Optimizing Outcomes for Patients With Growth Hormone Deficiency and Other Growth Disorders in Managed Care
The purpose of the Managed Care Tool Box is to provide examples of resources and tools that have been used successfully by clinicians, educators, peer review organizations, managed care organizations, and others to improve the management of growth hormone deficiency and other growth disorders. This Tool Box does not specifically endorse any of the enclosed tools.
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Guidelines and Consensus Statements

American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for Growth Hormone Use in Growth Hormone-Deficient Adults and Transition Patients—2009 Update.


In 2009, the American Association of Clinical Endocrinologists (AACE) substantially revised their 2004 medical guidelines for the accurate diagnosis and effective ethical treatment of growth hormone deficiency in affected patients.

The recently revised AACE guidelines address the accurate diagnosis and effective therapy for growth hormone-deficient patients, as well as cut points or benchmarks for stimulation testing of growth hormone deficiency. Stimulation testing measures normal secretion or low growth hormone secretion, making them an accurate barometer to gauge growth hormone deficiency.

Recommendations include:

- Patients with childhood-onset GH deficiency previously treated with GH therapy should be retested after achieving final height, and GH therapy should be discontinued for at least one month to determine GH status before restarting GH therapy.
- GH dosing regimens should be individualized, independent of body weight, particularly in those with GH deficiency and diabetes, obesity and previous gestational diabetes, or a family history of diabetes.
- The starting dose of GH therapy for patients in transition should be approximately 50% of the dose between the pediatric doses required for growth and the adult dose.
- For childhood treatment of Turner’s syndrome, idiopathic short stature, and conditions other than GH deficiency, there is no indication to retest when they achieve final height and no benefit to continuing GH therapy in adulthood.
- The insulin tolerance test is the preferred GH stimulation test to establish the diagnosis of adult GH deficiency in patients with childhood-onset GH deficiency, as well as in diagnosing adult GH deficiency in general. The arginine + GH-releasing hormone stimulation test, glucagon test, and the arginine test alone are acceptable alternatives.
- GH is not recommended for any reason other than the well-defined uses of the drug. No data are available suggesting that GH is beneficial in anti-aging or enhancing sport performance.
- Physicians should follow up on patients at one- to two-month intervals after initiating GH therapy.
Consensus Guidelines for the Diagnosis and Treatment of Adults With GH Deficiency II: A Statement of the GH Research Society in Association With the European Society for Pediatric Endocrinology, Lawson Wilkins Society, European Society of Endocrinology, Japan Endocrine Society, and Endocrine Society of Australia.


In 2007, the GH Research Society held a Consensus Workshop in Sydney, Australia, to incorporate the important advances in the management of GH deficiency in adults, which occurred since the inaugural 1997 Consensus Workshop.

Findings and recommendations of the Consensus Panel include:

- Testing for GHD should be extended from hypothalamic-pituitary disease and cranial irradiation to include traumatic brain injury.
- Idiopathic isolated GHD occurring de novo in the adult is not a recognized entity.
- The insulin tolerance test, combined administration of GHRH with arginine or growth hormone-releasing peptide, and glucagon are validated GH stimulation tests in the adult.
- A low IGF-1 is a reliable diagnostic indicator of GHD in the presence of hypopituitarism, but a normal IGF-1 does not rule out GHD.
- GH status should be reevaluated in the transition age for continued treatment to complete somatic development. Interaction of GH with other axes may influence thyroid, glucocorticoid, and sex hormone requirements.
- Response should be assessed clinically by monitoring biochemistry, body composition, and quality of life.
- There is no evidence that GH replacement increases the risk of tumor recurrence or de novo malignancy.
Consensus Statement on the Diagnosis and Treatment of Children With Idiopathic Short Stature: A Summary of the Growth Hormone Research Society, the Lawson Wilkins Pediatric Endocrine Society, and the European Society for Paediatric Endocrinology Workshop.


The Growth Hormone Research Society together with the Lawson Wilkins Pediatric Endocrine Society and the European Society for Pediatric Endocrinology convened in 2007 to review and weigh available evidence related to the evaluation and management of children with ISS. Leading experts in the field, including representatives of all international pediatric endocrine societies, were invited to participate in creating a consensus document on the topic. Evidence was obtained by extensive literature review and from clinical experience.

Findings and recommendations include:

- ISS is defined auxologically by a height below -2 SD score (SDS) without findings of disease as evident by a complete evaluation by a pediatric endocrinologist including stimulated GH levels.
- ISS may be a risk factor for psychosocial problems, but true psychopathology is rare.
- In the United States and seven other countries, the regulatory authorities approved GH treatment (at doses up to 53 µg/kg/d) for children shorter than -2.25 SDS, whereas in other countries, lower cutoffs are proposed.
- Psychological counseling is worthwhile to consider instead of or as an adjunct to hormone treatment.
- The predicted height may be inaccurate and is not an absolute criterion for GH treatment decisions.
- The shorter the child, the more consideration should be given to GH.
- Successful first-year response to GH treatment includes an increase in height SDS of more than 0.3–0.5.
- The mean increase in adult height in children with ISS attributable to GH therapy is 3.5–7.5 cm.
- Responses to GH therapy are highly variable.
- IGF-1 levels may be helpful in assessing compliance and GH sensitivity; levels that are consistently elevated (-2.5 SDS) should prompt consideration of GH dose reduction.
- GH therapy for children with ISS has a similar safety profile to other GH indications.
Members of several pediatric endocrine societies with expertise in obstetrics, peri- and neonatal medicine, pediatrics, pediatric and adult endocrinology, epidemiology, and pharmacology as well as representatives from the Growth Hormone Research Society convened in 2006 to examine data relevant to the early, mid-, and long-term outcome of children born small for gestational age (SGA). The goal of the meeting was to identify the key health issues facing a child born SGA and to propose management strategies. Published data was used to frame and support recommendations, and were not available or adequate, discussion was based on expert clinical opinions.

Findings and recommendations include:

- Diagnosis of SGA should be based on accurate anthropometry at birth including weight, length, and head circumference.
- Early surveillance in a growth clinic is recommended for children without catch-up.
- Early neurodevelopment evaluation and interventions are warranted in at-risk children.
- Endocrine and metabolic disturbances in the SGA child are recognized, but infrequent.
- For the 10% who lack catch-up, GH treatment can increase linear growth.
- Early intervention with GH for those with severe growth retardation (height SD score, -2.5; age, 2–4 yrs) should be considered at a dose of 35–70 µg/kg/d.
- Long-term surveillance of treated patients is essential.
- The associations at a population level between low birth weight, including SGA, and coronary heart disease and stroke in later life are recognized, but there is inadequate evidence to recommend routine health surveillance of all adults born SGA outside of normal clinical practice.
Consensus Statement on the Management of the GH-treated Adolescent in the Transition to Adult Care.


In 2005, the European Society for Paediatric Endocrinology published this consensus statement on issues relating to the care of GH-treated patients in the transition from pediatric to adult life workshop. Clinicians experienced in the care of pediatric and adult patients on GH treatment from a wide range of countries participated.

Findings and recommendations include:

- Reassess etiology and disease-specific management.
- Reassess GH treatment regimen to mimic the diminishing production of endogenous GH secretion.
- Achieve full adult somatic development including lean body mass and bone mineral accrual completion of pubertal, sexual, and reproductive maturation.
- Reduce metabolic and cardiovascular risks attainment of adult psychosocial development.
- Educate patients to ensure they have an understanding of their disease to develop autonomy in health care decision making.
Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline.


A Task Force was convened by The Endocrine Society to develop guidelines for the evaluation and treatment of adults with GH deficiency. Only fully published, peer-reviewed literature was reviewed. This Consensus Statement was published in 2006.

Findings and recommendations include:

- GHD can persist from childhood or be newly acquired.
- Confirmation through stimulation testing is usually required unless there is a proven genetic/structural lesion persistent from childhood.
- GH therapy offers benefits in body composition, exercise capacity, skeletal integrity, and quality of life measures and is most likely to benefit those patients who have more severe GHD.
- The risks of GH treatment are low.
- GH dosing regimens should be individualized.
- The final decision to treat adults with GHD requires thoughtful clinical judgment with a careful evaluation of the benefits and risks specific to the individual.
# Managed Care Tool Box

## Diagnostic Coding of Growth Hormone Deficiency

### ICD-9 Codes Associated With a Diagnosis of Pediatric Growth Hormone Deficiency

<table>
<thead>
<tr>
<th>ICD-9 Code</th>
<th>Primary Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>253.2</td>
<td>Panhypopituitarism</td>
</tr>
<tr>
<td>253.3</td>
<td>Growth hormone deficiency</td>
</tr>
<tr>
<td>585</td>
<td>Chronic renal insufficiency</td>
</tr>
<tr>
<td>759.81</td>
<td>Prader-Willi Syndrome</td>
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<td>759.89</td>
<td>Noonan’s Syndrome</td>
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<tr>
<td>758.6</td>
<td>Turner’s Syndrome</td>
</tr>
<tr>
<td>764.00</td>
<td>Small for Gestational Age</td>
</tr>
<tr>
<td>783.43</td>
<td>Idiopathic Short Stature</td>
</tr>
</tbody>
</table>

### Coding for Children and Adolescents With ISS

- ICD-9: 783.43
- ICD-10: E34.3 Short stature due to endocrine disorder
  - R62.52 Short stature (child)

### Coding for Children Born SGA

- ICD-9: 764.00
- CD-10: PO5.1 codes, broken out by weight
  - PO5.10, Unspecified weight
  - PO5.11, Less than 500 grams
  - PO5.12, 500–749 grams
  - PO5.13, 750–999 grams
  - PO5.14, 1000–1249 grams
  - PO5.15, 1250–1499 grams
  - PO5.16, 1500–1749 grams
  - PO5.17, 1750–1999 grams
  - PO5.18, 2000–2499 grams
Growth Hormone Administration Devices

Norditropin NordiFlex®

The Norditropin NordiFlex® is a disposable, premixed, prefilled pen for the administration of Norditropin (somatropin [rDNA origin] injection). Norditropin NordiFlex® uses NovoFine® needles which have an ultra-sharp, low-angle point designed to increase injection comfort. These administration devices are prefilled and premixed and are available in 5 mg/1.5 mL, 10 mg/1.5 mL, 15 mg/1.5 mL, and 30 mg/3 mL sizes. After initial use, the pens can be stored at up to 77°F for use within 3 weeks. The Norditropin NordiFlex® is manufactured by Novo Nordisk®.

Complete instructions for the use of the Norditropin NordiFlex® are available at: http://www.norditropin-us.com/parents/nordiflex.asp

Norditropin FlexPro®

Norditropin FlexPro® is a prefilled pen for the administration of Norditropin (somatropin [rDNA origin] injection). The device requires no reconstitution or loading of cartridges. It is available in 3 doses (5 mg/1.5 mL, 10 mg/1.5 mL, and 15 mg/1.5 mL). After first use, FlexPro® 5 mg/1.5 mL and 10 mg/1.5 mL pens can be stored at room temperature. The Norditropin FlexPro® is manufactured by Novo Nordisk®.

Complete instructions for the use of the Norditropin FlexPro® are available at: http://www.norditropin-us.com/flexpro/index.html

FlexPro® pens come in 3 strengths:

- 5 mg/1.5 mL pen (0.025 mg increments)
- 10 mg/1.5 mL pen (0.05 mg increments)
- 15 mg/1.5 mL pen (0.1 mg increments)
Genotropin MiniQuick®

The Genotropin MiniQuick® is a disposable device manufactured by Pfizer Inc., used to mix and administer a single dose of Genotropin Lyophilized Powder (somatropin [rDNA origin] for injection). Each Genotropin MiniQuick® comes preloaded with a two-chamber cartridge of Genotropin. The device is available in ten different dose sizes.

Complete instructions for the use of the Genotropin MiniQuick® are available at: http://www.genotropin.com/content/resources_mini_quick_instructions.aspx

Genotropin Pen®

The Genotropin Pen® is a reusable administration device used to mix and inject doses of Genotropin Lyophilized Powder (somatropin [rDNA origin] for injection). This device is manufactured by Pfizer Inc.

Complete instructions for the use of the Genotropin Pen® are available at: http://www.genotropin.com/content/Resources_pen_instructions.aspx
HumatroPen®

The HumatroPen® is used to mix and inject doses of Humatrope (somatropin [RNA origin] for injection). This device is manufactured by Eli Lilly and Company and is available in 3 sizes: 6 mg, 12 mg, and 24 mg.

Complete instructions for the use of the HumatroPen® are available at:
http://www.humatrope.com/Pages/index.aspx

Tev-Tropin Tjet®

The Tev-Tropin Tjet® is a needle-free device used for the administration of Tev-Tropin (somatropin [rDNA origin] for injection). It is manufactured by Gate Pharmaceuticals, a division of Teva Pharmaceuticals USA.

Complete instructions for the use of Tev-Tropin Tjet® are available at:
**Nutropin AQ NuSpin™**

The Nutropin AQ NuSpin™ is a multi-dose, dial-a-dose injection device prefilled with Nutropin AQ [somatropin (rDNA origin) injection] in 5, 10, and 20 mg/2 mL cartridges for subcutaneous use. It is recommended that Nutropin AQ be administered using sterile, disposable needles. It is manufactured by Genentech Inc.

Complete instructions for the use of Nutropin AQ NuSpin™ are available at: http://www.nutropin.com/about/devices-formulas/nuspin.jsp

**Saizen easypod®**

The Saizen easypod® is an automated drug delivery device for Saizen [somatropin (rDNA origin) for injection]. easypod® automatically inserts a needle and delivers a preset dose of Saizen. It is the first of its kind for growth hormone delivery and is intended for use with Saizen 8.8 mg click.easy® cartridges. The Saizen easypod® is manufactured by EMD Serono, Inc.

Complete instructions for the use of the Saizen easypod® are available at: http://www.saizenus.com/abouteasypod.aspx
Saizen cool.click™2

The Saizen cool.click™2 is one of the latest needle-free drug delivery devices for growth hormone. A spring mechanism is used to disperse Saizen [somatropin (rDNA origin) for injection] through a tiny hole in the skin. cool.click™2 incorporates an improved nozzle and a digital display for reading the dose compared to the original cool.click™. cool.click™2 is designed for use with Saizen in 5-mg and 8.8-mg vials. The Saizen cool.click™2 is manufactured by EMD Serono, Inc.

Complete instructions for the use of the Saizen cool.click™2 are available at:
http://www.saizenus.com/aboutEasyPod/aboutCoolClick2.aspx
Additional Resources

Growth Charts

The Centers for Disease Control (CDC) growth charts consist of a series of percentile curves that illustrate the distribution of selected body measurements in U.S. children. Pediatric growth charts have been used by pediatricians, nurses, and parents to track the growth of infants, children, and adolescents in the United States since 1977. The 1977 growth charts were revised and updated in 2000 to make them a more valuable clinical tool for health professionals. Most of the data used to construct these charts come from the National Health and Nutrition Examination Survey (NHANES), which has periodically collected height and weight and other health information on the American population since the early 1960s.

Growth charts are not intended to be used as a sole diagnostic instrument. Instead, growth charts are tools that contribute to forming an overall clinical impression for the child being measured. The revised growth charts provide an improved tool for evaluating the growth of children in clinical and research settings.

Additional information on CDC growth charts is available at:
http://www.cdc.gov/growthcharts/cdc_charts.htm
Advocacy Groups

The Magic Foundation®
The Magic Foundation is a national non-profit organization created to provide support services for the families of children afflicted with a wide variety of chronic and/or critical disorders, syndromes, and diseases that affect a child’s growth. Since its inception, the Foundation has grown to include support services for adults who were also impacted by these disorders.

Additional information on the Magic Foundation and its services is available at:
http://www.magicfoundation.org/www/docs/905

The Human Growth Foundation
The Human Growth Foundation is a voluntary, non-profit organization whose mission is to help children and adults with disorders of growth and growth hormone through research, education, support, and advocacy. The Foundation is dedicated to helping medical science better understand the process of growth. It is composed of concerned parents and friends of children and adults with growth problems; physicians; and other interested health professionals.

Additional information on the Human Growth Foundation and its services is available at:
http://www.hgfound.org/

The Pituitary Network Association (PNA)
The PNA is an international non-profit organization for patients with pituitary tumors and disorders, their families, loved ones, and the physicians and health care providers who treat them.

Additional information on the PNA and its services is available at:
http://www.pituitary.org/about/about.aspx

Prader-Willi Syndrome Association
The Prader-Willi Syndrome Association is an organization of families and professionals working together to promote and fund research, provide education, and offer support to enhance the quality of life of those affected by Prader-Willi syndrome.

Additional information on the Prader-Willi Syndrome Association and its services is available at:
http://www.pwsausa.org/
Professional Organizations

Pediatric Endocrine Society (PES)
The PES has over 1200 members representing the multiple disciplines of Pediatric Endocrinology. The members are dedicated to the research and treatment of children with endocrine disorders, including reproductive, bone, thyroid, growth, pituitary and adrenal, as well as children with diabetes and obesity. The Society works to promote the continuing education of its membership.

Additional information is available at: http://www.lwpes.org/

American Academy of Pediatrics
The American Academy of Pediatrics is an organization of 60,000 pediatricians committed to the attainment of optimal physical, mental, and social health and well-being for all infants, children, adolescents, and young adults.

Additional information is available at: http://www.aap.org/

Pediatric Endocrine Nursing Society
The Pediatric Endocrinology Nursing Society (PENS) is a voluntary non-profit specialty nursing organization committed to the advancement of the art and science of pediatric endocrine nursing.

Additional information is available at: http://www.pens.org/