

Pharmacy Medical Necessity Guidelines: Growth Hormone Replacement Therapy

Effective: January 1, 2021

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	RX	Department to Review	RXUM
<p>These pharmacy medical necessity guidelines apply to the following:</p> <p>Commercial Products</p> <ul style="list-style-type: none"> <input checked="" type="checkbox"/> Tufts Health Plan Commercial products – large group plans <input checked="" type="checkbox"/> Tufts Health Plan Commercial products – small group and individual plans <input checked="" type="checkbox"/> Tufts Health Freedom Plan products – large group plans <input checked="" type="checkbox"/> Tufts Health Freedom Plan products – small group plans • CareLinkSM – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization <p>Tufts Health Public Plans Products</p> <ul style="list-style-type: none"> <input checked="" type="checkbox"/> Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product) <input type="checkbox"/> Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans <input checked="" type="checkbox"/> Tufts Health RITogether – A Rhode Island Medicaid Plan 		<p>Fax Numbers:</p> <p>RXUM: 617.673.0988</p>	

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

Endogenous human growth hormone (HGH) is a product of the pituitary gland within the endocrine system. This system produces hormones that are secreted into the blood or lymph and circulated through the body. The hormones released by these glands can have a particular effect on a specific tissue or organ or they can initiate a more general effect manifested through the body. The body's regulation of the release of these hormones through the endocrine system is important for maintaining a proper hormonal balance.

Growth hormone has been shown to increase growth by stimulating the production of insulin-like growth factor I (IGF-I), which facilitated cartilage production and its subsequent development into bone, as well as other related proteins. Recombinant human growth hormone is used to increase the growth rate in children with documented growth retardation due to deficiency of growth hormone, to reverse small stature in cases for which growth hormone stimulation has been found beneficial (Hayes Report, October 1996: pg. 1-2). A pediatric endocrinologist must oversee the treatment. Monitoring frequency is recommended at the following intervals upon initiation of therapy: 3 months, 6 months, then annually thereafter. Treatment consists of SC or IM self-administered injections 6 or 7 times a week (except for Nutropin Depot which is once or twice a month). Initial training of Members in the administration of growth hormone is usually performed in the endocrinologist office.

HGH is produced throughout a person's lifetime. It promotes growth in children and is important in adult metabolism. A deficiency of HGH in adults can cause alterations in body composition, affect lipid and bone metabolism, reduce strength and work capacity and impair psychological wellbeing. Adults can become growth hormone deficient (GHD) in a variety of ways, but most often the cause is a pituitary or parasellar tumor or as a result of the treatment of these tumors.

HIV wasting syndrome is defined as unintentional and progressive weight loss (cachexia) often accompanied by weakness, fever, nutritional deficiencies and diarrhea. The wasting can be caused by opportunistic infections that interfere with the gut's ability to absorb nutrients, altered metabolism of nutrients or by inadequate food intake due to nausea and vomiting. The syndrome reduces the quality of life, exacerbates the illness and increases the risk of death for people with HIV. (Therapies that have been tried to reverse the weight loss in HIV-infected persons include appetite stimulants, anabolic agents, cytokine inhibitors and hormones.) The goal of therapy is to increase the person's body weight and promote an increase in lean body mass (muscle).

Somatropin and Somatrem are synthetic forms of human growth hormone that are produced by using recombinant DNA (rDNA) technology. Somatropin (i.e., Norditropin[®], Norditropin Nordiflex[®], Norditropin FlexPro[®], Nutropin[®], Nutropin AQ[®], Genotropin[®], Humatrope[®], Saizen[®], Omnitrope[®], Zomacton[®]) is used in GH deficient adults to maintain body composition and metabolism. Serostim[®] can help to reduce the

signs and symptoms of AIDS wasting syndrome and was granted orphan drug status (7-year marketing exclusivity for this indication) from the FDA in 1996 for the treatment of HIV wasting.

COVERAGE GUIDELINES

The plan may authorize coverage of recombinant human growth hormone (GH) (**Norditropin, Norditropin FlexPro and Norditropin Nordiflex**) for Members when the following criteria are met:

Initial therapy for pediatric growth hormone deficiency (GHD), chronic renal insufficiency prior to transplantation, Turner Syndrome, Prader-Willi Syndrome, Noonan Syndrome, mutation of Short-Stature Homebox (SHOX) gene, and Small for Gestational Age (SGA) (see Limitations)

1. Documentation diagnosis of pediatric GHD defined as all of the following:
 - a. Member must be evaluated and therapy must be prescribed and monitored by a pediatric endocrinologist or pediatric nephrologist
 - b. Member must not have attained epiphyseal closure as determined by X-ray
 - c. Member must have failed to respond to at least TWO standard GH stimulation tests (insulin, levodopa, arginine, propranolol, clonidine, or glucagon), defined as a peak measured GH level <10 ng/mL after stimulation no more than 6 months apart
 - d. Height at initiation of therapy must be >2 standard deviations below normal mean for age and gender or below the 3rd percentile for age and gender

OR

- 2a. Documented diagnosis of any of the following
 - a) Chronic renal insufficiency prior to transplantation
 - b) Turner Syndrome
 - c) Prader-Willi Syndrome
 - d) Noonan Syndrome
 - e) Mutation of SHOX gene
 - f) SGA defined as all of the following:
 - Child born SGA, defined as birth weight or length 2 or more standard deviations below the mean for gestational age (including infants born with intrauterine growth restriction or Russell-Silver Syndrome resulting in SGA)
 - Child does not show catch up growth between ages 2 and 4 years of age, defined as height 2 or more standard deviations below the mean for age and gender
 - Other causes for short stature such as growth inhibiting medication, endocrine disorders and emotional deprivation or syndromes have been ruled out

AND

- 2b. Height at initiation of therapy must be greater than 2 standard deviations below normal mean for age and gender

Continuation therapy for pediatric GHD, chronic renal insufficiency prior to transplantation, Turner Syndrome, Prader-Willi Syndrome, Noonan Syndrome, mutation of SHOX gene, and SGA (see Limitations)

1. Continuation of therapy prior to completion of linear growth
 - Documentation of the following:
 - Medical history as it relates to growth, including any test results and growth chart
 - Continuing care plan
 - At least a doubling of the annualized pre-treatment growth rate after the first 6 months of therapy then an increase in growth of at least 3 cm per year thereafter
2. Continuation of therapy after completion of linear growth (therapy will be continued at standard adult doses)
 - a) Member will be re-evaluated after GH treatment has been stopped for at least 3 months to determine GH status

AND

- b) Member must have failed to respond to at least ONE standard GH stimulation test (insulin, levodopa, arginine, propranolol, clonidine, glucagon), defined as a peak measured GH level <5 ng/mL after stimulation

Acquired Growth Hormone Deficiency (GHD) (see Limitations)

Note: Acquired GHD can be due to, but is not limited to the following: Central nervous system tumors, cranial irradiation, panhypopituitarism, pituitary insufficiency, pituitary surgery, pituitary tumor, radiation treatments, or trauma.

1. Documentation the Member has failed to respond to at least one standard growth hormone stimulation test (with insulin, levodopa, arginine, propranolol, clonidine, glucagon), defined as a peak measure growth hormone level of <5 ng/mL after stimulation

Note: Not required for Members who have had surgical removal of the pituitary

AIDS Wasting Syndrome

The plan may authorize coverage of recombinant human growth hormone (**Serostim**) for Members when the following criteria are met:

1. A documented diagnosis of AIDS

AND

2. A weight loss of at least 10% from baseline weight OR a body mass index (BMI) of less than 20

AND

3. Documentation that the Member has had an adequate nutritional evaluation and has failed to respond adequately to a high calorie diet

AND

4. Member is concurrently receiving antiviral therapy indicated for the treatment of the human immunodeficiency virus

Short Bowel Syndrome (see Limitations)

The plan may authorize coverage of recombinant human growth hormone (**Zorbitive**) for Members when the following criteria are met:

1. A documented diagnosis of Short Bowel Syndrome from a gastroenterologist

AND

2. A documented dependence on intravenous parenteral nutrition (IPN) for nutritional support

Chronic Renal Insufficiency

The plan may authorize coverage of recombinant human growth hormone (**Nutropin, Nutropin AQ and Nutropin NuSpin**) for Members when the following criteria are met:

1. A documented diagnosis of growth failure associated with chronic renal insufficiency

LIMITATIONS

- The plan does not provide coverage of growth hormone therapy for other conditions that include, but are not limited to, the following:
 - Constitutional delay
 - Idiopathic short stature
 - Genetic short stature
 - Glucocorticoid-induced growth failure
 - Down's Syndrome
- Patients who present with, or develop, an active neoplasm (tumor), or with an active intracranial lesion, will be excluded from coverage.
- For the diagnosis of pediatric growth hormone deficiency (GHD), initial authorization will be for 6 months. Subsequent authorizations will be authorized 1 year and must be reviewed annually except for Members with pituitary damage (e.g., tumor, radiation, stroke or trauma).
- Initial authorizations will be limited to 1 year for the following diagnoses: chronic renal insufficiency, Turner Syndrome, Prader-Willi Syndrome, Noonan Syndrome, mutation of Short-Stature (SHOX) gene, and Small for Gestational Age. Subsequent authorizations will be authorized for 1 year and must be reviewed annually except for Members with pituitary damage (e.g., tumor, radiation, stroke or trauma).
- For the diagnosis of acquired GHD, Members at least 18 years of age will be authorized for 1 year. Members <18 years of age will be authorized until the Member is 18 years of age.
- For the diagnosis of short bowel syndrome, Members will be authorized for a one time authorization for 28 days only.
- The plan will not cover other growth hormone medications, unless a Member has either failed an adequate trial or has a contraindication to **Norditropin, Norditropin FlexPro** or **Norditropin Nordiflex** (with the exception of Serostim for AIDS Wasting Syndrome and Zorbitive for Short Bowel Syndrome).
- The plan will not cover Nutropin or Nutropin AQ except for the treatment of growth failure associated with chronic renal insufficiency.

Note: Non-covered growth hormone medications include: Genotropin, Humatrope, Nutropin, Nutropin AQ, Nutropin AQ NuSpin, Omnitrope, Saizen, and Zomacton.

CODES

Medical billing codes may not be used for this medication. This medication must be obtained via the Member's pharmacy benefit.

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APPROVAL HISTORY

October 1998: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. January 11, 2005: Add the indication of Short Bowel Syndrome
2. January 10, 2006: Add to criteria #2, Continuation of Therapy for Pediatric GHD (1 year authorization), "except for Members with pituitary damage (e.g., tumor, radiation, stroke or trauma)."
3. August 8, 2006: Changed criteria 1C from, "Member must have failed to respond to at least one standard GH stimulation tests" to, "Member must have failed to respond to at least TWO standard GH stimulation tests." Added the following to criteria 1C, "NOTE: For children with the following conditions, only ONE failed GH stimulation test is required: Central nervous system tumors, Cranial irradiation, Panhypopituitarism. Removed, "NOTE: Not required for diagnosis of Turner Syndrome or Prader-Willi Syndrome" from criteria #1d. Removed, "NOTE: Not required for diagnosis of Turner Syndrome, Prader-Willi Syndrome or subnormal growth hormone levels due to pituitary surgery, radiation therapy or multiple pituitary deficiency" from criteria #1e. Removed, "Growth hormone deficient short stature including but not limited to pituitary dwarfism, panhypopituitarism, pituitary insufficiency, growth hormone deficiency" from criteria #2. Changed criteria #3 heading from, "Continuation of Therapy for Pediatric GHD (1 year authorization)" to, "Continuation of Therapy Prior to Completion of Linear Growth (1 year authorization)". Changed criteria #4 heading from, "Continuation of Therapy After Completion of Linear Growth" to, "Continuation of Therapy After Completion of Linear Growth (Therapy will be continued at standard adult doses)". Removed criteria #4c: "Member will resume growth hormone therapy, if GHD has been determined, at adult doses." Changed second bullet under Limitation #1 from, "Non-growth hormone deficient short stature" to, "Idiopathic short stature"
4. July 10, 2007: Added Noonan Syndrome to criteria #2
5. September 11, 2007: Specified that Serostim (only) will be covered AIDS wasting syndrome (previously criteria #5). Specified that Zorbtive (only) will be covered for short bowel syndrome (previously criteria #6). Added exception statement to limitation #3, "(with the exception of Serostim for AIDS Wasting Syndrome and Zorbtive for Short Bowel Syndrome)." Specified that Nutropin and Nutropin AQ will be covered for treatment of growth failure associated with chronic renal insufficiency and added limitation #4.
6. September 9, 2008: Removed the following conditions from criteria 1c, that required only 1 GH stimulation test: central nervous system tumors, cranial irradiation, panhypopituitarism. Added the following conditions to criteria #5 (Acquired GHD), which require only 1 GH stimulation test: central nervous system tumors, cranial irradiation, panhypopituitarism. Changed the "Note" under criteria #5 for Acquired GHD from, "Note: Approval is for a maximum of 1 year and must be reviewed annually" to, "Note: For Members aged 18 years or older, approval is for a maximum of 1 year and must be reviewed annually."
7. September 8, 2009: Removed Protropin from the list of non-covered growth hormone medications. Protropin has been discontinued.
8. January 1, 2010: Removal of Tufts Medicare Preferred language (separate criteria have been created specifically for Tufts Medicare Preferred)
9. September 13, 2010: No changes
10. August 14, 2012: No changes

11. August 6, 2013: No changes
12. August 12, 2014: Included pediatric nephrologist as specialists under 1a and or below the 3rd percentile for age and gender under 1d of the Pediatric Growth Hormone Deficiency section. Specified for criteria requiring failure of two GH tests, failed tests must be no more than 6 months apart for consideration of failing two tests. Replaced Intrauterine Growth Retardation with Small for Gestational Age defined as all of the following Child born SGA defined as birth weight or length 2 or more standard deviations below the mean for gestational age (including infants born with intrauterine growth restriction or Russell-Silver Syndrome resulting in SGA); AND Child does not show catch up growth before 2 years of age, defined as height 2 or more standard deviations below the mean for age and gender; AND Other causes for short stature such as growth inhibiting medication, endocrine disorders and emotional deprivation or syndromes have been ruled out. Added the diagnoses of Mutation of Short-Stature Homeobox (SHOX) gene and Height at initiation of therapy must be > 2 standard deviations below normal mean for age and gender to guidelines. Modified criterion 1b under AIDS Wasting Syndrome to require Member to concurrently be receiving antiviral therapy indicated for the treatment of the human immunodeficiency virus.
13. August 11, 2015: Drug name change from Tev-Tropin to Zomacton.
14. January 1, 2016: Administrative change to rebranded template.
15. September 13, 2016: No changes
16. April 11, 2017: Administrative update. Effective 6/1/2017, Medical Necessity Guideline applies to Tufts Health RITogether.
17. September 12, 2017: No changes
18. December 12, 2017: Administrative update effective 1/1/18 Tufts Health Together removed from the Medical Necessity Guideline. Reformatted clinical criteria to help specify clinical criteria for approvable diagnoses and duration of authorizations; no changes to clinical criteria made.
19. August 7, 2018: No changes
20. August 13, 2019: August 13, 2019: Updated the definition of SGA to the "Child does not show catch up growth between ages 2 and 4 years of age..." from previous language of "before 2 years of age."
21. December 8, 2020: No changes

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. 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.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

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.