Highmark Medical Policy Bulletin

Section:	Injections
Number:	I-12
Topic:	Growth Hormone, Human Recombinant Somatrem/Somatropin
Effective Date:	March 2, 2009
Issued Date:	May 3, 2010
Date Last Reviewed:	

General Policy Guidelines

Indications and Limitations of Coverage

Somatrem (e.g., Protropin) and Somatropin (e.g., Nutropin)(codes J2940, J2941) are polypeptide hormones which are of a recombinant DNA origin. The amino acid sequence of these products are identical to that of human growth hormone. The drugs are indicated for the long-term treatment of children who have growth failure due to an inadequate secretion of normal endogenous growth hormone. Growth hormone (GH) therapy can also be used in the treatment of adults with proven growth hormone deficiency, for patients with AIDS wasting, or to promote wound healing in patients with third-degree burns.

The administration of growth hormone to children with growth hormone deficiency has resulted in increased linear growth and subsequent normal adult stature. Patients should be closely monitored for growth hormone antibodies and continued response to the therapy.

In children, GH therapy is typically discontinued when growth velocity is less than 2 cm per year, when epiphyseal fusion has occurred, or when the height reaches the 5th percentile of adult height. In patients with chronic renal failure undergoing transplantation, GH therapy is discontinued at the time of transplant.

Coverage for growth hormone is determined according to individual or group customer benefits.

The following indications are appropriate for coverage of GH therapy:

1. The use of this drug in the long-term treatment of children who have a lack of adequate endogenous growth hormone resulting from the following conditions:

   A. Primary Pituitary Disease
      - genetic syndromes such as aplasia, hypoplasia, familial panhypopituitarism, familial isolated growth hormone deficiency, or deletion of growth hormone gene.
      - intrasellar tumors such as adenomas and craniopharyngioma.
      - nontumorous destruction such as trauma, infection, central nervous system (CNS) irradiation.

   B. Pituitary Deficiency secondary to hypothalamic destruction
      - idiopathic which may result from perinatal insult, multiple deficiencies such as panhypopituitarism.
      - postinfectious
      - hypothalamic tumor such as craniopharyngioma, hamartoma, neurofibroma, germinoma.

      NOTE: In addition to the indications in 1.A. or 1.B., the child's hormone deficiency must be substantiated by the

NOTE: In addition to the indications in 1.A. or 1.B., the child's hormone deficiency must be substantiated by the following:

a. The height is less than the 3rd percentile;
b. The growth velocity is less than or equal to 4 cm/year as determined by measurement;
c. The bone age is greater than or equal to 2 years behind chronologic age; and
d. The patient has had an abnormal response of less than 10 ng/ml to **two** provocative stimulation tests, such as levadopa, clonidine, glucagon, propanalol, arginine, or insulin.

The above data should be documented in the medical record on appropriate growth charts. A period of at least six months (ideally, a year or longer) is necessary for reliable calculation.

2. Children with Turner's syndrome - Turner's syndrome is defined as a 45, XO genotype.

3. Children with chronic renal failure - Chronic renal insufficiency is defined as a creatinine clearance between 5 and 75 ml/min per 1.73 m2. [In children with a height less than the 3rd percentile for chronologic age with chronic renal insufficiency prior to renal transplant.]

4. Adults with proven congenital or acquired GH deficiency - (See items 1.A. and 1.B. for applicable diagnoses codes). Proven growth hormone deficiency is defined as a negative response to a standard growth hormone stimulation test, i.e., maximum peak of less than 5 ng/ml when measured by polyclonal antibody (RIA) or less than 2.5 ng/ml when measured by monoclonal antibody (IRMA).

5. AIDS Wasting - AIDS wasting is defined as a greater than 10% of baseline weight loss that cannot be explained by a concurrent illness other than HIV infection. Patients must simultaneously be treated with antiviral agents. Therapy is continued until this definition is no longer met. Serostim (Somatropin)(J2941) is FDA approved for this indication.

6. To promote wound healing in burn patients - GH therapy for burn patients should be limited to hospital inpatients with 3rd degree burns.

7. Children with Prader-Willi Syndrome - Prader-Willi syndrome is a genetic disorder characterized by a microdeletion in the long arm of chromosome 15. Clinically, the syndrome presents as a complex multisystem disorder characterized by excessive appetite, obesity, short stature, characteristic appearance, developmental disability, and significant behavioral dysfunction. GH deficiency has been demonstrated in most tested patients with Prader-Willi syndrome.

8. Short bowel syndrome - Short bowel syndrome is a rare, serious, and potentially life-threatening condition that follows extensive surgical removal of portions of the small intestine as a treatment for acute or chronic disorders of the intestine. Zorbtive (Somatropin)(J2941) is FDA approved for this indication in patients receiving specialized nutritional support, and should be used in conjunction with optimal management of short bowel syndrome.

   Specialized nutritional support may consist of a high carbohydrate, low-fat diet, adjusted for individual patient requirements and preferences. Nutritional supplements may be added according to the discretion of the treating physician. Optimal management of short bowel syndrome may include dietary adjustments, enteral feedings, parenteral nutrition, fluid and micronutrient supplements, as needed.

   Administration for more than four weeks has not been adequately studied.

9. Noonan syndrome - Treatment of short stature in children associated with Noonan syndrome.

   Noonan syndrome is defined as an autosomal-dominant genetic syndrome commonly characterized by short stature, congenital heart defects, and unique facial features. Up to 80% of children with Noonan syndrome experience significant short stature.

Coverage is limited to those indications noted above. Each case and the necessary documentation will be reviewed for medical necessity prior to payment.

NOTE: 24 hour continuous measurements of GH, serum levels of insulin-like growth factors (IGF) or insulin-like growth factor binding protein (IGFBP) are considered inadequate to document growth hormone deficiency. GH therapy is considered ineligible for coverage in patients with the diagnosis of partial growth hormone deficiency, neurosecretory GH dysfunction, constitutional growth and delay, GH bioresistance, or pediatric patients born small for gestational age (SGA) who fail to show catch-up growth by age two.

All claims for growth hormone therapy should be referred for medical review on a yearly basis for ongoing approval.

Use of this drug for any condition other than those listed above should be denied as not medically necessary and, therefore, not covered. A participating, preferred, or network provider cannot bill the member for the denied service unless the provider has given advance written notice, informing the member that the service may be deemed not medically necessary and providing an estimate of the cost. The member must agree in writing to assume financial responsibility, in advance of receiving the service. The signed agreement should be maintained in the provider's records.

The use of this drug for short stature is considered cosmetic, and therefore, not covered. A participating, preferred, or network provider can bill the member for the non-covered service.

NOTE: This policy is designed to address medical guidelines that are appropriate for the majority of individuals with a particular disease, illness, or condition. Each person's unique clinical circumstances may warrant individual consideration, based on review of applicable medical records.

Procedure Codes

J2940 J2941

Traditional (UCR/Fee Schedule) Guidelines

Refer to General Policy Guidelines

FEP Guidelines

Under the Federal Employee Program, all services that utilize FDA-approved drugs, devices, or biological products are eligible when intended for the treatment of a serious or life-threatening condition and when medically necessary and appropriate for the patient's condition.

Comprehensive / Wraparound / PPO / Major Medical Guidelines

Refer to General Policy Guidelines

Any reference in this bulletin to non-billable services by a network provider may not be applicable to Major Medical

Any reference in this bulletin to non-billable services by a network provider may not be applicable to Major Medical.

Managed Care (HMO/POS) Guidelines

Refer to General Policy Guidelines

Publications

PRN References

04/1998, Growth hormone therapy eligible for some conditions
08/2002, Growth hormone therapy eligible for Prader-Willi Syndrome
12/2003, Growth hormone for short stature considered cosmetic
08/2004, Growth hormone therapy eligible for short bowel syndrome
04/2009, Growth hormone therapy eligible for the treatment of short stature in Noonan syndrome

References

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Human Growth Hormone, National Blue Cross Blue Shield Association Medical Policy Reference Manual, Policy No. 5.01.06, issued June 2008.

Persistent Short Stature, Other Potential Outcomes, and the Effect of Growth Hormone Treatment in Children Who are Born Small for Gestational Age, Pediatrics, Vol. 112, No. 1, 07/2003

Vance ML, Mauras N. Growth hormone therapy in adults and children. *N Engl J Med*. 1999;341:1206-1216.

MacFarlane CE, Brown DC, Johnstown LB, et al. Growth hormone therapy and growth in children with Noonan's syndrome: results of 3 years' follow-up. *J Clin Endocrinol Metab*. 2001;86:1953-1956.

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Accretropin™ (somatropin) Injection [package insert]. Winnipeg. Canada:Cangene Corporation; 2007.

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Albertson-Wikland K, Aronson AS, Gustafsson J, et al. Dose-dependent effect of growth hormone on final height in children with Short Stature without growth hormone deficiency. *J Clin Endocrinol Metab*. 2008;93:4342-4350.

VandenBerg J, Bannink E, Wielopolski P, et al. Cardiac status after childhood growth hormone treatment of Turner syndrome. *J Clin Endocrinol Metab*. 2008;93:(7).

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View Previous Versions

[Version 013 of I-12]
[Version 012 of I-12]
[Version 011 of I-12]
[Version 010 of I-12]
[Version 009 of I-12]
[Version 008 of I-12]
[Version 007 of I-12]
[Version 006 of I-12]
[Version 005 of I-12]
[Version 004 of I-12]
[Version 003 of I-12]
[Version 002 of I-12]
[Version 001 of I-12]

Table Attachment

Text Attachment

Procedure Code Attachments

Diagnosis Codes

194.3	198.89	213.0	213.1
215.0	215.2	215.3	215.4
215.5	215.6	215.7	215.8
215.9	227.3	234.8	237.0
237.70	237.71	237.72	239.7
253.0	253.1	253.2	253.3
253.4	253.5	253.6	253.7
253.8	253.9	579.3	585.1
585.2	585.3	585.4	585.5
585.6	585.9	757.32	758.6
759.2	759.6	759.81	759.89
783.43			

Glossary