Human Growth Hormone

Somatropin (Genotropin®, Norditropin®, Nutropin®, Nutropin® AQ, Humatrope®, Serostim®, Saizen®, Zomacton/TevTropin®, Zorbtive®, Omnitrope®)

**Description:**
The primary action of these drugs is stimulation of linear growth. Other actions include stimulation of skeletal growth, increase in cell growth, increase in organ growth, and effects on metabolism of protein, carbohydrates, lipids, minerals, and connective tissue.

**Indications:**
Genotropin®, Norditropin®, Nutropin®, Nutropin® AQ, Humatrope®, Saizen®, Zomacton/TevTropin®, Zorbtive®, Omnitrope® are indicated for the following conditions:

1. Treatment of pediatric patients who have growth failure due to an inadequate secretion of normal endogenous growth hormone
2. Treatment of idiopathic short stature, also called non-growth hormone deficient short stature, defined by height standard deviation score (SDS) ≤ -2.25 (1.2 percentile), and associated with growth rates unlikely to permit attainment of adult height in the normal range, in pediatric patients whose epiphyses are not closed and for whom diagnostic evaluation excludes other causes associated with short stature that should be observed or treated by other means
3. Replacement of endogenous growth hormone in adults with growth hormone deficiency (GHD) who meet either of the following two criteria: Adult Onset: Patients who have GHD, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes
4. Treatment of growth failure in children with chronic kidney disease (CKD) up to the time of kidney transplantation
5. Treatment of children with short stature associated with Noonan syndrome
6. Treatment of pediatric patients who have growth failure due to Prader Willi syndrome
7. Treatment of short stature or growth failure in children with short stature homeobox-containing gene (SHOX) deficiency whose epiphyses are not closed
8. Treatment of growth failure in children born small for gestational age (SGA) who fail to manifest catch-up growth by age 2 to 4 years
9. Treatment of short stature associated with Turner syndrome in patients whose epiphyses are not closed

Genotropin®, Norditropin®, Nutropin®, Nutropin® AQ, Humatrope®, Saizen®, Zomacton/TevTropin®, Zorbtive®, Omnitrope® are indicated for the following conditions:

10. Treatment of short bowel syndrome (SBS) in patients receiving specialized nutritional support and in conjunction with optimal management of short bowel syndrome

Serostim® is indicated for the following condition:

11. Treatment of human immunodeficiency virus (HIV) infected patients with wasting or cachexia to increase lean body mass (LBM) and body weight, and improve physical endurance.

**Reasons for Prior Authorization:**
- ✗ Cost
- ✗ Potential for misuse
- ☐ Toxicity
Criteria for Approval:

1. Patient has been evaluated by an endocrinologist AND Coverage of Genotropin or Nordotropin is recommended in patients who meet one of the following criteria [2 or 3]:

2. Diagnosis is an FDA-labeled indication

   A. If patient has a diagnosis of GHD, child and adolescent. Approve for initial 1 year therapy in patients who meet the following criteria (i, ii, iii, iv, or v):

   i. The patient meets the following (a and b):

   a. The patient has had growth hormone stimulation testing with at least one of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND the peak growth hormone response to at least one test is < 10 ng/mL; AND

   b. The patient’s growth (height) velocity must be ONE of the following (1, 2, or 3):

      1. The child is < 3 years of age and has a pretreatment growth rate of < 7 cm/year; OR
      2. The child is aged ≥ 3 years and has a growth rate < 4 cm/year; OR
      3. The child or adolescent is ≤ 18 years of age and has a growth velocity that is less than the 10th percentile for age and gender based on at least 6 months of growth data

   ii. The patient has undergone brain radiation AND meets the following criteria (a and b):

   a. The patient meets at least ONE of the following criteria (1 or 2):

      1. The patient has had growth hormone stimulation testing with at least one of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND the peak growth hormone response to at least one test is < 10 ng/mL OR
      2. The patient has a deficiency in at least one other pituitary hormone (that is, adrenocorticotropic hormone [ACTH], thyroid-stimulating hormone [TSH], gonadotropin deficiency [luteinizing hormone (LH) deficiency and/or follicle stimulating hormone (FSH) deficiency are counted as one deficiency], or prolactin) AND

   b. The patient’s growth (height) velocity is ONE of the following (1, 2, or 3):

      1. The child is < 3 years of age and has a pretreatment growth rate of < 7 cm/year; OR
      2. The child is aged ≥ 3 years and has a growth rate < 4 cm/year; OR
      3. The child or adolescent is ≤ 18 years of age and has a growth velocity that is less than the 10th percentile for age and gender based on at least 6 months of growth data

   iii. The patient has congenital hypopituitarism AND meets the following criteria (a):

   a. The patient meets at least ONE of the following criteria (1 or 2):

   1. The patient has had growth hormone stimulation testing with at least one of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND the peak growth hormone response to at least one test is < 10 ng/mL OR
   2. The patient has a deficiency in at least one other pituitary hormone (that is, adrenocorticotropic hormone [ACTH], thyroid-stimulating hormone [TSH], gonadotropin deficiency [luteinizing hormone (LH) deficiency and/or follicle stimulating hormone (FSH) deficiency are counted as one deficiency], or prolactin) AND
   3. The patient’s growth (height) velocity is ONE of the following (1, 2, or 3):

      1. The child is < 3 years of age and has a pretreatment growth rate of < 7 cm/year; OR
      2. The child is aged ≥ 3 years and has a growth rate < 4 cm/year; OR
      3. The child or adolescent is ≤ 18 years of age and has a growth velocity that is less than the 10th percentile for age and gender based on at least 6 months of growth data
1. The patient has had growth hormone stimulation testing with at least one of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND the peak growth hormone response to at least one test is < 10 ng/mL OR  
2. The patient has a deficiency in at least one other pituitary hormone (that is, adrenocorticotropic hormone [ACTH], thyroid-stimulating hormone [TSH], gonadotropin deficiency [luteinizing hormone [LH] and/or follicle stimulating hormone (FSH) deficiency are counted as one deficiency], or prolactin) and/or the patient has the imaging triad of ectopic posterior pituitary and pituitary hypoplasia with abnormal pituitary stalk 

iv. The patient has panhypopituitarism and meets the following criteria (a):  
a. Patient meets at least ONE of the following criteria (1, 2, or 3):  
1. Patient has pituitary stalk agenesis, empty sella, sellar or supra-sellar mass lesion, or ectopic posterior pituitary “bright spot” on magnetic resonance image or computed tomography; OR  
2. Patient has three or more of the following pituitary hormone deficiencies: somatropin (growth hormone), adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), gonadotropin deficiency (luteinizing hormone [LH] and/or follicle stimulating hormone [FSH] deficiency are counted as one deficiency), and prolactin; OR  
3. The patient has had growth hormone stimulation testing with at least one of the following agents: levodopa, insulin-induced hypoglycemia, arginine, clonidine, or glucagon AND the peak growth hormone response to at least one test is < 10 ng/mL  
v. The patient has had a hypophysectomy (surgical removal of pituitary gland) 

B. If patient has a diagnosis of GHD, and is continuing Somatropin therapy (established on somatropin for ≥ 10 months), approve continuing therapy for 1 year in patients who meet ONE of the following (i, ii, or iii):  
i. Patients < 12 years of age. The height has increased by ≥ 4 cm/year in the most recent year or 
ii. Adolescents between ≥ 12 years and ≤ 18 years of age. The patient meets the following criteria (a and b):  
a. Height has increased by ≥ 4 cm/year in the most recent year; AND  
b. The epiphyses are open  
iii. Adolescents or young adults > 18 years of age. The patient meets the following criteria (a, b, and c):  
a. Height has increased by ≥ 4 cm/year in the most recent year; AND  
b. The epiphyses are open; AND  
c. Mid-parental height has not been attained 

C. If patient has a diagnosis of Non-growth hormone deficient short stature (idiopathic short stature). Approve for initial therapy for 1 year in patients who meet the following criteria (i, ii, iii, iv, v, and vi):  
i. The child is ≥ 5 years of age; AND  
ii. The patient’s baseline height is less than 1.2 percentile or a standard deviation score (SDS) < -2.25 for age and gender; AND  
iii. The patient’s growth (height) velocity is ONE of the following (a or b):
a. The child is ≥ 5 years of age AND has a growth rate < 4 cm/year; OR
b. The growth velocity is less than the 10th percentile for age and gender based on at least 6 months of growth data; AND

iv. Without growth hormone therapy, the patient’s predicted adult height is < 160 cm (63 inches) in males or < 150 cm (59 inches) in females; AND

v. The epiphyses are open; AND

vi. The patient does not have constitutional delay of growth and puberty (CDGP)

D. If patient is diagnosed with Non-Growth Hormone Deficient Short Stature, and is continuing therapy (established on somatropin for ≥ 10 months), approve continuing therapy for 6 months in patients who meet ONE of the following criteria (i, ii, iii, or iv)

i. Patients ≥ 5 years of age who received somatropin on an initial 6-month trial basis. The annualized growth rate has doubled in comparison to the previous year. For example, if the growth velocity was 3 cm/year for the year prior to treatment, then the growth velocity must be at least 3 cm in 6 months (baseline velocity was 1.5 cm/6 months) or for example, the growth velocity was 2 cm/year for the year prior to treatment, then after 6 months of somatropin therapy, the growth velocity must be at least 2 cm in 6 months (1 cm/6 months baseline); OR

ii. Patients ≥ 5 years and < 12 years of age (i.e., established on somatropin for ≥ 10 months). The height has increased by ≥ 4 cm/year in the most recent year; OR

iii. Patients ≥ 12 years of age and ≤ 18 years of age (i.e., established on somatropin for ≥ 10 months). The patient meets the following criteria (a and b):
   a. Height has increased by ≥ 4 cm/year in the most recent year; AND
   b. The epiphyses are open

iv. Adolescents and young adults > 18 years of age (i.e., established on somatropin for ≥ 10 months). The patient meets the following criteria (a, b, and c):
   a. Height has increased by ≥ 4 cm/year in the most recent year; AND
   b. The epiphyses are open; AND
   c. Mid-parental height has not been attained

E. If patient has a diagnosis of GHD, adult or transitioning adult. Approve for initial therapy for 1 year in patients who meet the following criteria (i, ii, and iii):

i. The endocrinologist must certify that somatropin is not being prescribed for anti-aging therapy or to enhance athletic ability or for body building; AND

ii. Childhood onset; OR Adult onset that results from one of the following: growth hormone deficiency (GHD) alone or multiple hormone deficiencies (hypopituitarism) resulting from pituitary disease, hypothalamic disease, pituitary surgery, cranial radiation therapy, tumor treatment, traumatic brain injury, or subarachnoid hemorrhage; AND

iii. Patient meets one of the following criteria (a, b, or c):
   a. The patient (adult or transition adolescent) had childhood-onset growth hormone deficiency (GHD) and has known mutations, embryopathic lesions, congenital defects, or irreversible structural hypothalamic-pituitary lesions/damage OR
   b. Patient meets all of the following criteria (1, 2, and 3)
      1. The patient (adult onset or transition adolescent) has three or more of the following pituitary hormone deficiencies: Adrenocorticotropic hormone (ACTH),
thyroid-stimulation hormone (TSH), gonadotropin
deficiency (luteinizing hormone [LH] and/or follicle
stimulating hormone (FSH) deficiency are counted as
one deficiency), and prolactin AND

2. The age and gender adjusted serum insulin-like
growth factor-1 (IGF-1) must be below the lower limits
of the normal reference range for the reporting
laboratory AND

3. Other causes of low serum insulin-like growth factor-1
(IGF-1) have been excluded (e.g., malnutrition,
prolonged fasting, poorly controlled diabetes mellitus,
hypothyroidism, hepatic insufficiency, oral estrogen
therapy)

OR

c. The patient has had a negative response to one of the
following standard growth hormone stimulation tests with the
response given for each test and depending on whether an
adult or transition adolescent

Adults: the patient meets ONE of the following (i, ii, iii, iv, or v):

i. Insulin tolerance test with peak response ≤
5.0 mcg/L; OR

ii. Glucagon stimulation test with peak response
≤ 3.0 mcg/L AND the patient’s body mass
index (BMI) is ≤ 25 kg/m2; OR

iii. Glucagon stimulation test with peak response
≤ 1.0 mcg/L AND the patient’s body mass
index (BMI) is > 25 kg/m2; OR

iv. If both the insulin tolerance test AND
glucagon stimulation test are contraindicated,
the arginine alone test can be used with a
peak response ≤ 0.4 mcg/L OR

v. Macrilen™ (macimorelin for oral solution) test
with peak responses < 2.8 ng/mL (2.8 mcg/L)
AND the patient’s body mass index (BMI) is ≤
40 kg/m2

Transition adults: the patient has been off somatropin therapy
for at least 1 month before retesting with a growth hormone
stimulation test and meets ONE of the following (i, ii, iii, or iv):

i. Insulin tolerance test with peak response ≤
5.0 mcg/L; OR

ii. Glucagon stimulation test with peak response
≤ 3.0 mcg/L AND the patient’s body mass
index (BMI) is < 25 kg/m2; OR

iii. Glucagon stimulation test with peak response
≤ 3.0 mcg/L AND the patient’s body mass
index (BMI) is ≥ 25 kg/m2 AND a second
growth hormone stimulation test with a peak
response as stated in transition adolescents
b1, b4, or b5 in this section; OR

iv. If both the insulin tolerance test AND
glucagon stimulation test are contraindicated,
the arginine alone test can be used with a
peak response ≤ 0.4 mcg/L

F. If the patient has a diagnosis of GHD, is an adult or transition adolescent, and
is continuing therapy (established on somatropin for ≥ 10 months), approve
continuing therapy for 1 year in patients who meet the following criteria (i, and
ii) every 12 months:

i. Childhood onset; OR Adult onset that results from one of the following:
growth hormone deficiency (GHD) alone or multiple hormone
deficiencies (hypopituitarism) resulting from pituitary disease, hypothalamic disease, pituitary surgery, cranial radiation therapy, tumor treatment, traumatic brain injury, or subarachnoid hemorrhage; AND

ii. The endocrinologist must certify that somatropin is not being used for anti-aging therapy or to enhance athletic performance/body building

G. If patient has a diagnosis of chronic kidney disease. Approve for initial therapy for 1 year in patients who meet the following criteria (i, and ii):
   i. Patient has been evaluated by an endocrinologist OR a nephrologist AND
   ii. Patient has CKD as defined by an abnormal creatinine clearance

H. If the patient has a diagnosis of CKD and is continuing therapy (established on somatropin for ≥ 10 months), approve continuing therapy for 1 year in patients who meet the following criteria (i, and ii):
   i. Height has increased by ≥ 2.5 cm/year in the most recent year AND
   ii. The epiphyses are open

I. If patient has a diagnosis of Noonan syndrome. Approve for initial therapy for 1 year in patients who meet the following criteria (i):
   i. The patient’s baseline height is less than the 5th percentile using a growth chart for children without Noonan syndrome

J. If the patient has a diagnosis of Noonan syndrome and is continuing therapy (established on somatropin for ≥ 10 months), approve continuing therapy for 1 year in patients who meet the following criteria (i, and ii):
   i. Height has increased by ≥ 2.5 cm/year in the most recent year AND
   ii. The epiphyses are open

K. If patient has a diagnosis of Prader-Willi syndrome. Approve for initial therapy for 1 year.

L. If the patient has a diagnosis of Prader-Willi syndrome and is continuing therapy (established on somatropin for ≥ 10 months), approve continuing therapy for 1 year in patients who meet the following criteria (i, or ii):
   i. Children and adolescents: Patient meets the following criteria (a and b):
      a. Height has increased by ≥ 2.5 cm/year in the most recent year AND
      b. The epiphyses are open (When the epiphyses are closed and/or the height velocity is < 2.5 cm/year, the patient can be reviewed for continuation of therapy as an adult with Prader-Willi syndrome)
   ii. Adults or adolescents whose epiphyses are closed and/or whose height velocity is < 2.5 cm/year: Patient meets all of the following (a):
      a. The endocrinologist must certify that somatropin is not being used for anti-aging therapy or to enhance athletic performance/body building

M. If patient has a diagnosis of Short Stature Homeobox-Containing Gene Deficiency (SHOX). Approve for initial therapy for 1 year in patients who meet the following criteria (i, ii, and iii):
   i. Patient has short stature homeobox-containing gene (SHOX) deficiency demonstrated by chromosome analysis; AND
   ii. Epiphyses are open; AND
   iii. The patient’s baseline height is less than the 3rd percentile for age and gender

N. If the patient has a diagnosis of SHOX and is continuing therapy (established on somatropin for ≥ 10 months), approve continuing therapy for 1 year in patients who meet the following criteria (i, and ii):
   i. Height has increased by ≥ 2.5 cm/year in the most recent year AND
   ii. The epiphyses are open

O. If patient has a diagnosis of children born small for gestational age or with intrauterine growth restriction (retardation) including those with Silver-Russell syndrome. Approve for initial therapy for 1 year in patients who meet the following criteria (i, ii, and iii):
i. Patient is ≥ 2 years of age; AND

ii. Patient was born small for gestational age (SGA), which is defined as birth weight and/or birth length that is > 2 standard deviations (SD) below the mean (< -2 SD) for gestational age and gender, and the patient did not have sufficient catch-up growth before age 2 to 4 years; AND

iii. The patient’s baseline height is less than the 5th percentile for age and gender

P. If the patient has a diagnosis of small for gestational age or with in utero growth restriction (retardation) including those with Silver-Russell syndrome and is continuing therapy (established on somatropin for ≥ 10 months), approve continuing therapy for 1 year in patients who meet the following criteria (i, ii, or iii):

i. Patients < 12 years of age. Height has increased by ≥ 4 cm/year in the most recent year.

ii. Patients ≥ 12 years and ≤ 18 years of age. The patient meets the following criteria (a and b):
   a. Height has increased by ≥ 4 cm/year in the most recent year; AND
   b. The epiphyses are open

iii. Adolescents and young adults > 18 years of age. The patient meets the following criteria (a, b, and c):
   a. Height has increased by ≥ 4 cm/year in the most recent year; AND
   b. Epiphyses are open; AND
   c. Mid-parental height has not been attained

Q. If patient has a diagnosis of Turner syndrome. Approve for initial therapy for 1 year

R. If patient has a diagnosis of Turner syndrome and is continuing therapy (established on somatropin for ≥ 10 months), approve continuing therapy for 1 year in patients who meet the following criteria (i and ii):

i. Height has increased by ≥ 2.5 cm/year in the most recent year; AND

ii. The epiphyses are open

OR

3) If patient has a diagnosis is Short Bowel Syndrome in adults. Approve of initial therapy for 1 month if the patients meets the following criteria (A and B):

A. Patient is receiving specialized nutritional support (defined as a high carbohydrate, low-fat diet that is adjusted for individual patient requirements and preferences); AND

B. Patient is ≥ 18 years of age

4) If patient has diagnosis of SBS and is continuing therapy (established on somatropin for ≥ 10 months), approve continuing therapy for a second 1-month course if the adult responded with a decrease in requirement for specialized nutritional support according to the prescribing physician

Coverage of Serostim is recommended in patients who meet the following criteria:

5) If patient has diagnosis is HIV with wasting or cachexia in adults. Approve of initial therapy for 6 months in patients who meet all of the following criteria (A, B, C, D, and E):

A. Patient is ≥ 18 years of age; AND

B. Patient has ONE of the following (i, ii, or iii):
   i. Documented unintentional weight loss of ≥ 10% from baseline; OR
   ii. Weight < 90% of the lower limit of ideal body weight; OR
   iii. Body mass index (BMI) ≤ 20 kg/m2; AND

C. Patient has wasting or cachexia that is due to malabsorption, poor diet, opportunistic infection, or depression, and other causes have been addressed prior to starting somatropin; AND
D. The patient has been on antiretroviral therapy or highly active antiretroviral treatment (HAART) for ≥ 30 days prior to beginning Serostim therapy and will continue antiretroviral therapy throughout the course of Serostim treatment; AND
E. Serostim is not being used solely for treatment of alterations in body fat distribution such as increased abdominal girth, lipodystrophy and excess abdominal fat, or buffalo hump

6) If patient has diagnosis of HIV with wasting or cachexia and is continuing serostim therapy, approve up to a 6 month course of Serostim if the patient meets all the above criteria (5A-E), AND patient has to have been OFF Serostim for at least 1 month

7) For indications 2), approval of Nutropin®, Nutropin® AQ, Humatrope®, Saizen®, Zomacton/TevTropin®, Omnitrope® only after trial of Genotropin® or Norditropin®

8) For indications 3), approval of Nutropin®, Nutropin® AQ, Humatrope®, Saizen®, Zomacton/TevTropin®, Omnitrope®, Zorbtive® only after trial of Genotropin®, or Norditropin®

9) Patient has no conditions not recommended for approval to treatment

Reasons for Denial of Benefit:

1) Patient does not meet Criteria for Approval
2) Patient has any of the following conditions not recommended for approval:
   i. Acute critical illness due to complications following surgery, multiple accidental trauma, or with acute respiratory failure
   ii. Anti-aging, to improve functional status in elderly patients and somatopause
   iii. Athletic ability enhancement
   iv. Bony dysplasias (achondroplasia, hypochondroplasia)
   v. Burn injury (extensive) in children or adults
   vi. Cardiac transplantation
   vii. Central precocious puberty
   viii. Chronic fatigue syndrome
   ix. Congenital adrenal hyperplasia (CAH)
   x. Constitutional delay of growth and puberty (CDGP)
   xi. Corticosteroid-induced short stature
   xii. Crohn’s disease
   xiii. Cystic fibrosis
   xiv. Dilated cardiomyopathy and heart failure
   xv. Down’s syndrome
   xvi. End-stage renal disease in adults undergoing hemodialysis
   xvii. Familial dysautonomia (Riley-Day syndrome, Hereditary Sensory Autonomic Neuropathy)
   xviii. Fibromyalgia
   xix. Hematopoietic stem cell transplant without total body irradiation or cranial radiation
   xx. HIV-Infected patients with alterations in body fat distribution
   xxi. Infertility
   xxii. Kidney transplant patients (children) with a functional renal allograft
   xxiii. Liver transplant
   xxiv. Multiple system atrophy (MSA)
   xxv. Myelomeningocele
   xxvi. Obesity
   xxvii. Osteogenesis imperfecta
   xxviii. Osteoporosis
   xxix. Thalassemia
X-linked hypophosphatemria rickets (familial hypophosphatemria, hypophosphatemria rickets)

Policy History:
- Created: July 2003
- Reason: Adoption of ESI standard, customized for co-prefering Genotropin and Norditropin

Benefit Approval:
- All approvals for initial therapy and continuation specifics per indication found in monograph above.

References: