



Growth Hormone Prior Authorization Program Summary

This program applies to MN Medicaid only.

All products in this program are targeted, formulary and non-formulary. Additional FE review required for non-formulary drugs.

For Medicaid, the preferred products are the MN Medicaid Preferred Drug List (PDL) preferred drugs: Norditropin and Nutropin AQ.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

FDA APPROVED INDICATIONS AND DOSAGE **1-8,26,28

Available Products	GHD* IN CHILD-REN	GHD IN ADULTS±	CKD	PWS	TS	SGA	ISS	SHOX	HIV	NS	SBS
Genotropin® (mg/kg/week)	✓ 0.16-0.24	✓ 0.04-0.08		✓ 0.24	✓ 0.33	✓ Up to 0.48	✓ Up to 0.47				
Humatrope® (mg/kg/week^)	✓ 0.18-0.3	✓ 0.006-0.0125^ mg/kg/day			✓ Up to 0.375	✓ Up to 0.47	✓ Up to 0.37	✓ 0.35			
Norditropin® (mg/kg/day)	✓ 0.024-0.034	✓ 0.004-0.016		✓ 0.24	✓ Up to 0.067	✓ Up to 0.067	✓ Up to 0.47			✓ Up to 0.066	
Nutropin® AQ (mg/kg/week)	✓ 0.3-0.7	✓ 0.006-0.025 (≤35 y.o.) or up to 0.0125 (>35 y.o.) mg/kg/day	✓ Up to 0.35		✓ Up to 0.375		✓ Up to 0.3				
Omnitrope (mg/kg/week)	✓ 0.16-0.24	✓ 0.04-0.08		✓ 0.24	✓ 0.33	✓ Up to 0.48	✓ Up to 0.47				
Saizen® (mg/kg/week)	✓ 0.18	✓ 0.005 initial mg/kg/day May be increased to no more than 0.01 mg/kg/day after 4 weeks									
Serostim® (mg/kg/day)									✓ 0.1		

Available Products	GHD* IN CHILD-REN	GHD IN ADULTS [±]	CKD	PWS	TS	SGA	ISS	SHOX	HIV	NS	SBS
									(up to 6 mg daily) ^a		
Zomacton® (mg/kg 3 times/week)	✓ 0.1 (up to 0.3 mg/kg/week)	✓ Non-weight based: initial 0.15-0.3 mg/day and may increase every 1-2 months by 0.1-0.2 mg/day Weight based (not recommended for obese: Initial 0.006 mg/kg daily with maximum of 0.0125 mg/kg)			✓ Up to 0.375 mg/kg /week	✓ Up to 0.47 mg/kg /week	✓ Up to 0.37 mg/kg /week	✓ 0.35 mg/kg/week			
¥ Zorbtive® (SC: mg/kg/day)											✓ 0.1 (up to 8 mg daily)

* - GHD-growth hormone deficiency, CKD-chronic kidney disease, PWS-Prader Willi Syndrome, TS-Turner's Syndrome, SGA-Small for Gestational Age, ISS-Idiopathic Short Stature, SHOX-SHOX deficiency, HIV- HIV patients with wasting or cachexia, NS-Noonan Syndrome, SBS-Short Bowel Syndrome
^ - Max dose for Humatrope adult GHD is 0.0125 mg/kg/day (12.5 µg/kg/day);
± - Can also dose by *Non-weight based dosing*: A starting dose of approximately 0.2 mg/day (range, 0.15-0.30 mg/day) may be used without consideration of body weight, and increased gradually every 1-2 months by increments of approximately 0.1-0.2 mg/day.
¥ - Administration for more than 4 weeks has not been adequately studied
** - Current guidelines recommend adult non-weight based dosing be initiated at 0.1 -0.2 mg/day and gradually titrated to the minimal dose that normalizes serum IGF-1 levels.
^a - Most of the effect of Serostim on work output and lean body mass was apparent after 12 weeks of treatment. The effect was maintained during an additional 12 weeks of therapy. There are no safety or efficacy data available from controlled studies in which patients were treated with Serostim continuously for more than 48 weeks.

CLINICAL RATIONALE

Idiopathic short stature (ISS) refers to extreme short stature that does not have a diagnostic explanation. "Short stature" has been defined by the American Association of Clinical Endocrinologists as height more than two standard deviations (SD) below the mean for age and sex. ISS refers to a height of more than 2.25 SD below the mean for age and sex, or the shortest 1.2% of children.¹⁷

Short bowel syndrome (SBS) is a malabsorption disorder caused by either the surgical removal of the small intestine or the loss of its absorptive function due to various diseases. In clinical studies, the administration of GH enhanced the transmucosal transport of water, electrolytes, and nutrients.⁴

Short stature may be the only apparent feature present in children with GHD.²⁰ The following features indicate a need for further investigation: severe short stature (height more than three SD below the mean), height more than 1.5 SD below the midparental height, height more than two SD below the mean and a height velocity over one year more than one SD below the mean for chronological age, or a decrease in height SD of more than 0.5 over one year in children over two years of age.²⁰ Patients who have GHD presenting at infancy or have acquired GHD, short stature may not yet be apparent. These patients may present with height velocities more than 2 SD below the mean over one year or more than 1.5 SD sustained over two years.²⁰

A trial of GH therapy should be approved for children with otherwise unexplained short stature who pass GH stimulation tests, but who meet most of the following criteria: (1) height >2.25 SD below the mean for age or >2 SD below the mid-parental height percentile; (2) growth velocity 2 SD below the mean for age; (4) low serum insulin-like growth factor 1 (IGF-I) and/or insulin-like growth factor binding protein 3 (IGFBP3); and/or (5) other clinical features suggestive of GHD.²¹

UptoDate states the following for the diagnosis of growth hormone deficiency in children:³

- A more comprehensive evaluation is warranted in children with one or more of the following:
 - Growth failure – suggested by a height for age curve that has deviated downwards across two major height percentile curves or the child is growing slower than the following rates:
 - Age 2-4 years: height velocity (HV) less than 5.5 cm/year (<2.2 inches/year)
 - Age 4-6 years: HV less than 5 cm/year (<2 inches/year)
 - Age 6 to puberty:
 - HV less than 4 cm/year for boys (<1.6 inches/year)
 - HV less than 4.5 cm/year for girls (<1.8 inches/year)
 - Severe short stature (e.g. height \leq 2.5 SD [0.6th percentile]), or less severe short stature combined with growth failure
 - Features that raise concerns for hypothalamic-pituitary hormones, either congenital or acquired
 - Evidence for deficits in other hypothalamic-pituitary hormones, either congenital or acquired
- Once decision is made for further evaluation, other causes for growth failure should be ruled out and once ruled out, the possibility of GHD should be investigated with the following test:
 - Insulin-like growth factor I (IGF-I)
 - Insulin-like growth factor binding protein 3 (IGFBP-3)
 - Bone age
- The IGF-I, IGFBP-3, and bone age testing results may be interpreted as follows:
 - Moderately or severely reduced IGF-I and IGFBP-3 (e.g. <1.3 SD) with delayed bone age
 - In most cases, the possibility of GHD should be further examined by provocative GH testing
 - If growth failure is severe, bone age is significantly delayed, and IGF-I and IGFBP-3 are definitively low (e.g. <-2 SD), it is reasonable to make the diagnosis of GHD without performing GH stimulation testing, especially in the setting of known hypothalamic-pituitary disease and/or its treatment (e.g. brain surgery and/or radiations).

- Somewhat low IGF-I and IGFBP-3 (e.g. between 0 and -1.3 SD) – The decision about whether to perform provocative GH testing depends on individual patient characteristics, including the severity of growth failure, degree of bone age delay, and whether the low levels can be explained by other factors, such as poor nutrition.
 - Clearly normal IGF-I and IGFBP-3 (SD ≥ 0 , i.e. in the upper half of the normal range) – GHD is extremely unlikely, and no further testing is required
 - If the IGF-I and IGFBP-3 are discordant, IGF-I takes precedence except for infants and young children, in whom IGFBP-3 should take precedence.
- Provocative (stimulation) GH testing is indicated for most patients to confirm GHD, however, because this testing has limitations, it should not be the sole diagnostic criterion.
- Provocative GH testing is not necessary for the following patients whose other clinical criteria are sufficient for diagnosis of GHD
 - Pituitary abnormality and a known deficiency of at least one other pituitary hormone, as well as auxological criteria
 - Newborn with congenital pituitary abnormality or known deficiency of a pituitary hormone, along with hypoglycemia, at which time a simultaneous serum GH concentration is < 5 mcg/L
 - Infant or young child with extreme short stature (e.g. height < -3 SD), normal nutrition, significantly reduced IGF-I and IGFBP-3 (e.g. < -2 SD) and delayed bone age.
- In general, two different stimuli should be used for provocative GH testing. Those with known pathology of the central nervous system, other pituitary hormone defects, or a genetic defect, one test is sufficient to establish GHD.

UptoDate states the following for growth hormone deficiencies in adults:²⁹

- The diagnosis of GHD in adults is likely in the patient has documented panhypopituitarism and a low serum IGF-1 concentration confirms the diagnosis of GHD.
- An IGF-I level lower than the gender and age specific lower limit of normal in a patient who has organic pituitary disease confirms the diagnosis of GHD.
- If IGF-I is equivocal, a subnormal GH response to a provocative test will confirm the diagnosis.
- A subnormal increase in serum GH level in a patient who has organic pituitary disease confirms the diagnosis of GHD.
- Recommend two GH stimulation test to help confirm GHD.

The 2016 Hormone Research in Paediatrics Clinical Practice Committee states the following:⁹

- The use of GH provocative testing is not required for diagnosis of GHD
 - In patients possessing all of the following three conditions: auxological criteria, hypothalamic-pituitary defect (such as major congenital malformation [ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk], tumor or irradiation), and deficiency of at least one additional pituitary hormone
 - In a newborn with hypoglycemia who does not attain a serum GH concentration above 5 mcg/L and has deficiency of at least one additional pituitary hormone and/ or the classical imaging triad (ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk)
- GH provocative testing should not be used as a sole diagnostic criterion
- For those transitioning after childhood GH treatment
 - Patients with multiple (≥ 3) pituitary hormone deficiencies regardless of etiology, or GHD with a documented causal genetic mutation or specific pituitary/hypothalamic structural defect except ectopic posterior pituitary, should be diagnosed with persistent GHD
 - Re-evaluation of the somatotrophic axis should be performed to identify persistent GHD in persons with GHD and deficiency of only one additional pituitary hormone,

- idiopathic isolated GHD (IGHD), IGHD with or without a small pituitary/ectopic posterior pituitary, and in patients after irradiation
- Measurement of the serum IGFI concentration should be the initial test of the somatotrophic axis if re-evaluation of the somatotrophic axis is clinically indicated
- GH provocative testing should be performed to evaluate the function of the somatotrophic axis in the transition period if indicated by a low IGF-I level.
- GH treatment should be offered to individuals with persistent GHD in the transition period.

The International Societies of Pediatric Endocrinology and the Growth Hormone Research Society state that the definition of short gestation age (SGA) is not straightforward; however, they recommend that SGA should be defined as a weight and/or length less than -2 SD because this will identify the majority of those in whom ongoing growth assessment is required (this definition is also mirrored in other publications).²⁷ It is believed that identification of SGA is important since these infants are at an increased risk for perinatal morbidity, associated health problems (e.g. neurodevelopmental disorders), persistent short stature, and metabolic alterations in later life.²⁷ Approximately 90 % of term SGA infants display sufficient catch-up growth to attain a height above -2 SD by the age of 2 years, whereas 10 percent remain short throughout childhood and adolescence.³ Regarding GH therapy, they state that there should be a positive response to GH treatment (height velocity SD score more than +0.5 in the first year of treatment). If there is an inadequate response, reevaluation is indicated, including consideration of compliance, GH dose, diagnosis, and the decision to discontinue treatment. In those with a positive response to GH, withdrawal of GH therapy after 2–3 yr leads to catch-up growth and is not recommended. Discontinuation of GH treatment in adolescence is recommended when the growth rate falls to less than 2 cm/yr.²⁷

Growth hormone products are considered clinically identical, without differences in efficacy and safety. The variations are in how the GH product is stored, dosed, and administered by device.²⁵

Laboratory Tests for Diagnosis of GHD

Evaluation for GHD should be considered if the following conditions exist:^{10-12,19}

- A child with a standing height of more than 3 standard deviation below the mean for chronological age, sex, and ethnic background
- A child with a height velocity below the fifth to tenth percentile for age, with no clear etiology
- A child with a standing height that is 2 SD to 3 SD below the mean for chronologic age, and with growth deceleration (growth velocity less than the twenty-fifth percentile) that cannot otherwise be explained
- Hypothalamic-pituitary dysfunction (e.g., microphallus, septo-optic dysplasia, intracranial tumor, history of cranial irradiation) with decelerating growth
- Deficits in other hypothalamic-pituitary hormones, either congenital or acquired
- Adults with manifestations suggestive of GHD

In newborns who present with hypoglycemia in the absence of a metabolic disorder, a serum growth hormone level of < 20 mcg/L is highly suggestive of GHD.²⁰

Guidelines recommend that the presence of deficiencies in three or more pituitary axes (panhypopituitarism) and serum IGF-I levels below the age- and sex-appropriate reference range when off GH therapy are deemed GHD, and do not require further stimulation testing.^{17,22,24}

GH stimulation (provocative) tests play a critical role in the diagnosis of GHD. The most frequently used tests include the insulin tolerance test (ITT); arginine; growth hormone releasing hormone (GHRH), with or without arginine; levodopa (L-dopa); glucagon, with or without a beta blocker, such as propranolol; and clonidine.^{10,11,19}

Most endocrinologists use a cutoff serum growth hormone concentration of more than 10 mcg/L in children and of more than 3 mcg/L (some authorities use 5 mcg/L) in adults to define normal response on provocative tests. The following are the most recent guidelines regarding stimulation testing; however, they are both outdated (2009 and 2011) and not up-to-date with current clinical practice.^{10,11,17,19}

- The Growth Hormone Research Society has recommended the ITT as the standard test for the diagnosis of GHD in adults.¹¹
- In an ITT, insulin is administered intravenously to produce a nadir in the plasma glucose level of less than 40 mg/dL (2.2 mmol/L); serum (or blood) glucose and serum growth hormone levels are measured at times 0, 15, 30, 60, 90, and 120 minutes after administering insulin. An experienced staff under the direct supervision of a physician should perform the test. GHD is diagnosed when the growth hormone level is less than 5 mcg/L.
- An ITT is contraindicated in patients with cardiovascular disease, cerebrovascular disease, or seizure disorders, or in patients older than 65 years.
- The GHRH-arginine test was used by many centers as an alternative to the ITT. When the GHRH-arginine test was employed, a GHD was diagnosed when the growth hormone level was < 4.1 mcg/L. However, manufacture of Geref (GHRH) was indefinitely discontinued in 2008 and unavailability of recombinant GHRH in the United States has created a need for a reliable alternative to this test. To establish the diagnosis of adult GHD in patients with child-onset GHD, the ITT is the preferred test. The glucagon test, and rarely the ARG test, are acceptable alternatives.
- In patients with a GHD of hypothalamic origin (as a result, for example, of irradiation), GHRH can give falsely normal testing. In such patients, ITT or glucagon should be used.¹⁷
- In patients where the ITT is not desirable and when recombinant GHRH is not available, the glucagon test is a reliable alternative, but not the levodopa and clonidine tests.¹⁷

Some clinicians require that these criteria occur on 2 provocative tests because of the high frequency of false-negative results for each single test.^{10,19}

Treatment of Growth Hormone Deficiency

All somatotropin (GH) therapy is indicated in children with growth hormone deficiency (GHD) with an abnormal growth velocity curve, and an untreated growth velocity less than the tenth percentile for bone age and gender.¹³ The American Association of Clinical Endocrinologists (AACE) and the National Institute for Health and Clinical Excellence (NICE) recommend somatotropins in children with GHD, Turner's syndrome, chronic renal insufficiency, and Prader-Willi Syndrome.¹⁷⁻¹⁸ The NICE 2010 updated guidelines also include the recommendation for the use of somatotropins in children born small for gestational age with subsequent failure at 4 years of age or later and short stature homeobox-containing gene (SHOX) deficiency.¹⁸

The American Association of Clinical Endocrinologists Medical Guidelines for GH use in GH Deficient Adults and Transition Patients-2009 Update recommendations include¹⁷:

- GH should only be prescribed to patients with clinical features suggestive of adult GHD and biochemically proven evidence of adult GHD.
- No data are available to suggest that GH has beneficial effects in treating aging and age-related conditions and the enhancement of sporting performance; therefore, we do not recommend the prescription of GH to patients for any reason other than the well-defined approved uses of the drug.
- For childhood GH treatment of conditions other than GHD, such as Turner's syndrome and idiopathic short stature, there is no proven benefit to continuing GH treatment in adulthood; hence, there is no indication to retest these patients when final height is achieved.
- On restarting GH therapy, the starting dose of GH in transition patients should be approximately 50% of the dose between the pediatric doses required for growth and the adult dose.
- "There is no evidence that one GH product is more advantageous over the other, apart from differences in pen devices, dose increments and decrements, and whether or not

the product requires refrigeration; therefore, we do not recommend the use of one commercial GH preparation over another.”

The Endocrine Society Clinical Practice guideline (2011) for evaluation and treatment of adult growth hormone deficiency recommends that 2 stimulation tests be performed for patients with idiopathic GHD due to the difficulty in accurately diagnosing this condition. These guidelines also advise that deficiencies in 3 or more pituitary axes is strongly suggestive of GHD and stimulation testing is optional in this situation.²²

HIV/AIDS wasting was historically common, particularly in later stages of the disease. The incidence of wasting has declined since the introduction of anti-retroviral therapy (ART). Tissue wasting responds rapidly to ART, and the primary therapy for HIV wasting is ART.¹⁵ The diagnosis of HIV wasting requires one of the following:^{16,23}

- Weight loss of greater than:
 - 10% within 12 months or from baseline visit
 - 7.5% within 6 months
 - 5% within 3 months
- At least 5% total body cell mass (BCM) loss within 6 months
- Body mass index (BMI) <20 kg/m²
- In men: BCM <35% of total body weight and BMI <27 kg/m²
- In women: BCM <23% of total body weight and BMI <27 kg/m²

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Growth Hormone Prior Authorization

TARGET AGENTS - For Medicaid, the preferred products are the MN Medicaid Preferred Drug List (PDL) preferred drugs: Norditropin and Nutropin AQ.

Omnitrope® (somatropin)
Genotropin® (somatropin)
Humatrope® (somatropin)
Norditropin® NordiFlex, Norditropin Flexpro (somatropin)
Nutropin AQ® (somatropin)
Nutropin AQ Nuspin® (somatropin)
Saizen®, Saizen Click.Easy (somatropin)
Serostim® (somatropin)
Zomacton® (somatropin)
Zorbtive® (somatropin)

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Growth Hormone (GH) products will be approved as below.

For **Children – Initial Evaluation** when ALL of the following are met:

1. ONE of the following:
 - a. The request is for a preferred agent or Zorbtive or Serostim
OR
 - b. ONE of the following:
 - i. The patient has tried and had an inadequate response to the preferred agents
OR
 - ii. The patient has documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred agents
OR
 - iii. The prescriber has submitted documentation in support of the use of the non-preferred agent, for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist
- AND**
2. The patient is a child (as defined by the prescriber)
AND
3. ONE of the following:
 - a. If the request is for Zorbtive, the patient has a diagnosis of short bowel syndrome (SBS) AND is receiving enteral or parenteral nutritional support or other specialized nutritional support
OR
 - b. BOTH of the following:
 - i. The patient has ONE of the following diagnoses:
 1. Hypoglycemia in newborns (patient is ≤ 4 months of age) AND has a diagnosis of hypopituitarism or panhypopituitarism
OR
 2. Turner's Syndrome
OR
 3. Noonan Syndrome
OR
 4. Prader-Willi Syndrome
OR
 5. Leri-Weill Dyschondrosteosis
OR

- 6. Chronic renal insufficiency
OR
- 7. Acquired growth hormone deficiency (GHD), which can be due to, but is not limited to: pituitary surgery, pituitary insufficiency, radiation treatments, pituitary tumor, trauma, central nervous system tumors, cranial irradiation or panhypopituitarism
OR
- 8. Pediatric growth hormone deficiency or another diagnosis AND ALL of the following:
 - a. The patient has not attained epiphyseal closure as determined by X-ray
AND
 - b. The patient has a height more than 2 SD below the mean for age and sex
AND
 - c. The patient has a growth velocity more than 1 SD below the mean for chronological age over one year
AND
 - d. The patient has failed at least 2 GH stimulation tests (with insulin, levodopa, arginine, propranolol, clonidine, or glucagon), defined with a peak GH value of <10 ng/mL after stimulation
AND
 - e. The patient has a documented gender-specific delayed bone age
AND
- ii. The prescriber is a pediatric endocrinologist or a pediatric nephrologist, or prescriber has had at least one annual consultation about the patient with the pediatric specialty (endocrinology or nephrology)

Length of Approval: 6 months

For **Children – Renewal Evaluation** when ALL of the following are met:

- 1. ONE of the following:
 - a. The request is for a preferred agent or Zorbtive or Serostim
OR
 - b. ONE of the following:
 - i. The patient has tried and had an inadequate response to the preferred agents
OR
 - ii. The patient has documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred agents
OR
 - iii. The prescriber has submitted documentation in support of the use of the non-preferred agent, for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist
AND
- 2. The patient is a child (as defined by the prescriber)
AND
- 3. ONE of the following:
 - a. The patient has been approved for therapy with GH previously through the Prime Therapeutics PA process
OR
 - b. The patient has undergone a 6 month trial of GH supplied by a manufacturer

- AND**
4. ONE of the following:
 - a. If the request is for Zorbtive, the patient has a diagnosis of short bowel syndrome (SBS) AND has shown clinical benefit from treatment with growth hormone
OR
 - b. The patient has a diagnosis of hypopituitarism or panhypopituitarism
OR
 - c. The patient has any other diagnosis AND ALL of the following:
 - i. The patient's height is less than 5'6" for males or 5'1" for females
AND
 - ii. The patient has not attained epiphyseal closure. (Epiphyseal closure is defined as a bone age of 16 years in a male or 14 years in a female on wrist films)
AND
 - iii. The patient's growth velocity has improved since initiation or last GH approval, defined as >4.5 cm/year in a pre-pubertal child or >2.5 cm/year in a post-pubertal child

Length of Approval: 12 months

For **Adults – Initial Evaluation** when ALL of the following are met:

1. ONE of the following:
 - a. The request is for a preferred agent or Serostim or Zorbtive
OR
 - b. ONE of the following:
 - i. The patient has tried and had an inadequate response to the preferred agents
OR
 - ii. The patient has documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred agents
OR
 - iii. The prescriber has submitted documentation in support of the use of the non-preferred agent, for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist
- AND**
2. The patient is an adult (as defined by the prescriber)
AND
3. ONE of the following:
 - a. If the request is for Serostim, the patient has a diagnosis of AIDS wasting/cachexia AND BOTH of the following:
 - i. If the patient is acidemic, attempts have been made to increase serum bicarbonate
AND
 - ii. ONE of the following:
 1. The patient has tried and had an inadequate response to an appetite stimulant (dronabinol or megestrol)
OR
 2. The patient has documented intolerance, FDA labeled contraindication, or hypersensitivity to an appetite stimulant (dronabinol or megestrol)
 - OR**
 - b. If the request is for Zorbtive, the patient has a diagnosis of short bowel syndrome (SBS) AND is receiving enteral or parenteral nutritional support or other specialized nutritional support

OR

c. BOTH of the following:

i. ONE of the following:

1. The patient has a diagnosis of childhood onset symptomatic growth hormone deficiency (GHD) AND has failed at least one GH stimulation test (with insulin, levodopa, L-arginine, clonidine, or glucagon) performed at least 3 months after the cessation of prior GH therapy (peak GH value of <5 ng/mL after stimulation measured by radioimmunoassay or <2.5 ng/mL measured by immunoradiometric assay)

OR

2. BOTH of the following:

a. The patient has a diagnosis of adult onset symptomatic GHD associated with multiple hormone deficiencies (i.e., panhypopituitarism) as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma

AND

b. ONE of the following:

i. The patient is deficient in at least 3 or more pituitary hormones (other than GH) requiring hormone replacement therapy where clinically appropriate (e.g., thyroid-stimulating hormone, adrenocorticotrophic hormone, prolactin, luteinizing hormone, follicle-stimulating hormone, antidiuretic hormone, oxytocin) AND the patient's serum IGF-1 (insulin-like growth factor-1) levels are below the age- and sex-appropriate reference range when off GH therapy

OR

ii. The patient is deficient in at least 2 additional pituitary hormones (other than GH) requiring hormone replacement therapy (e.g., thyroid-stimulating hormone, adrenocorticotrophic hormone, prolactin, luteinizing hormone, follicle-stimulating hormone, antidiuretic hormone, oxytocin) AND has failed at least one GH stimulation test (with insulin, levodopa, L-arginine, clonidine, or glucagon; peak GH value of <5 ng/mL after stimulation measured by radioimmunoassay or <2.5 ng/mL measured by immunoradiometric assay)

OR

3. The patient has a diagnosis of adult onset symptomatic GHD or another diagnosis AND the patient has failed at least two GH stimulation tests (with insulin, levodopa, L-arginine, clonidine, or glucagon) as an adult following a GH washout period of 1 to 3 months (peak GH value of <5 ng/mL after stimulation measured by radioimmunoassay or <2.5 ng/mL measured by immunoradiometric assay)

AND

ii. The prescriber is an endocrinologist specializing in the treatment of adult growth hormone deficiency, or prescriber has had at least one annual consultation about the patient with an endocrinology specialist

Length of Approval: 12 weeks for AIDs wasting/cachexia;
12 months for other indications

For **Adults – Renewal Evaluation** when ALL of the following are met:

1. ONE of the following:

a. The request is for a preferred agent or Serostim or Zorbtive

OR

b. ONE of the following:

i. The patient has tried and had an inadequate response to the preferred agents

OR

ii. The patient has documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred agents

OR

iii. The prescriber has submitted documentation in support of the use of the non-preferred agent, for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

AND

2. The patient is an adult (as defined by the prescriber)

AND

3. The patient has been approved for therapy with GH previously through the Prime Therapeutics PA process

AND

4. ONE of the following:

a. If the request is for Zorbtive, the patient has a diagnosis of short bowel syndrome (SBS) AND has shown clinical benefit from treatment with growth hormone

OR

b. If the request is for Serostim, the patient has a diagnosis of AIDS wasting/cachexia AND shows evidence of benefit of GH treatment (improvement in lean body mass or weight measurements)

OR

c. The patient has any other diagnosis AND BOTH of the following:

i. The patient's IGF-1 level has been evaluated to confirm the appropriateness of the current dose

AND

ii. The patient has had benefits from GH therapy in any of the following response parameters: body composition, cardiovascular health, bone mineral density, serum cholesterol, or physical strength

Length of Approval: 12 weeks for AIDs wasting/cachexia;
12 months for other indications



Step Therapy Supplement

This program applies to Medicaid.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT OBJECTIVE

The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL

The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
 - a. A statement by the prescriber that the patient is currently taking the requested agent
AND
 - b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
AND
 - c. The prescriber states that a change in therapy is expected to be ineffective or cause harm
- OR**
2. BOTH of the following
 - a. The patient's medication history includes the required prerequisite/preferred agent(s) or a drug in the same pharmacological class with the same mechanism of action as indicated by ONE of the following:
 - i. Evidence of a paid claim(s) within the past 999 days
OR
 - ii. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days**AND**
 - b. ONE of the following:
 - i. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
OR
 - ii. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)
- OR**
3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria

STEP THERAPY SUPPLEMENT QUESTION SET

- S1. Is the patient currently being treated with the requested agent as indicated by ALL of the following:
- a. A statement by the prescriber that the patient is currently taking the requested agent
 - b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
 - c. The prescriber states that a change in therapy is expected to be ineffective or cause harm
- If yes, continue to program specific criteria.
If no, continue to S2.

- S2. Does the patient’s medication history include the required prerequisite/preferred agent(s) or a drug in the same pharmacological class with the same mechanism of action as indicated by:
- a. Evidence of a paid claim(s) within the past 999 days
 - b. A statement by the prescriber that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days
 - c. No evidence of prerequisite/preferred agent trial
- If a or b, continue to S3.
If c, continue to S5.

- S3. Was the required prerequisite/preferred agent(s) discontinued due to lack of effectiveness or an adverse event?
- If yes, continue to program specific criteria.
If no, continue to S4.

- S4. Has the prescriber submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)?
- If yes, pharmacist must review and may continue to program specific criteria.
If no, continue to S5.

- S5. Has the prescriber provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm?
- If yes, pharmacist must review and may continue to program specific criteria.
If no, deny.

Document History

Original Client Specific Review Client Specific criteria, approved by BCBS MN Pharmacy Clinical Team (PCT) 10/2019
Original Implementation 1/1/2020