Growth Hormone Prior Authorization Program Summary

This program applies to Medicaid.

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.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
04-01-2024	03-01-2017

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Genotropin® (somatropin) Subcutaneous injection	Pediatric: Treatment of children with growth failure due to growth hormone deficiency (GHD), Prader-Willi syndrome (PWS), Small for Gestational Age (SGA), Turner syndrome (TS), and Idiopathic Short Stature (ISS) Adult: Treatment of adults with either adult onset or childhood onset GHD		4
Humatrope® (somatropin) Subcutaneous injection	Pediatric: Growth failure due to inadequate secretion of endogenous growth hormone (GHD); short stature associated with TS; Idiopathic Short Stature (ISS), height standard deviation score (SDS) less than -2.25, and associated with growth rates unlikely to permit attainment of adult height in the normal range; short stature or growth failure in short stature homeobox-containing gene (SHOX) deficiency; short stature born small for gestational age (SGA) with no catch-up growth by 2 years to 4 years of age Adult: Replacement of endogenous GH in adults with GH deficiency		5
Ngenla™ (somatrogon-ghla) Subcutaneous pen-injection	- Treatment of pediatric patients aged 3 years and older who have growth failure due to inadequate secretion of endogenous growth hormone		38
Norditropin® (somatropin) Subcutaneous injection	Pediatric: Treatment of pediatric patients with growth failure due to inadequate secretion of endogenous growth hormone (GH), short stature associated with NS, TS, and SGA with no catch-up growth by age 2 to 4 years, ISS, and growth failure due to PWS		6

Agent(s)	FDA Indication(s)	Notes	Ref#
	Adult: Replacement of endogenous GH in adults with growth hormone deficiency		
Nutropin® AQ (somatropin) Subcutaneous injection	Pediatric: Treatment of children with growth failure due to growth hormone deficiency (GHD), ISS, TS, and chronic kidney disease (CKD) up to the time of renal transplantation Adult: Treatment of adults with either childhood-onset or adult onset GHD		8
Omnitrope® (somatropin) Subcutaneous injection	Pediatric: Treatment of children with growth failure due to GHD, PWS, SGA, TS, and ISS Adult: Treatment of adults with either adult onset or childhood onset GHD		7
Saizen® (somatropin) Subcutaneous injection	Pediatric: Treatment of children with growth failure due to GHD Adult: Treatment of adults with either adult onset or childhood onset GHD		1
Serostim® (somatropin) Subcutaneous injection	- Treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance		2
Skytrofa® (lonapegsomatropin-tcgd) Subcutaneous injection	- Treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone		37
Sogroya® (somapacitan-beco) Subcutaneous injection	Pediatric: Treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone Adult: Replacement of endogenous growth hormone in adults with growth hormone deficiency		38
Zomacton® (somatropin) Subcutaneous injection	Pediatric: Treatment of pediatric patients with growth failure due to inadequate secretion of endogenous growth hormone (GH), short stature associated with TS, ISS, short stature or growth failure in short stature homeobox-containing gene (SHOX) deficiency, and SGA with no catch-up growth by 2 years to 4 years Adult: Replacement of endogenous GH in adults with GH deficiency		9
Zorbtive® (somatropin)	-Treatment of short bowel syndrome in adult patients receiving specialized nutritional support		3

Agent(s)	FDA Indication(s)	Notes	Ref#
Subcutaneous injection			

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Growth Hormone Deficiency in Children and Adults	Growth hormone deficiency (GHD) can be divided into congenital and acquired forms. The single most important clinical manifestation of GHD is growth failure, and careful documentation of height velocity is critical to making the correct diagnosis. Patients with congenital GHD have only a slightly reduced birth length and may not immediately show growth failure. Neonatal morbidity may include hypoglycemia. Children with acquired GHD present with severe growth failure, delayed bone age, and increased weight:height ratios. Causes of acquired GHD include intracranial tumors involving the hypothalamic-pituitary region, cranial irradiation, and head trauma.(10) Clinical presentation, diagnosis, and treatment of GHD in children and adolescents, as described by the 2016 Pediatric Endocrine Society Guidelines for Growth Hormone and Insulin-Like Growth Factor-1 (IGF-1) Treatment in Children and Adolescents(11), the 2019 Growth Hormone Research Society (GRS) Guidelines for the Diagnosis, Genetics, and Therapy of Short Stature Children(12), the 2000 Growth Hormone Research Society (GRS) Consensus Guidelines for the Diagnosis and Treatment of Growth Hormone (GH) Deficiency in Childhood and Adolescence(13), and UpToDate(10,14), is stated as follows: • A more comprehensive evaluation is warranted in children with one or more of the following: ○ Height-for-age curve that has deviated downward across two major height percentile curves (e.g., from above the 25th percentile to below the 10th percentile)(10,14) ○ Age 2-4 years: height velocity (HV) less than 5.5 cm/year (less than 2.2 inches/year)(10,14) ○ Age 4-6 years: HV less than 5 cm/year (less than 2 inches/year)(10,14) ○ Age 6 years to puberty: ▪ HV less than 4 cm/year for boys (less than 1.6 inches/year)(10,14) ▪ HV less than 4.5 cm/year for girls (less than 1.8 inches/year)(10,14) ○ Decrease in height standard deviation (SD) of more than 0.5 over one year in children over 2 years of age(13) ○ Height velocity more than 2 SD below the mean over one year, or more than 1.5 SD sustained over 2 years(13) ○ Height more than 1.5 SD below the midparental height(12,13) ○ Height greater than 2 SD below the mean for age and sex(12,14) ○ Severe short stature (e.g., height less than or equal to -2.5 standard deviations [SD], i.e., 0.6th percentile), or less severe short stature combined with growth failure(10,12,13) ○ Features that raise concerns for hypothalamic-pituitary dysfunction, either congenital or acquired, with decelerating growth, even if the child's height is within the normal range(10) ○ Evidence for deficits in other hypothalamic-pituitary hormones, either congenital or acquired(10) • Once the decision to evaluate a short child has been made, a variety of different tests can be performed. Assessment of pituitary GH production is difficult because GH secretion is pulsatile. Between normal pulses of GH secretion, serum GH levels are often low, below the limits of sensitivity of most conventional assays. Because of these issues, the diagnosis of GHD is made with a combination of clinical assessment and auxology, levels of

	insulin-like growth factor I (IGF-I) and insulin-like growth factor binding protein 3 (IGFBP-3), and GH stimulation (provocation) tests.(10,12,13)
	• The IGF-I, IGFBP-3, and bone age testing results may be interpreted as follows:
	  ○ *Moderately or severely reduced*: IGF-I and IGFBP-3 less than -2 SD with delayed bone age; possibility of GHD should be explored by provocative testing in most cases(10,13)
	  ○ *Somewhat low*: IGF-I and IGFBP-3 between 0 and -2 SD; decision about whether to perform provocative testing depends on other factors(10)
	  ○ *Clearly normal*: IGF-I and IGFBP-3 SD greater than or equal to 0; no further testing required(10)
	  ○ If the IGF-I and IGFBP-3 are discordant, IGF-I takes precedence except for infants and young children, in whom IGFBP-3 should guide the decision about further testing.(10,12)
	• 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.(10,11) In general, two different tests should be used for provocative GH testing. For those with known pathology of the central nervous system, history of irradiation, other pituitary hormone defects (e.g., multiple pituitary hormone deficiency [MPHD]), or a genetic defect, one test is sufficient.(10,12,13)
	• The use of GH provocative testing is not required for diagnosis of GHD in the following conditions:
	  ○ 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(10,11,12)
	  ○ 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 congenital pituitary abnormality (ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk)(10,11,12)
	  ○ Infant or young child with extreme short stature (e.g., height less than -3 SD), normal nutrition, significantly reduced IGF-1 and IGFBP-3 (e.g., less than -2 SD), and delayed bone age(10)
	  ○ In newborns who present with hypoglycemia in the absence of a metabolic disorder, a serum growth hormone level of less than 20 mcg/L suggests GHD. An IGFBP-3 measurement (e.g., less than -2 SD) is of value for the diagnosis of GHD in infancy.(13)
	  ○ When an alternative diagnosis for short stature is evident, such as Turner syndrome, Noonan syndrome, Prader-Willi syndrome (PWS), SHOX deficiency, chronic renal insufficiency, or in children born small for gestational age (SGA)(12)
	• Some guidelines acknowledge that a threshold test result distinguishing "normal" from GHD has not been well established.(11,12) Most pediatric endocrinologists define a "normal" response by a serum GH concentration of greater than 10 mcg/L, but a cutoff of 7.5 mcg/L is often used for modern assays.(10,12,13)
	• Treatment of children with GHD is the following:
	  ○ Weight-based or body-surface-area dosing should be used.(11,12,13,15)
	  ○ Measure serum IGF-1 levels to monitor adherence and for dose changes.(11,12,15)
	  ○ Serum levels of IGF-1 should be measured approximately 4 weeks after beginning GH treatment and/or making a dose adjustment(15)
	  ○ Routine follow-up (once IGF-1 levels are in target range) of pediatric patients should be conducted on a 3- to 6-month basis(13,15)

	○ Treatment is appropriate for children with GHD whose epiphyses are open(15) Guidelines for patients transitioning from pediatric to adult care, as described by the 2016 Pediatric Endocrine Society Guidelines for Growth Hormone and Insulin-Like Growth Factor-1 (IGF-1) Treatment in Children and Adolescents(11), the 2000 Growth Hormone Research Society (GRS) Consensus Guidelines for the Diagnosis and Treatment of Growth Hormone (GH) Deficiency in Childhood and Adolescence(13), the 2019 American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology Guidelines for Management of Growth Hormone Deficiency in Adults and Patients Transitioning from Pediatric to Adult Care(24), the 2011 Endocrine Society Clinical Practice Guidelines for Evaluation and Treatment of Adult Growth Hormone Deficiency(25), and UpToDate(27), is stated as follows: • Only a minority of children with childhood-onset GHD will remain deficient as adults and require ongoing GH therapy. The transition period is loosely defined as occurring from mid-to-late teens until 6-7 years after reaching near-adult height.(27) • For patients transitioning from pediatric to adult care: ○ Because the majority of isolated childhood-onset GHD patients will have normal results when tested as adults, it is important to repeat GH stimulation testing to determine if ongoing therapy is required.(11,24,27) ○ Measurement of the serum IGF-1 concentration should be the initial test of the somatotropic axis if re-evaluation of the somatotropic axis is clinically indicated.(11) ○ GH provocative testing should be performed to evaluate the function of the somatotropic axis in the transition period if indicated by a low IGF-I level.(11,24,25) ○ Patients with multiple (≥ 3) pituitary hormone deficiencies regardless of etiology, or GHD with an established causal genetic mutation, or GHD with a specific pituitary/hypothalamic structural defect (except ectopic posterior pituitary), should be diagnosed with persistent GHD.(11,13,24,27) GH treatment should be offered to individuals with persistent GHD in the transition period.(11,24,25,27) Clinical presentation, diagnosis, and treatment of GHD in adults, as described by the 2019 American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology Guidelines for Management of Growth Hormone Deficiency in Adults and Patients Transitioning from Pediatric to Adult Care(24), the 2011 Endocrine Society Clinical Practice Guidelines for Evaluation and Treatment of Adult Growth Hormone Deficiency(25), and UpToDate(26), is stated as follows: • The diagnosis of adult GHD should be based on the combination of documented pituitary or hypothalamic disease, panhypopituitarism, and a subnormal serum IGF-1 concentration (lower than the gender- and age-specific lower limit of normal).(26) GH levels decline with aging, whereas serum IGF-1 levels can be lowered by factors such as malnutrition and various comorbidities (e.g., diabetes, renal and/or hepatic disease). Stimulation (provocative) tests should only be performed based on the clinical context of each patient with a history suggestive of a reasonable clinical suspicion of GHD, and with the intent to initiate GH therapy if the diagnosis is confirmed.(24) • Diagnosis of adult GHD, without the need for stimulation/provocation tests, can be made in the following patient subtypes: ○ Patients with organic hypothalamic-pituitary disease (e.g., suprasellar mass with previous surgery and cranial irradiation) and presence of deficiencies in three or more pituitary axes (multiple pituitary hormone deficiency [MPHD]) together with subnormal serum IGF-1 levels (less than -2 SD)(24,25,26)

	○ Patients with genetic defects affecting the hypothalamic-pituitary axes(24,25) ○ Patients with hypothalamic-pituitary structural brain defects(24,25) • GH stimulation tests are needed to confirm diagnosis in the following patient subtypes: ○ In patients with less than or equal to 2 pituitary hormone deficiencies, subnormal IGF-1 levels alone are not sufficient to make a diagnosis of adult GHD; one GH stimulation test should be performed to confirm the diagnosis.(24) In transition patients who have completed longitudinal growth: ▪ After at least one month of discontinuation of therapy, patients with childhood-onset GHD and subnormal serum IGF-1 levels should be retested for GHD with provocation tests.(24,25) ▪ Patients with idiopathic childhood-onset GHD with organic hypothalamic-pituitary disease should have at least one stimulation test performed.(24) ▪ In the past, a level of serum GH less than or equal to 5 mcg/L on the insulin tolerance test was considered confirmation of GHD. However, experts increasingly report the disuse of this test and instead the glucagon-stimulation test (GST) and the macimorelin test should be utilized.(24,26)
Idiopathic Short Stature	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. A consensus conference of the International Societies of Pediatric Endocrinology and the Growth Hormone Research Society proposed that children with ISS whose heights are less than -2.0 SDS and who are more than 2.0 SDS below their mid-parental target height or had a predicted height less than -2.0 SDS warrant consideration for treatment.(34) If the initial growth response is good while on GH therapy, (at least 2.5 cm/year above the baseline height velocity after one year of treatment), treatment continues until linear growth decreases to less than 2.0 to 2.5 cm (approximately 1 inch)/year. This decrease usually occurs in late puberty, equating to a bone age of 13 to 13.5 years in girls or 15.5 to 16 years in boys.(16) GH therapy was approved in the United States for children with ISS with height at or less than -2.25 SDS (1.2 percentile) below the mean for age and sex, associated with growth rates unlikely to permit attainment of adult height in the normal range (this corresponds to an adult height less than 63 inches for males and less than 59 inches for females), in whom diagnostic work up excluded other causes for short stature that should be observed or treated by other means, and in pediatric patients whose epiphyses are not closed.(33,34) The evaluation should attempt to identify children with growth patterns consistent with constitutional delay of growth and puberty (CDGP) because they are likely to have catch-up growth without GH treatment. Clinical evidence supporting CDGP includes delayed bone age and/or history of delayed growth and puberty in a parent. Moreover, adolescent boys with CDGP and moderate short stature (taller than -2.5 SD) are more appropriately treated with testosterone replacement rather than GH. However, treatment of children with ISS with GH is controversial because of variable efficacy and high costs.(16,17)
Growth Failure in Chronic Kidney Disease	The goal of GH therapy in children with chronic kidney disease (CKD) is normalization of final height. GH therapy should be initiated when the following criteria have been met:(18,19) • All other amenable risk factors for growth impairment have been addressed • There is evidence of growth impairment, defined as HV for age less than -1.88 SD OR a HV for age less than 3rd percentile

Short Bowel Syndrome	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. Zorbtive is indicated for the treatment of SBS in adult patients receiving specialized nutritional support.(3) The beneficial effect of growth hormone (GH) as an aid to wean parenteral nutrition (PN) in short bowel syndrome (SBS) is controversial and a considerable amount of skepticism surrounds the long-term benefits. Four randomized placebo controlled studies have been performed using growth hormone to stimulate mucosal growth. In three studies there was no significant increase in absorption but one showed a small improvement in nutrient absorption.(31) A phase 3, prospective, randomized, placebo-controlled trial enrolled 41 PN-dependent SBS patients who were studied in an inpatient-like setting for 6 weeks, with 2 weeks of diet and medication optimization and PN stabilization followed by a 4-week treatment period. Patients were randomized into 3 groups: recombinant human growth hormone plus glutamine, growth hormone without glutamine, and placebo plus glutamine. A significant reduction was seen in PN requirements in both groups treated with growth hormone at the end of the 4-week treatment period. PN reduction remained significantly reduced during a 12-week observation period only in the group treated with growth hormone plus glutamine.(32)
Growth Failure in Children Born Small for Gestational Age	Low birth weight remains a major cause of morbidity and mortality in early infancy and childhood throughout the world. The International Societies of Pediatric Endocrinology and the Growth Hormone Research Society (GRS) 2007 Consensus Statement Guidelines on the Management of the Child Born Small for Gestational Age (SGA) recommend that SGA should be defined as a birth weight and/or birth length less than -2 SD below the population average. 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.(20-22) A child who reaches 24 months of age and fails to manifest catch-up growth (i.e., height remains less than 2 SD below the mean for age and gender) meets the indication to receive GH therapy.(22,23)
HIV Patients with Wasting or Cachexia	HIV/AIDS wasting syndrome is defined by the Centers for Disease Control and Prevention (CDC) as an involuntary weight loss of greater than 10% of body weight. The incidence of wasting has declined since the introduction of anti-retroviral therapy (ART), but many patients still meet the criteria for serious weight loss and wasting. Tissue wasting responds rapidly to ART, and the primary therapy for HIV wasting is ART.(28,30) The diagnosis of HIV wasting requires one of the following:(29) • 10% unintentional weight loss over 12 months • 7.5% unintentional weight loss over 6 months • Greater than 5% unintentional weight loss over 4 months • 5% body cell mass (BCM) loss within 6 months • Body mass index (BMI) less than 20 kg/m^2 • In men: BCM less than 35% of total body weight and BMI less than 27 kg/m^2 • In women: BCM less than 23% of total body weight and BMI less than 27 kg/m^2
Growth Hormone Statute	U.S. Code Title 21 Chapter 21 Chapter § 333(e) states: Prohibited distribution of human growth hormone (1) Except as provided in paragraph (2), whoever knowingly distributes, or possesses with intent to distribute, human growth hormone for any use in humans other than the treatment of a disease or other recognized medical condition, where such use has been authorized by the Secretary of Health and Human Services under section 355 of this title and pursuant to the order of a physician, is guilty of an offense punishable by not more than 5 years in prison, such fines as are authorized by title 18, or both. (2) Whoever commits any offense set forth in paragraph (1) and such offense involves an individual under 18 years of age is punishable by not more than 10 years imprisonment, such fines as are authorized by title 18, or both. (3) Any conviction for a violation of paragraphs (1) and (2) of this subsection shall be considered a felony violation of the Controlled Substances Act [21 U.S.C. 801 et seq.] for the purposes of forfeiture under section 413 of such Act [21

	U.S.C. 853]. (4) As used in this subsection the term ''human growth hormone'' means somatrem, somatropin, or an analogue of either of them. (5) The Drug Enforcement Administration is authorized to investigate offenses punishable by this subsection.(35)
Efficacy	Recombinant growth hormone products are considered clinically identical, with no evidence that one commercial product is different or more advantageous than another, apart from differences in how the GH product is stored, dosed, and administered by device. Therefore, one commercial GH product is not recommended over another because there are no prospective head-to-head trials comparing the clinical efficacy of one commercial product with another.(24)
Safety(1-9, 37, 38)	Genotropin, Humatrope, Norditropin, Nutropin AQ, Omnitrope, Saizen, Zomacton have the following contraindications: • Acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure • Children with Prader-Willi syndrome who are severely obese, have a history of upper airway obstruction or sleep apnea, or have severe respiratory impairment • Active malignancy • Active proliferative or severe non-proliferative diabetic retinopathy • Children with closed epiphyses • Hypersensitivity to somatropin or diluents/excipients Serostim has the following contraindications: • Acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma or acute respiratory failure • Active malignancy • Active proliferative or severe non-proliferative diabetic retinopathy • Hypersensitivity to somatropin or diluent Skytrofa has the following contraindications: • Acute critical illness • Hypersensitivity to somatropin or any excipients in Skytrofa • Children with close epiphyses • Active malignancy • Active proliferative or severe non-proliferative diabetic retinopathy • Children with Prader-Willi syndrome who are severely obese or have severe respiratory impairment due to risk of sudden death Sogroya has the following contraindications: • Acute critical illness • Active malignancy • Hypersensitivity to somapacitan-beco or excipients • Active proliferative or severe non-proliferative diabetic retinopathy • Closed epiphyses in children used for longitudinal growth promotion • Children with Prader-Willi syndrome who are severely obese or have severe respiratory impairment due to risk of sudden death Zorbtive has the following contraindications: • Acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma or acute respiratory failure • Active neoplasia

	• Known hypersensitivity to growth hormone

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POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Genotropin ; Genotropin miniquick ; Humatrope ; Ngenla ; Norditropin flexpro ; Nutropin aq nuspin 10 ; Nutropin aq nuspin 20 ; Nutropin aq nuspin 5 ; Omnitrope ; Saizen ; Saizenprep reconstitution ; Serostim ; Skytrofa ; Sogroya ; Zomacton ; Zorbtive	lonapegsomatropin-tcgd for subcutaneous inj cart ; lonapegsomatropin-tcgd for subcutaneous inj cartridge ; somapacitan-beco solution pen-injector ; somatrogon-ghla solution pen-injector ; somatropin (non-refrigerated) for inj ; somatropin (non-refrigerated) for subcutaneous inj ; somatropin for inj ; somatropin for inj	0.2 MG ; 0.4 MG ; 0.6 MG ; 0.8 MG ; 1 MG ; 1.2 MG ; 1.4 MG ; 1.6 MG ; 1.8 MG ; 10 MG ; 10 MG/1.5ML ; 10 MG/2ML ; 11 MG ; 12 MG ; 13.3 MG ; 15 MG/1.5ML ; 2 MG ; 20 MG/2ML ; 24	M ; N ; O ; Y	N		

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
	cartridge ; somatropin for subcutaneous inj ; somatropin for subcutaneous inj cartridge ; somatropin for subcutaneous inj prefilled syr ; somatropin solution cartridge ; somatropin solution pen-injector	MG ; 24 MG/1.2ML ; 3 MG ; 3.6 MG ; 30 MG/3ML ; 4 MG ; 4.3 MG ; 5 MG ; 5 MG/1.5ML ; 5 MG/2ML ; 5.2 MG ; 5.8 MG ; 6 MG ; 6.3 MG ; 60 MG/1.2ML ; 7.6 MG ; 8.8 MG ; 9.1 MG				

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Genotropin ; Genotropin miniquick ; Humatrope ; Ngenla ; Norditropin flexpro ; Nutropin aq nuspin 10 ; Nutropin aq nuspin 20 ; Nutropin aq nuspin 5 ; Omnitrope ; Saizen ; Saizenprep reconstitution ; Serostim ; Skytrofa ; Sogroya ; Zomacton ; Zorbtive	lonapegsomatropin-tcgd for subcutaneous inj cart ; lonapegsomatropin-tcgd for subcutaneous inj cartridge ; somapacitan-beco solution pen-injector ; somatrogon-ghla solution pen-injector ; somatropin (non-refrigerated) for inj ; somatropin (non-refrigerated) for subcutaneous inj ; somatropin for inj ; somatropin for inj cartridge ; somatropin for subcutaneous inj ; somatropin for subcutaneous inj cartridge ; somatropin for subcutaneous inj prefilled syr ; somatropin solution cartridge ; somatropin solution pen-injector	0.2 MG ; 0.4 MG ; 0.6 MG ; 0.8 MG ; 1 MG ; 1.2 MG ; 1.4 MG ; 1.6 MG ; 1.8 MG ; 10 MG ; 10 MG/1.5ML ; 10 MG/2ML ; 11 MG ; 12 MG ; 13.3 MG ; 15 MG/1.5ML ; 2 MG ; 20 MG/2ML ; 24 MG ; 24 MG/1.2ML ; 3 MG ; 3.6 MG ; 30 MG/3ML ; 4 MG ; 4.3 MG ; 5 MG ; 5 MG/1.5ML ; 5 MG/2ML ; 5.2 MG ; 5.8 MG ; 6 MG ; 6.3 MG ; 60 MG/1.2ML ; 7.6 MG ; 8.8 MG ; 9.1 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Adult	**TARGET AGENTS:** **For Medicaid, the preferred products are the MN Medicaid Preferred Drug List (PDL) preferred drugs: Norditropin and Nutropin AQ** Omnitrope® (somatropin) Genotropin® , Genotropin® MiniQuick (somatropin) Humatrope® (somatropin) Ngenla™ (somatrogon-ghla) Norditropin FlexPro® (somatropin) Nutropin AQ NuSpin® (somatropin) Saizen®, Saizenprep® (somatropin) Serostim® (somatropin) Skytrofa™ (lonapegsomatropin-tcgd)

Module	Clinical Criteria for Approval
	Sogroya® (somapacitan-beco) Zomacton® (somatropin) Zorbtive® (somatropin)

Adults – Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The patient is an adult (as defined by the prescriber) **AND**
2. The patient has ONE of the following diagnoses:
    A. If the request is for Serostim, the patient has a diagnosis of AIDS wasting/cachexia AND ALL of the following:
        1. The patient is currently treated with antiretroviral therapy **AND**
        2. The patient will continue antiretroviral therapy in combination with the requested agent **AND**
        3. BOTH of the following:
            A. ONE of the following:
                1. The patient has had weight loss that meets ONE of the following:
                    A. 10% unintentional weight loss over 12 months **OR**
                    B. 7.5% unintentional weight loss over 6 months **OR**
                2. The patient has a body cell mass (BCM) loss greater than or equal to 5% within 6 months **OR**
                3. The patient's sex is male and has BCM less than 35% of total body weight and body mass index (BMI) less than 27 kg/m^2 **OR**
                4. The patient's sex is female and has BCM less than 23% of total body weight and BMI less than 27 kg/m^2 **OR**
                5. The prescriber has provided information that the patient's BCM less than 35% or less than 23% and BMI less than 27 kg/m^2 are medically appropriate for diagnosing AIDS wasting/cachexia for the patient's sex **OR**
                6. The patient's BMI is less than 20 kg/m^2 **AND**
            B. All other causes of weight loss have been ruled out **OR**
    B. If the request is for Zorbtive, then BOTH of the following:
        1. The patient has a diagnosis of short bowel syndrome (SBS) **AND**
        2. The patient is receiving specialized nutritional support **OR**
    C. The patient has a diagnosis of growth hormone deficiency (GHD) or growth failure due to inadequate secretion of endogenous growth hormone AND ONE of the following:
        1. The patient had a diagnosis of childhood-onset growth hormone deficiency AND has failed at least one growth hormone (GH) stimulation test as an adult **OR**
        2. The patient has a low insulin-like growth factor-1 (IGF-1) level AND ONE of the following:
            A. Organic hypothalamic-pituitary disease **OR**
            B. Pituitary structural lesion or trauma **OR**
            C. The patient has panhypopituitarism or multiple (greater than or equal to 3) pituitary hormone deficiency **OR**
        3. The patient has an established causal genetic mutation OR hypothalamic-pituitary structural defect other than ectopic posterior pituitary **OR**
        4. The patient has failed at least two growth hormone (GH) stimulation tests as an adult **OR**
        5. The patient has failed at least one GH stimulation test as an adult AND the patient has an organic pituitary disease **OR**

Module	Clinical Criteria for Approval
	D. The patient has another FDA approved indication for the requested agent and route of administration **OR** E. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 3. The request is for a long-acting GH agent AND if the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 6. The requested quantity (dose) is within FDA labeled dosing (or supported in compendia) for the requested indication **AND** 7. ONE of the following: A. The request is for a preferred agent, Serostim or Zorbtive **OR** B. ONE of the following: 1. The patient's medication history includes two preferred agents AND ONE of the following: A. The patient has had an inadequate response to two preferred agents **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over ALL the preferred agents **OR** 2. The patient has an intolerance or hypersensitivity to two preferred agents that is not expected to occur with the requested nonpreferred agent (medical record required) **OR** 3. The patient has an FDA labeled contraindication to ALL preferred agents that is not expected to occur with the requested nonpreferred agent (medical record required) **OR** 4. The prescriber has provided information to support the efficacy of the requested non-preferred agent over the preferred agents, for the intended diagnosis (medical record required) **OR** 5. 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** 6. The prescriber has provided information that ALL preferred agents 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 **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** SBS: 4 weeks AIDS wasting/cachexia: 12 weeks Any other indication: 12 months

Module	Clinical Criteria for Approval
	Adults – Renewal Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been approved for therapy with GH previously through the plan's prior authorization process **AND** 2. The patient is an adult (as defined by the prescriber) **AND** 3. ONE of the following: A. The request is for a preferred agent or Serostim or Zorbtive **OR** B. ONE of the following: 1. The patient's medication history includes two preferred agents AND ONE of the following: A. The patient has had an inadequate response to two preferred agents **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over ALL the preferred agents **OR** 2. The patient has an intolerance or hypersensitivity to two preferred agents that is not expected to occur with the requested nonpreferred agent (medical record required) **OR** 3. The patient has an FDA labeled contraindication to ALL preferred agents that is not expected to occur with the requested nonpreferred agent (medical record required) **OR** 4. The prescriber has provided information to support the efficacy of the requested non-preferred agent over the preferred agents, for the intended diagnosis (medical record required) **OR** 5. 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** 6. The prescriber has provided information that ALL preferred agents 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 **AND** 4. ONE of the following: A. The patient has a diagnosis of short bowel syndrome (SBS) AND has had clinical benefit with the requested agent **OR** B. The patient has a diagnosis of AIDS wasting/cachexia AND ALL of the following: 1. The patient is currently treated with antiretroviral therapy **AND** 2. The patient will continue antiretroviral therapy in combination with the requested agent **AND** 3. The patient has had clinical benefit with the requested agent (i.e., an increase in weight or weight stabilization) **OR** C. The patient has growth hormone deficiency (GHD) or growth failure due to inadequate secretion of endogenous growth hormone AND BOTH of the following: 1. The patient's IGF-I level has been evaluated to confirm the appropriateness of the current dose **AND** 2. The patient has had clinical benefit with the requested agent (i.e., body composition, hip-to-waist ratio, cardiovascular health, bone mineral density, serum cholesterol, physical strength, or quality of life) **OR**

<table>
<tr><th>Module</th><th>Clinical Criteria for Approval</th></tr>
<tr><td></td><td>
D. The patient has a diagnosis other than SBS, AIDS wasting/cachexia, GHD, or growth failure due to inadequate secretion of endogenous growth hormone AND has had clinical benefit with the requested agent AND
5. The patient does NOT have any FDA labeled contraindications to the requested agent AND
6. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or has consulted with a specialist in the area of the patient's diagnosis AND
7. The requested quantity (dose) is within FDA labeled dosing (or supported in compendia) for the requested indication AND
8. The patient is being monitored for adverse effects of GH

Compendia Allowed: CMS Approved Compendia

Length of Approval:

<table>
<tr><td>SBS</td><td>4 weeks</td></tr>
<tr><td>AIDS wasting/cachexia</td><td>12 weeks</td></tr>
<tr><td>Any other indication</td><td>12 months</td></tr>
</table>
</td></tr>
<tr><td>Child</td><td>
<table>
<tr><td>TARGET AGENTS:

For Medicaid, the preferred products are the MN Medicaid Preferred Drug List (PDL) preferred drugs: Norditropin and Nutropin AQ</td></tr>
<tr><td>Omnitrope® (somatropin)

Genotropin® , Genotropin® MiniQuick (somatropin)

Humatrope® (somatropin)

Ngenla™ (somatrogon-ghla)

Norditropin FlexPro® (somatropin)

Nutropin AQ NuSpin® (somatropin)

Saizen®, Saizenprep® (somatropin)

Serostim® (somatropin)

Skytrofa™ (lonapegsomatropin-tcgd)

Sogroya® (somapacitan-beco)

Zomacton® (somatropin)

Zorbtive® (somatropin)</td></tr>
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Growth Hormone (GH) products will be approved as below.
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Module	Clinical Criteria for Approval
	Children – Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient is a child (as defined by the prescriber) **AND** 2. The patient has ONE of the following diagnoses: A. ALL of the following: 1. The patient is a newborn (less than or equal to 4 months of age) with hypoglycemia **AND** 2. The patient has a serum growth hormone (GH) concentration less than or equal to 5 mcg/L **AND** 3. ONE of the following: A. Congenital pituitary abnormality (e.g., ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk) **OR** B. Deficiency of at least one additional pituitary hormone **OR** B. ALL of the following: 1. The patient is a newborn (less than or equal to 4 months of age) with hypoglycemia **AND** 2. The patient has a growth hormone (GH) concentration less than 20 mcg/L **AND** 3. The patient does not have a known metabolic disorder **AND** 4. The patient has a reduced IGFBP-3 level (e.g., less than -2 SD) **OR** C. The patient has a diagnosis of Turner syndrome **OR** D. The patient has a diagnosis of Noonan syndrome **OR** E. The patient has a diagnosis of Prader-Willi syndrome **OR** F. The patient has a diagnosis of SHOX gene deficiency **OR** G. If the request is for Zorbtive, the patient has a diagnosis of short bowel syndrome (SBS) AND is receiving specialized nutritional support AND ONE of the following: 1. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** 2. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **OR** H. The patient has a diagnosis of panhypopituitarism or has deficiencies in at least 3 or more pituitary axes AND serum IGF-I levels below the age- and sex-appropriate reference range when off GH therapy **OR** I. The patient has a diagnosis of chronic renal insufficiency and BOTH of the following: 1. The patient's height velocity (HV) for age is less than -1.88 standard deviations (SD) OR HV for age is less than the third percentile **AND** 2. Other etiologies for growth impairment have been addressed **OR** J. The patient has a diagnosis of small for gestational age (SGA) and ALL of the following: 1. The patient is 2 years of age or older **AND** 2. The patient has a documented birth weight and/or birth length that is 2 or more standard deviations (SD) below the mean for gestational age **AND** 3. At 24 months of age, the patient failed to manifest catch-up growth evidenced by a height that remains 2 or more standard deviations (SD) below the mean for age and sex **OR** K. The patient has a diagnosis of idiopathic short stature (ISS) AND ALL of the following: 1. The patient has a height less than or equal to -2.25 SD below the corresponding mean height for age and sex **AND** 2. The patient has open epiphyses **AND** 3. ONE of the following: A. The patient has a predicted adult height that is below the normal range AND ONE of the following: 1. The patient's sex is male and predicted adult height is less than 63 inches **OR** 2. The patient's sex is female and predicted adult height is less than 59 inches **OR**

Module	Clinical Criteria for Approval
	B. The patient is more than 2 SD below their mid-parental target height **AND** 4. BOTH of the following: A. The patient has been evaluated for constitutional delay of growth and puberty (CDGP) **AND** B. The patient does NOT have a diagnosis of CDGP **OR** L. The patient has a diagnosis of growth hormone deficiency (GHD) or growth failure due to inadequate secretion of endogenous growth hormone AND ONE of the following: 1. The patient has extreme short stature (e.g., height less than or equal to -3 SD), normal nutrition, significantly reduced IGF-1 and IGFBP-3 (e.g., less than -2 SD), and delayed bone age **OR** 2. BOTH of the following: A. The patient has ONE of the following: 1. Height more than 2 SD below the mean for age and sex **OR** 2. Height more than 1.5 SD below the midparental height **OR** 3. A decrease in height SD of more than 0.5 over one year in children greater than 2 years of age **OR** 4. Height velocity (HV) more than 2 SD below the mean over one year or more than 1.5 SD sustained over two years **OR** 5. Height-for-age curve that has deviated downward across two major height percentile curves (e.g., from above the 25th percentile to below the 10th percentile) **OR** 6. BOTH of the following: A. The patient's age is 2-4 years **AND** B. The patient has a HV less than 5.5 cm/year (less than 2.2 inches/year) **OR** 7. BOTH of the following: A. The patient's age is 4-6 years **AND** B. The patient has a HV less than 5 cm/year (less than 2 inches/year) **OR** 8. The patient's age is 6 years to puberty AND ONE of the following: A. The patient's sex is male and HV is less than 4 cm/year (less than 1.6 inches/year) **OR** B. The patient's sex is female and HV is less than 4.5 cm/year (less than 1.8 inches/year) **AND** B. ONE of the following: 1. The patient has failed at least 2 growth hormone (GH) stimulation tests (e.g., peak GH value of less than 10 mcg/L after stimulation, or otherwise considered abnormal as determined by testing lab) **OR** 2. The patient has failed at least 1 GH stimulation test (e.g., peak GH value of less than 10 mcg/L after stimulation, or otherwise considered abnormal as determined by testing lab) AND ONE of the following: A. Pathology of the central nervous system **OR** B. History of irradiation **OR** C. Other pituitary hormone defects (e.g., multiple pituitary hormone deficiency [MPHD]) **OR** D. A genetic defect **OR** 3. The patient has a pituitary abnormality and a known deficit of at least one other pituitary hormone **OR** M. The patient has another FDA approved indication for the requested agent and route of administration **OR** N. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 3. ONE of the following:

Module	Clinical Criteria for Approval
	A. The request is for a preferred agent or Zorbtive or Serostim **OR** B. ONE of the following: 1. The patient's medication history includes two preferred agents AND ONE of the following: A. The patient has had an inadequate response to two preferred agents **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over ALL the preferred agents **OR** 2. The patient has an intolerance or hypersensitivity to two preferred agents that is not expected to occur with the requested nonpreferred agent (medical record required) **OR** 3. The patient has an FDA labeled contraindication to ALL preferred agents that is not expected to occur with the requested nonpreferred agent (medical record required) **OR** 4. The prescriber has provided information to support the efficacy of the requested non-preferred agent over the preferred agents, for the intended diagnosis (medical record required) **OR** 5. 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** 6. The prescriber has provided information that ALL preferred agents 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 **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or has consulted with a specialist in the area of the patient's diagnosis **AND** 6. The requested quantity (dose) is within FDA labeled dosing (or supported in compendia) for the requested indication **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 4 weeks for SBS 12 months for other indications **Children – Renewal Evaluation** **Target Growth Hormone Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for therapy with GH through the plan's prior authorization process **AND** 2. The patient is a child (as defined by the prescriber) **AND** 3. ONE of the following: A. The request is for a preferred agent or Zorbtive or Serostim **OR** B. ONE of the following: 1. The patient's medication history includes two preferred agents AND ONE of the following: A. The patient has had an inadequate response to two preferred agents **OR**

Module	Clinical Criteria for Approval
	B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over ALL the preferred agents **OR** 2. The patient has an intolerance or hypersensitivity to two preferred agents that is not expected to occur with the requested nonpreferred agent (medical record required) **OR** 3. The patient has an FDA labeled contraindication to ALL preferred agents that is not expected to occur with the requested nonpreferred agent (medical record required) **OR** 4. The prescriber has provided information to support the efficacy of the requested non-preferred agent over the preferred agents, for the intended diagnosis (medical record required) **OR** 5. 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** 6. The prescriber has provided information that ALL preferred agents 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 **AND** 4. ONE of the following: A. The patient has a diagnosis of short bowel syndrome (SBS) AND has had clinical benefit with the requested agent AND ONE of the following: 1. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** 2. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **OR** B. The patient has a diagnosis of ISS and BOTH of the following: 1. The patient's height has increased greater than or equal to 2 cm over the previous year with GH therapy **AND** 2. Bone age is less than 16 years in patients with a sex of male and 15 years in patients with a sex of female AND the patient has open epiphyses **OR** C. The patient has a diagnosis of growth hormone deficiency (GHD), growth failure due to inadequate secretion of endogenous growth hormone, short stature disorder (i.e., Noonan's syndrome, SHOX deficiency, Turner Syndrome, small for gestational age), or renal function impairment with growth failure AND BOTH of the following: 1. The patient does NOT have closed epiphyses **AND** 2. The patient's height has increased greater than or equal to 2 cm over the previous year with GH therapy **OR** D. The patient has a diagnosis of Prader-Willi syndrome AND has had clinical benefit with the requested agent **OR** E. The patient has a diagnosis other than SBS, ISS, GHD, growth failure due to inadequate secretion of endogenous growth hormone, short stature disorder (i.e., Noonan's syndrome, SHOX deficiency, Turner syndrome, small for gestational age), or renal function impairment with growth failure, and Prader-Willi AND has had clinical benefit with the requested agent **AND** 5. The patient is being monitored for adverse effects of GH **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or has consulted with a specialist in the area of the patient's diagnosis **AND** 8. The requested quantity (dose) is within FDA labeled dosing (or supported in compendia) for the requested indication

Module	Clinical Criteria for Approval
	Compendia Allowed: CMS Approved Compendia **Length of Approval:** 4 weeks for SBS 12 months for other indications

