-like growth factor (IGF)-I treatment in short children with low IGF-I levels: first year results from a randomized clinical trial. *J Clin Endocrinol Metab* 95:611–619

## Policy Implementation/Update Information

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- 02/16/06 New policy implemented. Effective 2/16/2006.
- 6/19/06 Specialty Matched Consultant Advisory Panel review 5/18/2006. Added additional information to "When Growth Hormone is covered" section under the first bullet to indicate "(documentation should include sequential growth chart data utilizing clinical growth charts which are consistent with those available through the CDC at [http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/clinical\\_charts.htm](http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/clinical_charts.htm) )". References added.
- 6/30/08 Specialty Matched Consultant Advisory Panel review 5/29/08. No change to policy statement. References added.
- 8/25/08 Added HCPCS code J2170 to "Billing/Coding" section. Removed statement indicating; "Physicians will typically submit claims utilizing J3490 or J3590" from "Billing/Coding" section since there is a specific code for this biologic. (btw)
- 6/22/10 Policy Number(s) removed (amw)
- 9/28/10 Specialty Matched Consultant Advisory Panel review 8/2010. References updated
- 8/30/11 Specialty Matched Consultant Advisory Panel review 7/27/11. No change to coverage criteria. Policy accepted as written. (adn)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.