Growth Hormone
Effective 02/20/19

<table>
<thead>
<tr>
<th>Plan</th>
<th>× MassHealth</th>
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<tr>
<td></td>
<td>☐ Commercial/Exchange</td>
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<tr>
<th>Benefit</th>
<th>Program Type</th>
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<tr>
<td>× Pharmacy Benefit</td>
<td>× Prior Authorization</td>
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<tr>
<td>☐ Medical Benefit (NLX)</td>
<td>☐ Quantity Limit</td>
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<tr>
<td></td>
<td>☐ Step Therapy</td>
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**Specialty Limitations**
These medications have been designated specialty and must be filled at a contracted specialty pharmacy.

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**Contact Information**

**Specialty Medications**
All Plans
- Phone: 866-814-5506
- Fax: 866-249-6155

**Non-Specialty Medications**

<table>
<thead>
<tr>
<th>Plan</th>
<th>Phone</th>
<th>Fax</th>
</tr>
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<tbody>
<tr>
<td>MassHealth</td>
<td>877-433-7643</td>
<td>866-255-7569</td>
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<tr>
<td>Commercial</td>
<td>800-294-5979</td>
<td>888-836-0730</td>
</tr>
<tr>
<td>Exchange</td>
<td>855-582-2022</td>
<td>855-245-2134</td>
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</table>

**Medical Specialty Medications (NLX)**
All Plans
- Phone: 844-345-2803
- Fax: 844-851-0882

**Exceptions**
N/A

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**Overview**
Genotropin is the preferred Growth Hormone. Requests for all agents other than Genotropin, require clinical rationale for use of the requested agent instead of Genotropin.

**Coverage Guidelines**

**Pediatric Indications**

**Pediatric growth hormone (GH) deficiency/ panhypopituitarism:**
- Member has a diagnosis of GH deficiency or panhypopituitarism AND
- Member has a short stature or growth failure, documented by one of the following:
  - Pre-treatment height less than -2 standard deviations below mean or below 3rd percentile on standard pediatric growth chart
  - Height dropping below initial percentile curve on standard pediatric growth chart when monitored over 1 year AND
- Prescriber has provided documentation of ONE of the following*:
  a. Results of two abnormal tests, which can be either:
     i. Two abnormal GH stimulation tests
     ii. One abnormal stimulation test and one abnormal IGF-1/IGFBP-3 level
  b. ONE abnormal test (GH stimulation, IGF-1, or IGFBP-3 test), with either:
     i. Abnormal pituitary imaging
     ii. Deficiency of at least three other pituitary hormones (TSH, ACTH, LH, FSH, or AVP/ADH)
     iii. Appropriate current medication claims suggesting deficiency of at least three
other pituitary hormones (levothyroxine, hydrocortisone or other glucocorticoid, testosterone [for males] or estrogen/progesterone [for females], or desmopressin)

4. Prescriber has provided documentation of ONE of the following:
   a. Member is under the care of an endocrinologist
   b. Other possible causes of short stature or growth failure have been ruled out (i.e. hypothyroidism, malnutrition, chronic illness, skeletal disorders, pituitary tumor)

*Cases where imaging shows NO PITUITARY may be approved without requiring laboratory tests, if the member meets all other criteria.

Hypoglycemia due to growth hormone (GH) deficiency:
1. Member has a diagnosis of hypoglycemia due to growth hormone (GH) deficiency AND
2. Member has hypoglycemia-symptoms and a low glucose level* AND
3. Prescriber has provided laboratory results indicating GH deficiency (at least one abnormal GH stimulation test)

*Lower end of normal range is 75 mg/dL (4.2 mM/L) although symptoms are rare unless glucose is lower than 50 mg/dL

Noonan, Prader-Willi, or Turner syndrome:
1. Member has a diagnosis of Noonan, Prader-Willi, or Turner syndrome AND
2. Member has a short stature or growth failure, documented by one of the following:
   a. Pre-treatment height less than -2 standard deviations below mean or below 3rd percentile on standard pediatric growth chart
   b. Height dropping below initial percentile curve on standard pediatric growth chart when monitored over 1 year

3. Prescriber has provided documentation of ONE of the following*:
   a. Genetic testing confirming diagnosis
   b. Appropriate clinical rationale for why genetic testing cannot be provided (i.e. member is new to prescriber and current prescriber has no means of obtaining labs used for diagnosis, diagnosis made many years ago)

Chronic renal failure up to time of renal transplantation:
1. Member has a diagnosis of chronic renal failure up to time of renal transplantation AND
2. Member has a short stature or growth failure, documented by one of the following:
   a. Pre-treatment height less than -2 standard deviations below mean or below 3rd percentile on standard pediatric growth chart
   b. Height dropping below initial percentile curve on standard pediatric growth chart when monitored over 1 year

3. Prescriber has provided documentation of ONE of the following:
   a. Other CRF-associated etiologies have been excluded: acidosis, secondary hyperparathyroidism, malnutrition or zinc deficiency
   b. Member is under the care of a renal specialist
Small for gestational age/Intrauterine growth restriction (SGA/IUGR) with failed catch-up growth by age 2 to 4:

1. Member has a diagnosis of small for gestational age/intrauterine growth restriction (SGA/IUGR) with failed catch-up growth by age 2 to 4 AND
2. Member is at least 2 years of age or older AND
3. Member has a short stature or growth failure, documented by ONE of the following:
   a. Pre-treatment height less than -2 standard deviations below mean or below 3rd percentile on standard pediatric growth chart
   b. Height dropping below initial percentile curve on standard pediatric growth chart when monitored over 1 year
      AND
4. Diagnosis of SGA/IUGR, ONE of the following:*:
   a. Birth weight less than -2 standard deviations below mean or below 3rd percentile for gestational age
   b. Birth length less than -2 standard deviations below mean or below 3rd percentile for gestational age
      AND
5. Catch-up growth not achieved by age 2 to 4, documented as height continually less than -2 standard deviations below mean or below 3rd percentile from age 2 to current age. *

*For approval, members must meet both criteria 4 AND 5, independently.

Adult Indications

Growth hormone (GH) deficiency or panhypopituitarism:

1. Member has a diagnosis of GH deficiency or panhypopituitarism AND
2. Prescriber has provided documentation of ONE of the following*:
   a. Results of two abnormal tests, which can be either:
      i. Two abnormal GH stimulation tests
      ii. One abnormal stimulation test and one abnormal IGF-1/IGFBP-3 level
   b. ONE abnormal test (GH stimulation, IGF-1, or IGFBP-3 test), with either:
      i. Abnormal pituitary imaging
      ii. Deficiency of at least three other pituitary hormones (TSH, ACTH, LH, FSH, or AVP/ADH)
      iii. Appropriate current medication claims suggesting deficiency of at least three other pituitary hormones (levothyroxine, hydrocortisone or other glucocorticoid, testosterone [for males] or estrogen/progesterone [for females], or desmopressin)
      AND
3. Member has at least one complication of GH deficiency**

*Cases where imaging shows NO PITUITARY may be approved without requiring laboratory tests, if the member meets all other criteria including appropriate diagnosis and at least one complication of GHD.

Adults with a history of traumatic brain injury (TBI) or subarachnoid hemorrhage may present with GHD. This GHD may be transient, and may correct within one year’s time. If the documented diagnosis is adult isolated GHD (without organic/acquired causes such as septo-optic dysplasia, pituitary ablation, pan- or multiple hypopituitarism, or surgical resection), provocative stimulation testing in...
members with a TBI or subarachnoid hemorrhage should be performed at least 12 months after the event.

** A complication of GH deficiency is required:

1. Increased fat mass and reduced lean body mass (as documented, in part, by increased waist-hip ratio). Waist-hip ratio of = 1.0 for men and > 0.8 for woman is indicative of central obesity. Other methods of central obesity documentation include CT and/or MRI abdominal imaging results and waist measurement of > 40 inches in males or 35 inches in females.
2. Reduced extracellular volume (as documented by measurement of extracellular material)
3. Reduced bone mineral content and density (as documented by bone density study). As per the World Health Organization (WHO), bone density of -1 standard deviation (-1 S.D.) may indicate a 2.5 fold increased risk of fracture.
4. Elevated cholesterol (National Institutes of Health, National Heart, Lung, and Blood Institute: fasting total cholesterol = 240 mg/dL = high, LDL cholesterol 160 - 189 mg/dL = high, = 190 = very high).
5. Diminished renal function without other etiology (laboratory values and clinical rationale required)
6. Congestive heart failure (CHF)
7. Reduced exercise capacity (quantified, such as isometric/isokinetic strength, physical performance, maximal oxygen consumption and maximum work capacity increase)
8. Impaired quality of life-Quality of Life-Assessment of Growth Hormone Deficiency in Adults (QoLAGHDA) measure may be useful, although there are no studies to validate the predictive value of any specific cut off for a low score.

HIV/AIDS-associated wasting or cachexia (not covered for AIDS- or HAART-associated lipodystrophy)

1. Member has a diagnosis of HIV/AIDS-associated wasting or cachexia AND
2. Member is receiving concurrent antiretroviral therapy AND
3. Prescriber has provided evidence of wasting, as indicated by any of the following (with or without chronic fever, weakness, or diarrhea):
   a. An involuntary loss of at least 10% of body weight within one year
   b. An involuntary loss of at least 7.5% of body weight within six months
   c. A reduction in lean body mass (measured via bioelectrical impedance assay or BIA)
   d. A BMI of < 20 kg/m²
   **AND**
   Member has had a trial of an FDA-approved appetite stimulant, such as dronabinol or megestrol acetate oral suspension, prior to initiation of GH therapy if the etiology of wasting or cachexia is decreased caloric intake AND
4. Prescriber has provided documentation of ONE of the following:
   a. Other causes of weight loss have been ruled out:
      i. gastrointestinal tract opportunistic infections, decrease in food intake due to oral, pharyngeal, esophageal lesions or candidiasis, gonadal dysfunction, adverse effects due to medications, or psychosocial factors. Correction of factors such as these may alleviate the need for GH therapy.
   b. Member is under the care of an Infectious Disease specialist.

Adults-Short Bowel Syndrome (SBS)

1. Member has a diagnosis of SBS AND
2. Member is receiving specialized nutritional support, including enteral or parenteral nutrition and/or fluid and micronutrient supplements

**Continuation of Therapy**
Reauthorization requires physician documentation of continued medical necessity and the following Diagnosis-Specific criteria:

1. **For Pediatric GHD, SGA/IUGR with failed catch-up growth, Noonan Syndrome, Turner Syndrome, and Pediatric Prader-Willi Syndrome (PWS),** documentation indicating a measured growth velocity is at least 2.5 cm per year is required.
2. **For Adult GHD and panhypopituitarism (PHP),** documentation of appropriate IGF-1 or IGFBP-3 levels (within lab-specific reference range) **AND** continued positive response regarding documented GH complication are required.
3. **For Adult GHD from organic/acquired causes (i.e. septo-optic dysplasia, pituitary ablation, pan- or multiple hypopituitarism, or surgical resection),** documentation of appropriate IGF-1 or IGFBP-3 levels (within lab-specific reference range) is required.

**Limitations**
1. Initial approvals will be varied based on the treatment:
   a. **For Short Bowel Syndrome,** approvals will be for up to 4 weeks.
   b. **For adult GHD,** approvals will be for up to 12 months.
   c. **For ALL other indications,** approvals will be for up to 6 months.
2. Reauthorizations will be varied based on the treatment:
   a. **For adult GHD,** approvals will be for up to 12 months.
   b. **For ALL other indications,** approvals will be for up to 6 months.

**Appendix**

**Appendix A: Dosing**

<table>
<thead>
<tr>
<th>Medication</th>
<th>PEDIATRIC INDICATIONS</th>
<th>ADULT INDICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotropin® cartridge</td>
<td>Idiopathic Short Stature: up to 0.47 mg/kg subcutaneously (SC) weekly</td>
<td>Adult GHD: 0.04 mg/kg SC weekly to be increased as tolerated to not more than 0.08 mg/kg SC weekly at 4 to 8 week intervals, or a starting dose of approximately 0.2 mg SC daily (range, 0.15 to 0.30 mg SC daily) increased gradually by increments of 0.1 to 0.2 mg SC daily every 1 to 2 months</td>
</tr>
<tr>
<td>Genotropin® MiniQuick® cartridge</td>
<td>Pediatric GHD: 0.16 to 0.24 mg/kg SC weekly</td>
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<tr>
<td></td>
<td>Prader-Willi Syndrome: 0.24 mg/kg SC weekly</td>
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<tr>
<td></td>
<td>Small for Gestational Age: 0.48 mg/kg SC weekly</td>
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<tr>
<td></td>
<td>Turner Syndrome: 0.33 mg/kg SC weekly</td>
<td></td>
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<tr>
<td>Humatrope® Cartridge</td>
<td>Idiopathic short stature: up to 0.37 mg/kg SC weekly</td>
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<tr>
<td>Humatrope® vial</td>
<td>Pediatric GHD: 0.18 to 0.3 mg/kg SC weekly</td>
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<td></td>
<td>Turner Syndrome: up to 0.375 mg/kg SC weekly</td>
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<td></td>
<td>SHOX deficiency: 0.35 mg/kg SC weekly</td>
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<tr>
<td></td>
<td>Small for gestational age: up to 0.47 mg/kg SC weekly</td>
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<tr>
<td></td>
<td>Adult GHD:</td>
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<tr>
<td></td>
<td>Initial: not more than 0.006 mg/kg SC daily and may be increased up to a max of 0.0125 mg/kg SC daily.</td>
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<tr>
<td></td>
<td>Alternative schedule: 0.15 to 0.30 mg SC daily may be used without consideration of body weight and may be increased gradually by increments of approximately 0.1 to 0.2 mg SC daily every 1 to 2 months</td>
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</tbody>
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<thead>
<tr>
<th>Norditropin® FlexPro® Cartridge</th>
<th>Noonan Syndrome: Up to 0.066 mg/kg SC daily</th>
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<tbody>
<tr>
<td>Norditropin® NordiFlex® cartridge</td>
<td>Pediatric GHD: 0.024 to 0.034 mg/kg SC daily, 6 to 7 times a week</td>
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<tr>
<td></td>
<td>Small for gestational age: up to 0.067 mg/kg SC daily</td>
</tr>
<tr>
<td></td>
<td>Turner Syndrome: Up to 0.067 mg/kg SC daily</td>
</tr>
<tr>
<td></td>
<td>Adult GHD: 0.004 mg/kg SC daily to be increased as tolerated to not more than 0.016 mg/kg SC daily after approximately 6 weeks, or a starting dose of approximately 0.2 mg SC daily (range, 0.15 to 0.30 mg SC daily) increased gradually by increments of approximately 0.1 to 0.2 mg SC daily every 1 to 2 months</td>
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<thead>
<tr>
<th>Nutropin AQ® vial, pen cartridge</th>
<th>Chronic renal insufficiency: up to 0.35 mg/kg SC weekly</th>
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<tbody>
<tr>
<td>Nutropin AQ® NuSpin® pen cartridge</td>
<td>Idiopathic short stature: up to 0.3 mg/kg SC weekly</td>
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<tr>
<td></td>
<td>Pediatric GHD: up to 0.3 mg/kg SC weekly (up to 0.7 mg/kg SC weekly in pubertal patients)</td>
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<td></td>
<td>Turner Syndrome: up to 0.375 mg/kg SC weekly.</td>
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<td></td>
<td>Adult GHD: Initial: not more than 0.006 mg/kg SC daily. Dose may be increased to a maximum of 0.025 mg/kg SC daily in patients under 35 years old and to a maximum of 0.0125 mg/kg SC daily in patients over 35 years old.</td>
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<tr>
<td></td>
<td>Alternative schedule: starting dose of approximately 0.02 mg SC daily (range, 0.15 to 0.30 mg SC daily) may be used without consideration of body weight and may be increased gradually by increments of approximately 0.1 to 0.2 mg SC daily every 1 to 2 months.</td>
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<tr>
<td>Drug Type</td>
<td>Indication</td>
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<tr>
<td>Omnitrope® vial, cartridge</td>
<td>Idiopathic short stature: up to 0.47 mg/kg SC weekly</td>
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<tr>
<td></td>
<td>Pediatric GHD: 0.16 to 0.24 mg/kg SC weekly</td>
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<td>Prader-Willi syndrome: 0.24 mg/mg SC weekly</td>
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<td>Small for gestational age: up to 0.48 mg/kg SC weekly</td>
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<td></td>
<td>Turner syndrome: 0.33 mg/kg SC weekly</td>
</tr>
<tr>
<td>Saizen® vial</td>
<td>Pediatric GHD: 0.18 mg/kg SC weekly</td>
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<tr>
<td>Saizen® click easy® cartridge</td>
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<tr>
<td>Serostim® vial</td>
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<td></td>
<td>Pediatric GHD:</td>
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<tr>
<td>Zomacton® vial</td>
<td>Pediatric GHD: up to 0.1 mg/kg SC administered 3 times per week</td>
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<tr>
<td>Zorbtive® vial</td>
<td>Short Bowel Syndrome: dose of approximately 0.1 mg/kg SC to a maximum of 8 mg SC daily. Administration for more than 4 weeks has not been adequately studied.</td>
</tr>
</tbody>
</table>

Please note: The appearance of a medication in this chart does not indicate formulary coverage |

Appendix B: Pediatric Growth Charts – also available at http://www.cdc.gov/growthcharts/cdc_charts.htm
Length-for-age percentiles:
Boys, birth to 36 months

Published May 38, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).

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Stature-for-age percentiles: Boys, 2 to 20 years

Published May 30, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
Length-for-age percentiles: Girls, birth to 36 months

Published May 30, 2000.
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).

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Review History
06/16/08 – Reviewed
06/15/09 – Reviewed (I.S.S.)
06/21/10 – Reviewed
06/27/11 – Reviewed
06/25/12 – Reviewed
06/24/13 – Reviewed
06/23/14 – Reviewed
06/22/15 – Reviewed
06/2016 – Reviewed
02/2017 – Reviewed (adopted SGM) in P&T Meeting
11/20/17 – Reviewed (adopted MH RS)
02/20/19 – Reviewed in P&T Meeting

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