



Prior Authorization Approval Criteria

Human growth hormone - Adult

Generic name:	Human growth hormone, somatropin
Brand names:	Tev-Tropin, Humatrope, Nutropin, Genotropin, Norditropin, Saizen, Geref, Omnitrope
Medication class:	Growth hormone
FDA-approved uses:	For replacement of endogenous growth hormone in patients who have growth hormone deficiency (GHD) alone or with multiple hormone deficiencies as a result of pituitary disease, surgery, radiation or trauma. Also for adults who have had growth hormone deficiency as children and have confirmed growth hormone deficiency as adults.
Available dosage forms:	Subcutaneous solution and powder for solution; strength and vial size vary by brand. Tev-Tropin: One vial of 5mg somatropin with one 5ml vial of diluent
Usual dose:	Dosing regimen should be individualized independent of body weight, starting with a low dose, and then gradually increasing to the minimal dose that normalized IGF-1 without causing unacceptable side effects. Starting doses: Age <30: 0.4 to 0.5mg/day (may be higher for transition patients) Age 30-60: 0.2 to 0.3mg/day Age >60: 0.1 to 0.2mg/day Patients with diabetes: 0.1 to 0.2mg/day
Approximate monthly cost: (based on AWP 2010)	Tev-tropin (age <30, at 0.5mg/day): \$748 per month
Duration of therapy:	Indefinite or until no longer achieving benefits

Criteria (*bullet points below are all inclusive unless otherwise noted*):

- The indicated diagnosis (including any applicable labs and /or tests) and medication usage must be supported by documentation from the patient's medical records.
- If patient meets the criteria for growth hormone therapy, FCHP will only approve the preferred formulary product. Other products may be approved if the patient has tried and failed or was intolerant to the FCHP preferred product or if the patient is unable to use a traditional syringe and vial due to physical impairment (including visual impairment).
- Prescribed by endocrinologist only
- Patient should exhibit clinical features of the syndrome of GHD in adults as associated with abnormal body composition, reduced physical performance, altered lipid metabolism, decreased bone mass, increased insulin resistance, and reduced quality of life (QOL). Baseline levels of the following must be provided:
 - Cardiovascular
 - Systolic and diastolic blood pressure
 - Heart rate
 - Electrocardiogram results
 - Metabolic
 - Fasting glucose

- A1C
 - Fasting lipid profile
 - Body composition:
 - BMI, waist circumference, waist-to-hip ratio, lean and fat mass quantification using DEXA scans
 - Osteopenia/osteoporosis
 - Measurement of bone mineral content and BMD
 - Quality of life
 - Self-rating questionnaires such as Hopkins Symptom Checklist, Nottingham Health Profile, Psychological General Well-being Index, QOL Assessment of GHD in Adults (QOL-AGHDA), Questions on Life Satisfaction – Hypopituitarism (QLS-H)
 - **Transition patients with childhood-onset GHD (COGHD) continuing into adulthood:**
 - Patient must have had clinically documented COGHD
 - Patient must have stopped growing under the influence of GH therapy
 - GH therapy must be discontinued for at least 1 month
 - GH status must be re-evaluated:
 - Patient had clinically documented severe GHD in childhood due to
 - Irreversible hypothalamic-pituitary structural disease or central nervous system tumors or Multiple Pituitary Hormone Deficiency (MPHD, panhypopituitarism) (with a documented deficiency of at least 3 pituitary hormones) or receipt of high dose cranial radiation.
 - Patient has IGF-1 levels more than 2 standard deviations (< 3 percentile) below the mean.
- OR**
- Patient has a low IGF-1 (<50 percentile or <0 SD) and laboratory evidence of GHD as evidenced by subnormal response to at least 2 provocative stimulation tests:
 - Response less than 5ng/ml to the insulin tolerance test (ITT)
 - less than 3ng/ml to the glucagon test
 - less than 4ng/ml to the arginine test (ARG)
 - subnormal response to the GHRH+ARG test*

OR

- **Patients with adult-onset GHD (AOGHD):**
 - GH status must be evaluated:
 - Patient has clinically documented MPHD (panhypopituitarism)
 - Documented deficiency of at least 3 pituitary hormones
 - Patient has IGF-1 levels more than 2 standard deviations (<3 percentile) below the mean
- OR**
- Patient has low IGF-1 (<50 percentile or < 0 SD) and laboratory evidence of GHD as evidenced by subnormal response to at least 2 provocative stimulation tests:
 - Response less than 5ng/ml to the insulin tolerance test (ITT)
 - less than 3ng/ml to the glucagon test
 - less than 4ng/ml to the arginine test (ARG)
 - subnormal response to the GHRH+ARG test*

Criteria for Continuation:

- IGF-1 is in the middle (50 percentile or 0 SD) of the reference range for age and gender based on specific lab reference values. (If above normal, dose reduction required).
- Must not be experiencing any side effects of GH treatment
- Evidence of improvement or benefits from treatment in at least 2 of the following groups:
 - Cardiovascular
 - Systolic and diastolic blood pressure
 - Heart rate
 - Electrocardiogram results
 - Metabolic
 - Fasting glucose
 - A1C
 - Fasting lipid profile
 - Body composition:
 - BMI, waist circumference, waist-to-hip ratio, lean and fat mass quantification using DEXA scans
 - Osteopenia/osteoporosis
 - Measurement of bone mineral content and BMD (repeated after 2 yrs and then every 2-3 yrs)
 - Quality of life / physical activity tolerance
 - Must be documented on a self-rating questionnaire such as Hopkins Symptom Checklist, Nottingham Health Profile, Psychological General Well-being Index, QOL Assessment of GHD in Adults (QOL-AGHDA), Questions on Life Satisfaction – Hypopituitarism (QLS-H)

Monitoring (at 6 to 12 month intervals, unless otherwise indicated):

- IGF-1, fasting glucose, A1C, BMI, waist circumference, waste-to-hip ratio, Thyroid function, assessment of HPA axis, testosterone, fasting lipid panel, blood pressure, heart rate, electrocardiogram, BMD (at baseline and every 2-3 years), periodic MRI if patient had pituitary tumors or post surgery residual tumor, QOL questionnaire, glucocorticoid requirements.

Contraindications:

- Sensitivity to product or diluent
- Active malignant disease (The “waiting period” until it is considered inactive in unclear. It may vary on the type of tumor – shorter for leukemia and longer for breast cancer)
- Acute illness
- Benign intracranial hypertension (pseudotumor cerebri), proliferative or preproliferative diabetic retinopathy

Not approved if:

- Patient had childhood GH treatment for conditions other than GHD, such as Turner’s syndrome or ISS
- Patients with acute catabolism (including preoperative and postoperative patients), critically ill patients and burn patients. (Unless otherwise FDA approved)
- Pregnancy: GH therapy should be discontinued if pregnancy is confirmed
- Short stature/growth failure without growth hormone deficiency (except as indicated in criteria)
- Patients with Down Syndrome, Fanconi’s Syndrome, or Bloom Syndrome (These conditions have high risk of malignant tumor or leukemia, so it is recommended that GH therapy not be used since the occurrence of a malignant condition may be linked to GH.)
- Patients with Idiopathic short stature (ISS) or SHOX Deficiency
- Patients with Familial short stature
- Patients with constitutional delays
- Patients with Noonan Syndrome
- Patients with GH insensitivity (Laron Syndrome)
- Diagnosis of growth hormone deficiency not confirmed by biochemical test.

- Growth hormone use for patients with non-specific symptomology such as lipidemia, depression and weight gain.
- Used for Antiaging
- Performance enhancement for athletes
- Patient has any contraindications to the use of growth hormone.
- Not approved for continuation if there are no apparent or objective benefits of treatment achieved

Note:

- GHD in adults may be either adult-onset GHD (AOGHD) or childhood-onset GHD (COGHD) and may occur as isolated GHD or as multiple hormone deficiencies.
- For childhood GH treatment of conditions other than GHD, such as Turner’s syndrome or ISS, there is no proven benefit to continuing GH treatment in adulthood.
- Provocative tests of growth hormone stimulation include arginine (ARG), glucagon, and insulin (ITT). Gold standard is ITT; alternate is glucagon or ARG.
- Peak GH level must be adjusted if monoclonal-based assay or recombinant human GH reference preparations are used, based upon specific lab reference values.
- In adult patients with traumatic brain injury and aneurysmal subarachnoid hemorrhage, GH stimulation testing should be performed at least 12 months after the event
- GH doses may need to be increased in: young patients, low IGF-1 levels, addition of oral estrogen, change from transdermal to oral estrogen, to induce lipolysis
- GH doses may need to be decreased in: elderly patients, high IGF-1 levels, discontinuation of oral estrogen, change from oral estrogen to transdermal estrogen, addition of testosterone, worsening of glucose tolerance, side effects
- Dramatic changes in lipid levels are not consistently seen with GH treatment
- GH treatment has not been shown to change cardiovascular mortality
- ng/ml = mcg/L
- Dosing conversion: IU or mU to mg is 3:1
- There is no evidence that one commercial product is more advantageous over another, except for differences in pen devices, dose increments/decrements, and whether refrigeration is required. (from *American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use in Growth Hormone-Deficient Adults and Transition Patients – 2009 Update.*)

*GHRH is currently not available in the US. Also, GHRH+ARG test is dependent on BMI. Subnormal response is indicated as:

- < 11 ng/ml in patients with BMI < 25 kg/m²,
- < 8 ng/ml in patients with BMI > 25 and < 30 kg/m²
- < 4 ng/ml in patients with BMI > 30 kg/m²

Criteria based in part on *American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use in Adults and Children – 2003 Update* and *American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use in Growth Hormone-Deficient Adults and Transition Patients – 2009 Update*

FCHP Pharmacy and Therapeutics Committee approval: _____

Date: _____

Adopted: 12/10/2008
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