Growth Hormone (GH) in Children Somatropin (Humatrope®, NutropinAQ®, Genotropin®, Norditropin®, Saizen®, Omnitrope®, Zomacton®)	Place of Service Self-Administration – *May be covered under the pharmacy benefit* HCPCS: J2941 per 1 mg NDCs: (For preferred NutropinAQ) 50242-0043-14 10mg/2ml 50242-0073-01 20mg/2ml 50242-0074-01 10mg/2ml pen 50242-0075-01 5mg/2ml pen 50242-0076-01 20mg/2ml pen

Condition(s) listed in policy (*see criteria for details*)

- Chronic renal insufficiency leading to growth failure
- Noonan syndrome
- Pediatric growth hormone deficiency (GHD) **without** known pituitary disease
- Pediatric growth hormone deficiency (GHD) **with** known pituitary disease
- Prader-Willi Syndrome
- Small for gestational age (SGA)
- Short stature homeobox-containing gene (SHOX) deficiency
- Turner syndrome

AHFS therapeutic class: Pituitary

Mechanism of action: Somatropin (rDNA origin), a recombinant polypeptide hormone, possesses primary structural identity to that of human growth hormone.

(1) Special Instructions and pertinent Information

If member has a Prescription Benefit, please refer cases to Pharmacy Services for prior authorization.

If covered under the Medical Benefit, please submit clinical information for prior authorization review via fax. **Please include medical rationale why medication cannot be home self-administered.**

NutropinAQ® is the preferred formulary drug.

(2) Prior Authorization/Medical Review is required for the following condition(s)

All requests for Growth Hormone not listed in Section (3) must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Pediatric growth hormone deficiency (GHD) WITHOUT known pituitary disease

1. Use of non-preferred growth hormone therapy requires a contraindication or intolerance to Nutropin AQ that is not also expected with the requested non-preferred product, **AND**
2. Prescribed by a pediatric endocrinologist, **AND**
3. Patient's height must be 2 or more standard deviations below the mean (less than the 3rd percentile) for age and sex, **AND**
4. Patient's height velocity is less than 10th percentile of normal for age and sex, tracked over at least one year. (See chart on next page), **AND**
5. Meets ONE of the following:
    a. Patient has failed at least two standard GH provocative tests (e.g., clonidine, arginine, glucagon) defined as a peak < 10 ng/mL done within 1 year prior to initiating GH therapy, with peak value assessed using more than one point in time (e.g. 0, 30, 60, 90, 120 minutes), **OR**
    b. ***Effective through 5/31/2021***: Low Insulin-Like Growth Factor (IGF-1) test** and failure of one GH test, **OR**
    c. ***Effective through 5/31/2021***: Low IGF-1 test and evidence of pituitary disease (either Magnetic Resonance Imaging (MRI) proven abnormality or documented pituitary hormone deficiency.

Covered Doses

- Up to 0.30 mg/kg/week given in daily divided doses
- Up to 0.7mg/kg/week given in daily divided doses for growth hormone deficiency during puberty

Coverage Period

Initial: 1 year
Reauthorization: Continue yearly if no side effects, adequate patient compliance, AND growth velocity > 3 cm/yr.**

ICD-10:

E23.0, E23.1, E89.3

Pediatric growth hormone deficiency (GHD) WITH known pituitary disease

1. Use of non-preferred growth hormone therapy requires a contraindication or intolerance to Nutropin AQ that is not also expected with the requested non-preferred product, **AND**
2. Prescribed by a pediatric endocrinologist, **AND**
3. One of the of the following:
    a. Provider attestation of slowing in growth velocity, and Patient has hypothalamic pituitary abnormality [such as major congenital malformation (ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk), tumor, or irradiation], and one of the following:
        i. For patients without a pituitary gland:
            1. ***Through 5/31/2021:*** No additional requirement, or
            2. ***Effective 6/1/2021***: At least 1 pituitary hormone deficiency,

        OR

        ii. For patients with pituitary gland only: Failure of one standard growth hormone provocative test (e.g., clonidine, arginine, glucagon) done within 1 year prior to starting growth hormone therapy,

    OR

    b. Patient is a newborn and one of the following:
        i. Patient has congenital pituitary abnormality (ectopic posterior pituitary and pituitary hypoplasia with abnormal stalk), or
        ii. Patient has at least 1 pituitary hormone deficiency and hypoglycemia with a serum GH concentration <5 ug/L,

    OR

    c. Patient has a documented causal genetic mutation or specific pituitary/hypothalamic structural defect (not ectopic posterior pituitary), **OR**
    d. Patient has ≥3 multiple pituitary hormone deficiencies (MPHD), regardless of etiology

Covered Doses

- Up to 0.30 mg/kg/week given in daily divided doses
- Up to 0.7mg/kg/week given in daily divided doses for growth hormone deficiency during puberty

Coverage Period

Initial: 1 year
Reauthorization: Continue yearly if no side effects, adequate patient compliance, AND growth velocity > 3 cm/yr.**

ICD-10:

E23.0, E23.1, E89.3

Small for gestational age (SGA)

1. Use of non-preferred growth hormone therapy requires a contraindication or intolerance to Nutropin AQ that is not also expected with the requested non-preferred product, **AND**
2. Prescribed by a Pediatric Endocrinologist, **AND**
3. Patient's height at birth or birth weight must be 2 or more standard deviation (less than the 3rd percentile) below the mean for gestational age *(see Additional Information)*, **AND**
4. Patient's height must be 2 or more standard deviation below the mean (less than the 3rd percentile) at age 2 (boys: 80-81 cm; girls: 79-80 cm)

Covered Doses

- 0.16- 0.30 mg/kg/week given in 6-7 daily doses/wk.
- Up to 0.7mg/kg/week for growth hormone deficiency during puberty.

Coverage Period

Initial: 1 year
Reauthorization: Continue yearly if no side effects, adequate patient compliance, AND growth velocity > 3 cm/yr.**

ICD-10:

R62.52 with P05

Chronic renal insufficiency leading to growth failure

1. Use of non-preferred growth hormone therapy requires a contraindication or intolerance to Nutropin AQ that is not also expected with the requested non-preferred product, **AND**
2. GFR is <50ml/min

Covered Doses

Nutropin AQ®: up to 0.35 mg/kg/wk SC

Coverage Period

Initial: 1 year
Reauthorization: Continue yearly if patient has not had a kidney transplant in the past year

ICD-10:

N18.9

Short stature or growth failure in children with short stature homeobox-containing gene (SHOX) deficiency

1. Use of non-preferred growth hormone therapy requires a contraindication or intolerance to Nutropin AQ that is not also expected with the requested non-preferred product, **AND**
2. Documentation of SHOX gene deficiency, **AND**
3. Prescribed by a Pediatric Endocrinologist

Covered Doses
Nutropin AQ®: up to 0.35 mg/kg/wk SC

Coverage Period
Initial: 1 year
Reauthorization: Continue yearly if no side effects, adequate patient compliance, AND growth velocity > 3 cm/yr.**

ICD-10: R62.52

(3) The following condition(s) DO NOT require Prior Authorization/Preservice

All requests for Growth Hormone not listed in Section (3) must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Noonan syndrome

1. Use of non-preferred growth hormone therapy requires a contraindication or intolerance to Nutropin AQ that is not also expected with the requested non-preferred product, **AND**
2. Prescribed by a Pediatric Endocrinologist

Covered Doses
Nutropin AQ®: up to 0.35 mg/kg/wk SC

Coverage Period
Initial: 1 year
Reauthorization: Continue yearly if no side effects, adequate patient compliance, AND growth velocity > 3 cm/yr.**

ICD-10:
Q87.1 (growth failure due to Noonan Syndrome)

Prader-Willi Syndrome

1. Use of non-preferred growth hormone therapy requires a contraindication or intolerance to Nutropin AQ that is not also expected with the requested non-preferred product, **AND**
2. Prescribed by a Pediatric Endocrinologist

Covered Doses
Nutropin AQ®: up to 0.35 mg/kg/wk SC

Coverage Period
Initial: 1 year
Reauthorization: Continue yearly if no side effects, adequate patient compliance, AND growth velocity > 3 cm/yr.**

**For patients growth velocity <3 cm/yr, refer cases to Medical Director.

ICD-10:
Q87.1 (growth failure due to Prader-Willi Syndrome)

Turner Syndrome

1. Use of non-preferred growth hormone therapy requires a contraindication or intolerance to Nutropin AQ that is not also expected with the requested non-preferred product, **AND**
2. Prescribed by a Pediatric Endocrinologist

Covered Doses
Up to 0.375 mg/kg/wk

Coverage Period
Initial: 1 year
Reauthorization: Continue yearly if no side effects, adequate patient compliance, AND growth velocity > 3 cm/yr.**

ICD-10:
Q96.0 - Q96.9

(4) This Medication is NOT medically necessary for the following condition(s)

Blue Shield's research indicates there is inadequate clinical evidence to support off-label use of this drug for the following conditions (Health and Safety Code 1367.21):

- Athletic performance enhancement
- Anti-aging factor
- Burn injuries
- Cardiomyopathy
- Chronic catabolic states
- Constitutional delay in growth and development
- Crohn's disease
- Cystic fibrosis
- Growth retardation due to down syndrome or juvenile idiopathic arthritis
- Hand-Schuller Christian disease
- Hyperinsulinism
- Hypophospahtemic rickets
- Idiopathic short stature
- Idiopathic GHD with no history of GHD in childhood
- Infertility
- Kwashiorkor
- Malnutrition
- Muscular dystrophy

- Obesity
- Osteoporosis
- Osteogenesis imperfecta
- Skeletal dysplasias
- "Somatopause" in older adults
- Spina bifida

Coverage for a Non-FDA approved indication, requires that criteria outlined in Health and Safety Code § 1367.21, including objective evidence of efficacy and safety are met for the proposed indication.

Please refer to the Provider Manual and User Guide for more information.

(5) Additional Information

How supplied:

Humatrope:

- 5 mg vial and 5-mL vial of Diluent for Humatrope
- 6 mg (gold), 12 mg (teal) and 24 mg (purple) cartridge, and prefilled syringe of Diluent for Humatrope

Nutropin AQ:

- pen cartridge cartons contain one single pen cartridge containing 2 mL
    1. 10 mg pen= 10mg/2ml
    2. 20mg pen= 20mg/2ml
- NuSpin™ injection device
    1. 5mg/2ml, 10mg/2ml, 20mg/2ml

Genotropin:

- lyophilized powder in a two-chamber color-coded cartridge: 5.8 mg (green tip) and 12 mg (purple tip) (with preservative)
- Genotropin Miniquick Growth Hormone Delivery Device containing a two chamber cartridge (without preservative): 0.2 mg, 0.4 mg, 0.6 mg, 0.8 mg, 1.0 mg, 1.2 mg, 1.4 mg, 1.6 mg, 1.8 mg, and 2.0mg

Norditropin:

- Norditropin is preloaded in the Norditropin FlexPro pens
- 5 mg/1.5 mL (orange): FlexPro pen
- 10 mg/1.5 mL (blue): FlexPro pen
- 15 mg/1.5 mL (green): FlexPro pen
- 30 mg/3 mL (purple): FlexPro pen

Omnitrope:

- 5 mg/1.5ml cartridge
- 10 mg/1.5ml cartridge
- 5.8mg vial

Saizen:

5 mg and 8.8 mg vials.

Saizen clickeasy and Saizenprep 8.8 mg/1.51 ml cartridges

Zomacton: [somatropin (rDNA origin)] for injection is supplied as 5 mg and 10 mg of lyophilized, sterile somatropin per vial:

- Zomacton 5 mg carton (NDC 55566-1801-1) contains one vial of Zomacton (5 mg per vial) and one vial of diluent [5 mL of bacteriostatic 0.9% sodium chloride for injection, USP (benzyl alcohol preserved)], and is supplied in single cartons
- Zomacton 10 mg carton (NDC 55566-1901-1) contains one vial of Zomacton (10 mg per vial), one syringe of diluent [1 mL of bacteriostatic water for injection with 0.33% metacresol as preservative] and a 25G reconstitution needle, and is supplied in single cartons.
- Zomacton 10 mg carton (NDC 55566-1902-1) contains one vial of Zomacton (10mg per vial), one syringe of diluent [1 mL of bacteriostatic water for injection with 0.33% metacresol as preservative], 1 vial adapter, and is supplied in single cartons.

HEIGHT VELOCITY CHART

Tenth percentile of height velocity for boys age 2-17			
Age (years)	Height velocity (cm/y) 10th percentile	Age (years)	Height velocity (cm/y) 10th percentile
2.0	6.7	10.0	4.2
2.5	6.4	10.5	4.2
3.0	6.1	11.0	4.2
3.5	5.8	11.5	4.2
4.0	5.7	12.0	4.7
4.5	5.5	12.5	5.5
5.0	5.3	13.0	7.3
5.5	5.1	13.5	8.0
6.0	5.0	14.0	7.2
6.5	4.9	14.5	5.1
7.0	4.7	15.0	3.5
7.5	4.6	15.5	2.2
8.0	4.5	16.0	1.2
8.5	4.4	16.5	0.5
9.0	4.4	17.0	0.1
9.5	4.3		
Tenth percentile of height velocity for girls age 2-14 1/2			
Age (years)	Height velocity (cm/y) 10th percentile	Age (years)	Height velocity (cm/y) 10th percentile
2.0	7.1	8.5	4.7
2.5	6.7	9.0	4.8
3.0	6.3	9.5	4.9
3.5	6.0	10.0	5.0
4.0	5.8	10.5	4.6
4.5	5.4	11.0	6.4
5.0	5.2	11.5	6.9
5.5	5.0	12.0	6.3
6.0	5.0	12.5	4.6
6.5	4.9	13.0	3.0
7.0	4.8	13.5	1.7
7.5	4.8	14.0	0.8
8.0	4.7	14.5	0.1

1. The following associations define SGA as height or weight less than -2SD (< 3rd percentile):
   - The American Association of Clinical Endocrinologists Medical guidelines for growth hormone use in adults and children– 2003 Update (http://www.aace.com/pub/pdf/guidelines/hgh.pdf)
   - The International Small for Gestational Age Advisory Board Consensus Development Conference Statement: Management of Short Children Born Small for Gestational Age, April 24–October 1, 2001 (http://pediatrics.aappublications.org/cgi/content/full/111/6/1253#R15)
2. The AACE recommends children be evaluated for treatment with GH for the diagnosis of SGA if height or weight remains < 3rd percentile at age 2 or older.

(6) References

- Genotropin [Prescribing Information]. Pfizer Inc.: New York, NY. 2016.
- Humatrope [Prescribing Information]. Eli Lilly and Company: Indianapolis, IN. 2016.
- Norditropin [Prescribing Information]. Novo Nordisk Inc.: Plainsboro, NJ. 2018.
- Nutropin AQ [Prescribing Information]. Genentech: South San Francisco, CA. 2016.
- Omnitrope [Prescribing Information]. Sandoz Inc.: Princeton, NJ. 2014.
- Saizen [Prescribing Information]. EMD Serono Inc.: Rockland, MA. 2017.
- Zomacton [Prescribing Information]. Ferring Pharmaceuticals Inc.: Parsippany, NJ. 2018.
- AHFS®. Available by subscription at http://www.lexi.com
- DrugDex®. Available by subscription at http://www.micromedexsolutions.com

1. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children—2003 update. Endocr Pract 2003;9(1).
2. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. GH Research Society. J Clin Endocrinol Metab. 2000 Nov;85(11):3990-3.

(7) Policy Update

Date of last review: 2Q2022
Date of next review: 2Q2023
Changes from previous policy version:

- No clinical change to policy following routine annual review.

BSC Drug Coverage Criteria to Determine Medical Necessity
Reviewed by P&T Committee