Growth Hormones (Lonapegsomatropin, Somapacitan, Somatropin, Somatrogon)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

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Summary

Growth hormone (GH) is produced by the pituitary somatotroph cells. GH production begins early in fetal life and continues throughout life, although at a progressively lower rate. The plan covers treatment for the following FDA-approved indications: pediatric patients with growth failure due to any of the following - growth hormone (GH) deficiency, Turner syndrome, Noonan syndrome, small for gestational age (SGA), Prader-Willi syndrome, chronic kidney disease (CKD), short stature homeobox-containing gene (SHOX) deficiency and adults with childhood-onset or adult-onset GH deficiency. The plan also covers certain compendial uses for GH including human immunodeficiency, growth failure associated with any of the following - cerebral palsy, congenital adrenal hyperplasia, cystic fibrosis, and Russell-Silver syndrome. All other indications are considered experimental / investigational or not medically necessary.

The Plan's preferred growth hormone products are Humatrope (somatropin) and Norditropin (somatropin). Coverage for other (Non-Formulary) growth hormone products are preferred for certain conditions:

- Genotropin (somatropin) or Omnitrope (somatropin) is only provided when being prescribed for a member with Prader-Willi syndrome who is unable to use, or has tried and failed Norditropin (somatropin).
- Requests for non-formulary medications are also subject to Medical Necessity Criteria for Non-Formulary Products (PG069) Clinical Guideline.

Definitions

"Compendia" are summaries of drug information and medical evidence to support decision-making about the appropriate use of drugs and medical procedures. Examples include, but are not limited to:

1. American Hospital Formulary Service Drug Information
2. Clinical pharmacology
3. National Comprehensive Cancer Network Drugs and Biologics Compendium
4. Thomson Micromedex DrugDex
5. United States Pharmacopeia-National Formulary (USP-NF)

"Growth Hormone Deficiency" is a condition characterized by growth failure and can be divided into congenital and acquired forms.

"Noonan Syndrome" is an autosomal dominant condition that is associated with short stature and congenital heart disease (CHD).

"Prader-Willi Syndrome" is a syndrome caused by the absence of expression of the paternally active genes on the long arm of chromosome 15.

"Russell-Silver Syndrome" is a syndrome characterized by severe intrauterine growth restriction and postnatal growth retardation with a prominent forehead, triangular face, downturned corners of the mouth, and body asymmetry (hemihypertrophy).

"Short Stature Homeobox-containing (SHOX) Deficiency" is a syndrome in which there are variants in the SHOX-containing gene on the X chromosome.

"Small for Gestational Age" is defined as a weight and/or length at birth that is at least -2 standard deviations (SD) below the mean for gestational age with lack of catch up growth by the age of 2 years old.

"Turner Syndrome" is a sex chromosome disorder caused by loss of part or all of an X chromosome.

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers Growth Hormone medically necessary when ALL the following criteria are met:

1. The medication being requested meets BOTH of the following:
    a. Is being prescribed for an FDA-approved or compendia supported indication*; and*
    b. Is age-appropriate for the member based on FDA approval or is supported by evidence-based compendia*; AND*
2. Prescribed by, or in consultation with, a physician who specializes in the treatment of the specific condition such as an endocrinologist, pediatric endocrinologist, geneticist, or pediatric nephrologist; *AND*
3. The member is unable to use, or has tried and failed the Plan's preferred growth hormone product(s)*; AND*
4. The member meets the medical necessity criteria for the applicable indication listed below:

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

For the treatment of Adult Growth Hormone Deficiency

The Plan considers Growth Hormone medically necessary when BOTH of the following criteria are met:

1. The member has ONE (1) of the following:
    a. TWO (2) pre-treatment pharmacologic provocative GH tests demonstrating GH levels less than (<) 5 ng/mL:
        i. Unless the agent is Macrilen in which case a GH level of less than (<) 2.8 ng/mL confirms the presence of adult growth hormone deficiency; *or*
        ii. Unless the agent is a glucagon stimulation test, in which case a peak GH level ≤ 3.0 ng/mL in those with a body mass index (BMI) ≤ 30 kg/m2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m2 confirms the presence of adult growth hormone deficiency; *or*
        iii. Unless the agent is a Glucagon stimulation test, in which case with a peak GH level ≤ 1.0 ng/mL in those with a BMI of ≥ 25 kg/m2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m2 confirms the presence of adult growth hormone deficiency; *or*
    b. ONE (1) pre-treatment pharmacologic provocative GH test demonstrating a GH level less than (<) 5 ng/mL AND a pre-treatment IGF-1 level that is low for age and gender:
        i. Unless the agent is Macrilen in which case a GH level of less than (<) 2.8 ng/mL confirms the presence of adult growth hormone deficiency; *or*
        ii. Unless the agent is a glucagon stimulation test, in which case a peak GH level ≤ 3.0 ng/mL in those with a body mass index (BMI) ≤ 30 kg/m2 and a high pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI < 25 kg/m2 confirms the presence of adult growth hormone deficiency; *or*
        iii. Unless the agent is a Glucagon stimulation test, in which case with a peak GH level ≤ 1.0 ng/mL in those with a BMI of ≥ 25 kg/m2 and a low pretest probability of GHD (e.g., acquired structural abnormalities) OR a BMI > 30 kg/m2 confirms the presence of adult growth hormone deficiency; *or*
    c. A structural abnormality of the hypothalamus or pituitary AND BOTH of the following:
        i. Greater than > three (3) documented pituitary hormone deficiencies (e.g., adrenocorticotropic hormone [ACTH], antidiuretic hormone [ADH], follicle stimulating hormone [FSH], luteinizing hormone [LH], thyroid stimulating hormone [TSH], prolactin); *and*
        ii. A pre-treatment IGF-1 level that is low for age and gender; *or*
    d. A congenital abnormality of the hypothalamus or pituitary (e.g., pituitary transcription factor defects, GH-releasing hormone receptor gene defects) that persist throughout life and was diagnosed in infancy or childhood; *AND*
2. Chart documentation and supporting lab work are provided for review to substantiate the above-listed requirements.

<u>If the above prior authorization criteria are met, the requested medication will be approved for up to 12 months</u>.

For the treatment of Pediatric Growth Hormone (GH) Deficiency

The Plan considers Growth Hormone medically necessary when BOTH of the following criteria are met:

1. The member meets ONE (1) of the following:
    a. The member is a neonate or was diagnosed with GH deficiency as a neonate; *or*
    b. The member is a newborn who has GH deficiency due to congenital hypopituitarism and meets ALL of the following:
        i. The member is a newborn with hypoglycemia who does not attain a serum GH concentration above 5 mcg/L in the first week of life AND meets ONE (1) of the following:
            1. Deficiency of at least one (1) additional pituitary hormone; *or*
            2. Has classical imaging triad (i.e., congenital malformation) of ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk; *or*
    c. The member meets ALL of the following clinical parameters:
        i. The member has ONE (1) of the following:
            1. Two (2) pre-treatment pharmacologic provocative GH tests with both results demonstrating a peak GH level less than (<)10 ng/mL; *or*
            2. A documented pituitary or CNS disorder and a pre-treatment Insulin-like growth factor 1 (IGF-1) level greater than (>) 2 standard deviations (SD) below the mean; *and*
        ii. The member has ONE (1) of the following:
            1. The member is under 2.5 years of age at initiation of treatment, a pre-treatment height greater than (>) 2 standard deviations (SD) below the mean; *or*
            2. The member is above 2.5 years of age at initiation of treatment AND ONE (1) of the following:
                a. A pre-treatment height greater than > 2 SD below the mean and a 1-year height velocity greater than > 1 SD below the mean; *or*
                b. A pre-treatment 2-year height velocity greater than > 1.5 SD below the mean; *or*
                c. A pre-treatment 1-year height velocity greater than > 2 SD below the mean; *AND*
2. Chart documentation and supporting lab work are provided for review to substantiate the above-listed requirements.

If the above prior authorization criteria are met, the requested medication will be approved for up to 12 months.

For the treatment of Turner Syndrome

The Plan considers Growth Hormone medically necessary when ALL of the following criteria are met:

1. The member has a diagnosis of Turner Syndrome confirmed by karyotyping (genetic condition where one of the X chromosomes is partially or completely absent); *AND*

2. The member's pre-treatment height is less than (<) the 5th percentile for age; *AND*
3. The member's epiphyses are open; *AND*
4. Chart documentation and supporting lab work are provided for review to substantiate the above-listed requirements.

If the above prior authorization criteria are met, the requested medication will be approved for up to 12 months.

For the treatment of persons who are/were Small for Gestational Age

The Plan considers Growth Hormone medically necessary when ALL of the following criteria are met:

1. The member meets ONE (1) of the following:
    a. Birth weight less than < 2500 g at gestational age greater than > 37 weeks; *or*
    b. Birth weight or length less than less than < the 3rd percentile for gestational age; *or*
    c. Birth weight or length greater than or equal to ≥2 SD below the mean for gestational age; *AND*
2. The member's pre-treatment age is greater than or equal to ≥ 2 years; *AND*
3. The member failed to manifest catch up growth (i.e. pre-treatment height greater than or equal to ≥ 2 SD below the mean); *AND*
4. The member's epiphyses are open; *AND*
5. Chart documentation and supporting laboratory test results are provided for review to substantiate the above-listed requirements.

If the above prior authorization criteria are met, the requested medication will be approved for up to 12 months.

For the treatment of Noonan Syndrome

The Plan considers Growth Hormone medically necessary when ALL of the following criteria are met:

1. The member meets ONE (1) of the following:
    a. A pre-treatment height greater than > 2 SD below the mean and 1 year height velocity is greater than > 1 SD below the mean; *or*
    b. A pre-treatment 1-year height velocity greater than > 2 SD below the mean; *AND*
2. The member's epiphyses are open; *AND*
3. Chart documentation and supporting lab work are provided for review to substantiate the above-listed requirements.

If the above prior authorization criteria are met, the requested medication will be approved for up to 12 months.

For the treatment of Prader-Willi Syndrome

The Plan considers Growth Hormone medically necessary when BOTH of the following criteria are met:

1. The member has a diagnosis of Prader-Willi Syndrome confirmed by genetic testing showing ONE (1) of the following:
    a. Deletion in the chromosome 15q11.2-q13 region; *or*
    b. Maternal uniparental disomy in chromosome 15; *or*
    c. Imprinting defects or translocations involving chromosome 15; *AND*
2. Chart documentation and supporting lab work are provided for review to substantiate the above-listed requirements.

If the above prior authorization criteria are met, the requested medication will be approved for up to 12 months.

For the treatment of Short Stature homeobox-Containing Gene (SHOX) Deficiency

The Plan considers Growth Hormone medically necessary when ALL of the following criteria are met:

1. The member has a diagnosis of SHOX deficiency confirmed by molecular or genetic analyses; *AND*
2. The member meets ONE (1) of the following:
    a. A pre-treatment height greater than > 2 SD below the mean and 1 year height velocity is greater than > 1 SD below the mean; *or*
    b. A pre-treatment 1-year height velocity greater than > 2 SD below the mean; *AND*
3. The member's epiphyses are open; *AND*
4. Chart documentation and supporting lab work are provided for review to substantiate the above-listed requirements.

If the above prior authorization criteria are met, the requested medication will be approved for 12 months.

For the treatment of Growth Failure Associated with CKD, Cerebral Palsy, Congenital Adrenal Hyperplasia, Cystic Fibrosis, or Russell-Silver Syndrome

The Plan considers Growth Hormone medically necessary when ALL of the following criteria are met:

1. The member meets ONE (1) of the following:
    a. The member is less than < 2.5 years of age at initiation of treatment, a pre-treatment height greater than > 2 SD below the mean; *or*
    b. The member is greater than or equal to (≥) 2.5 years of age at initiation of treatment AND meets ONE (1) of the following:
        i. A pre-treatment height greater than > 2 SD below the mean and 1 year height velocity is greater than > 1 SD below the mean; *or*
        ii. A pre-treatment 2-year height velocity greater than > 1.5 SD below the mean; *or*
        iii. A pre-treatment 1-year height velocity greater than > 2 SD below the mean; *AND*
2. The member's epiphyses are open; *AND*
3. Chart documentation and supporting lab work are provided for review to substantiate the above-listed requirements.

If the above prior authorization criteria are met, the requested medication will be approved for 12 months.

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

For the treatment of Adult Growth Hormone Deficiency

Reauthorization for up to 12 months will be granted if clinical chart documentation is provided showing the member meets ONE of the following:

1. A clinical improvement, as evidenced by an improvement in the member's serum IGF-1; *OR*
2. Treatment plan indicating that the GH dose will be increased in response to a low IGF-1 serum concentration

For the treatment of Pediatric Growth Hormone Deficiency

Reauthorization for 12 months will be granted if clinical chart documentation is provided showing the member meets ALL of the following:

1. A clinical improvement in symptoms since starting the requested medication*; AND*
2. The member's epiphyses are open*; AND*
3. The member's growth rate is greater than > 2 cm per year unless there is a documented clinical reason for lack of efficacy (i.e. on treatment less than < a year, nearing final adult height).

For the treatment of Turner Syndrome

Reauthorization for 12 months will be granted if clinical chart documentation is provided showing the member meets ALL of the following:

1. A clinical improvement in symptoms since starting the requested medication*; AND*
2. The member's epiphyses are open*; AND*
3. The member's growth rate is greater than > 2 cm per year unless there is a documented clinical reason for lack of efficacy (i.e. on treatment less than < a year, nearing final adult height).

For the treatment of persons who are/were Small for Gestational Age

Reauthorization for 12 months will be granted if clinical chart documentation is provided showing the member meets ALL of the following:

1. A clinical improvement in symptoms since starting the requested medication*; AND*
2. The member's epiphyses are open*; AND*

3. The member's growth rate is greater than > 2 cm per year unless there is a documented clinical reason for lack of efficacy (i.e. on treatment less than < a year, nearing final adult height).

For the treatment of Noonan Syndrome

Reauthorization for 12 months will be granted if clinical chart documentation is provided showing the member meets ALL of the following:

1. A clinical improvement in symptoms since starting the requested medication*; AND*
2. The member's epiphyses are open*; AND*
3. The member's growth rate is greater than > 2 cm per year unless there is a documented clinical reason for lack of efficacy (i.e. on treatment less than < a year, nearing final adult height).

For the treatment of Prader-Willi Syndrome

Reauthorization for 12 months will be granted if clinical chart documentation is provided showing the member meeting ONE (1) of the following:

1. Clinical improvement in symptoms since starting the requested medication; *OR*
2. Stabilization in the member's body composition or psychomotor function.

For the treatment of Short Stature homeobox-Containing Gene (SHOX) Deficiency

Reauthorization for 12 months will be granted if clinical chart documentation is provided showing the member meets ALL of the following:

1. A clinical improvement in symptoms since starting the requested medication*; AND*
2. The member's epiphyses are open*; AND*
3. The member's growth rate is greater than > 2 cm per year unless there is a documented clinical reason for lack of efficacy (i.e. on treatment less than < a year, nearing final adult height).

For the treatment of Growth Failure Associated with CKD, Cerebral Palsy, Congenital Adrenal Hyperplasia, Cystic Fibrosis, or Russell-Silver Syndrome

Reauthorization for 12 months will be granted if clinical chart documentation is provided showing the member meets ALL of the following:

1. A clinical improvement in symptoms since starting the requested medication*; AND*
2. The member's epiphyses are open*; AND*
3. The member's growth rate is greater than > 2 cm per year unless there is a documented clinical reason for lack of efficacy (i.e. on treatment less than < a year, nearing final adult height).

Experimental or Investigational / Not Medically Necessary

Growth hormone products for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Achondroplasia
- Amyotrophic Lateral Sclerosis (ALS)
- Anorexia Nervosa (AN)
- Ataxia-Telangiectasia (A-T)
- Cognitive Developmental Disorder
- Crohn's Disease (CD)
- Dwarfism
- Eating Disorders
- Female Infertility
- Female Infertility Due to Diminished Ovarian Reserve
- Heart Failure
- Hypophosphatemic Rickets
- Idiopathic Short Stature (ISS)
- Juvenile Idiopathic Arthritis (JIA)
- Lipodystrophies
- Mucopolysaccharidosis IH
- Mucopolysaccharidosis Type I (MPS I)
- Mucopolysaccharidosis Type II (MPS II)
- Mucopolysaccharidosis Type VI
- Non-alcoholic Fatty Liver Disease, NAFLD
- Obesity
- Osteogenesis Imperfecta (OI)
- Osteopenia (Disorder)
- Osteoporosis
- Phelan McDermid Syndrome
- Polycystic Ovarian Syndrome (PCOS)
- Preimplantation Genetic Testing (PGT)
- Primary Disease Fascioscapulohumeral Dystrophy (FSHD)
- Septo-Optic Dysplasia
- Short Bowel Syndrome (SBS)
- Short Stature
- Still's Disease, Juvenile Onset
- Type 1 Diabetes Mellitus

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Appendix A

Table 1: Growth Hormones

Drug	FDA-Approved or Compendia-Supported Indications					
	Growth Hormone Deficiency		Turner Syndrome	SGA	Idiopathic Short Stature	Other
	Pediatric	Adults				
Genotropin (Somatropin)	✔	✔	✔	✔	✔	PWS
Humatrope (Somatropin)	✔	✔	✔	✔*	✔	SHOX
Ngenla (somatrogon-ghla)	✔					
Norditropin (Somatropin)	✔	✔	✔	✔*	✔	NS, PWS
Nutropin (Somatropin)	✔	✔	✔		✔	CKD
Omnitrope (Somatropin)	✔	✔	✔	✔	✔	PWS
Saizen (Somatropin)	✔	✔				
Serostim (Somatropin)						HIV
Skytrofa (Lonapegsomatropin-tcgd)	✔	✔				
Sogroya (Somapacitan-beco)	✔	✔				
Zomacton (Somatropin)	✔	✔	✔	✔*	✔	SHOX
Zorbtive[#] (Somatropin)						SBS

NOTE: All Growth Hormone medications require prior authorization.

Acronyms:

CKD = Growth failure due to chronic kidney disease

HIV = HIV-associated Wasting or Cachexia
NS = Noonan Syndrome
PWS = Prader-Willi Syndrome in children
SBS = Short Bowel Syndrome
SGA = Growth failure in children born Small for Gestational Age who fail to manifest catch-up growth by age 2 years of age (* – indicated in patients with no catch-up growth by 2 to 4 years of age)
SHOX = Short stature homeobox-containing gene deficiency
[#] Discontinued by Manufacturer

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