

# Indications for Recombinant Human Growth Hormone and Evaluation of Available Recombinant Human Growth Hormone Devices: Implications for Managed Care Organizations

Jeffrey D. Dunn, PharmD, MBA; and Nancy A. Nickman, PhD

## Abstract

There are now many recombinant human growth hormone (rhGH) products and delivery devices available for rhGH therapy. Not all products are approved to treat both children and adults, and they vary with respect to indications approved by the US Food and Drug Administration. Dosing of rhGH is based on weight, and a higher dose (per kg) is recommended in children than adults. This approximates the normal difference in growth hormone (GH) secretion between these 2 patient populations. Patient adherence to treatment is influenced by a number of factors, and patient inclusion in treatment decisions, such as the choice of delivery device, appears to be important. Unmet expectations are a key issue for many patients and families who decide to discontinue treatment. Counseling patients and families about predicted adult height with rhGH therapy should be based on realistic expectations. Managed care organizations face several challenges in providing rhGH therapy, including deciding who is most likely to benefit from treatment and when to discontinue treatment if the benefits appear to level off.

(*Am J Manag Care.* 2011;17:eS16-eS22)

For author information and disclosures, see end of text.

## Recombinant Human Growth Hormone Products, Indications, and Dosing

With the advent of a safe source of growth hormone (GH) in the form of recombinant human GH (rhGH), the number of US Food and Drug Administration (FDA)-approved indications for rhGH therapy has increased for children and adults. Currently, there are 11 rhGH products available, 9 of which are approved to treat growth hormone deficiency (GHD). The FDA-approved indications are not the same for all products. **Table 1** includes the most recent FDA-approved indications for each product.<sup>1-11</sup> The *International Classification of Diseases, 9th Revision, Clinical Modification* diagnostic codes for GHD and the etiologies of short stature are shown in **Table 2**.<sup>12</sup>

In general, dosing for rhGH therapy is based on weight; however, children receive a higher dose (per kg) than adults. Dosing is theoretically based on the level of GH secreted during development, with peak secretion during puberty and a subsequent reduction in adulthood (**Figure**).<sup>13,14</sup> Although there has been some difficulty obtaining a consensus on optimal dosing, many experts have proposed that rhGH therapy should be titrated, starting with low doses, and then the dose should be adjusted to attain serum insulin growth factor 1 levels that are normalized for the patient's age and sex. Titrating the dose has the added benefit of improved tolerability.<sup>15</sup>

When GH was first used as a treatment for GHD, there were limited supplies of GH available; therefore, only the most severe cases of GHD were treated. Due to the combination of rhGH availability and an increase in the number of conditions that were approved for rhGH therapy use, the demographics of those treated have changed dramatically. In 1990, an analysis showed that among children treated with GH therapy, 81% met the classic criteria for GHD (59% were classified with idiopathic GHD, 18% with organic GHD, and 4% with septo-optic dysplasia).<sup>16</sup> The remaining 19% had short stature of varied causes.<sup>16</sup> Before FDA approval of rhGH for the treatment of idiopathic short stature (ISS) and short for gestational age (SGA) (with failure to experience catch-up growth), many of these children were being treated off-label with rhGH. However, with FDA approvals, the number of children eligible for treatment has increased tremen-

**Table 1.** Recombinant Human Growth Hormone Products and FDA Indications<sup>1-11</sup>

Drug	FDA-Approved Indications				
	GHD (pediatric/adult)	Turner syndrome	CRI	ISS	Other
Genotropin <sup>1</sup>	X	X		X	PWS, SGA
Humatrope <sup>2</sup>	X	X		X	SGA, SHOX gene
Norditropin <sup>3</sup>	X	X			Noonan syndrome, SGA
Nutropin <sup>4</sup>	X	X	X	X	
Nutropin AQ <sup>5</sup>	X	X	X	X	
Omnitrope <sup>6</sup>	X			X	PWS, SGA
Saizen <sup>7</sup>	X				
Serostim <sup>8</sup>					HIV with wasting or cachexia
Tev-Tropin <sup>9</sup>	X (pediatric only)				
Valtropin <sup>10</sup>	X	X			
Zorbtive <sup>11</sup>					SBS

CRI indicates chronic renal insufficiency; FDA, US Food and Drug Administration; GHD, growth hormone deficiency; HIV, human immunodeficiency virus; ISS, idiopathic short stature; PWS, Prader-Willi syndrome; SBS, short bowel syndrome; SGA, small for gestational age (with no catch-up growth by age 2 to 4 years); SHOX, short stature homeobox.

dously given the much larger population of children who are diagnosed with conditions indicated for rhGH therapy. Current demographics suggest an increase in the proportion of children being treated for ISS and SGA compared with GHD. Guidelines for deciding which children will benefit most from rhGH therapy are important for managed care organizations (MCOs) so they allocate use of this treatment efficiently.

A wide variety of devices are available for delivery of rhGH, with most companies offering more than one

**Table 2.** ICD-9-CM Diagnostic Codes for GHD and Underlying Causes<sup>12</sup>

ICD-9-CM	Diagnosis
253.2	Panhypopituitarism
253.3	Pituitary dwarfism; isolated deficiency of human growth hormone
585	Chronic renal insufficiency
758.6	Turner's syndrome
759.81	Prader-Willi syndrome
759.89	Noonan syndrome
764.00	Small for gestational age, with failure to catch up <sup>a</sup>
783.43	Idiopathic short stature

GHD indicates growth hormone deficiency; ICD-9-CM, *International Classification of Diseases, 9th Revision, Clinical Modification*.  
<sup>a</sup>The new *International Classification of Diseases, 10th Revision, Clinical Modification* codes have delineations with respect to weight of newborn.

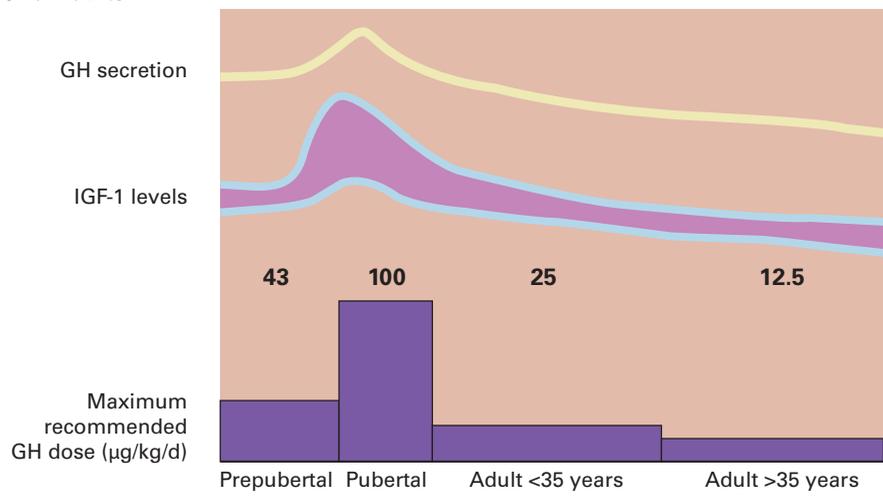
type of device.<sup>17-22</sup> These include the standard vial and syringe with needles, pens, prefilled pens, and needle-free devices (Table 3).<sup>1,7,9,10</sup> There are variations in the storage and handling requirements for devices, with some not requiring refrigeration until use, such as the Valtropin vial and prefilled syringe and the Saizen vial, pen, and cool.click.<sup>7,10</sup> Most need to be refrigerated after first use with the exception of the Norditropin 5-mg cartridge, NordiFlex 5 and 10 mg, and FlexPro 5 and 10 mg, which can be stored at room temperature (below 77°C) for 3 weeks.<sup>3</sup>

The convenience of various delivery devices with respect to storage and handling may be dependent on the lifestyle of patients and how use of the device fits into their normal routines.

The type of device selected may also affect how much of the drug is used. An economic analysis of delivery systems found that waste for vial and syringe delivery of rhGH was 23%.<sup>23</sup> Among pens, waste ranged from 19.5% in pediatric patients using the Humatrope 24-mg pen (14.3% in adult patients using this pen) to 1% in adult patients using Norditropin NordiFlex 5 mg (1.1% in pediatric patients using this pen).<sup>23</sup> These results suggested that although pens have a higher wholesale acquisition cost, using a pen delivery device may be more cost-effective than vial and syringe delivery.<sup>23,24</sup> Using a pen with a lower percentage of waste could potentially reduce the cost of treatment by approximately \$2000 per year for both pediatric and adult patients.<sup>23</sup>

Another factor that is important in evaluating a delivery system is the amount of time it takes to teach patients and caregivers how to use the device and the overall time required to prepare and administer the drug.<sup>25-27</sup> In 2009, results were published from an open-label study of 70 pediatric patients (mean age, 14 years) that assessed the ease of use and comfort of delivery with the disposable Norditropin FlexPro pen.<sup>25</sup> This delivery system was determined to be easy to use, and overall, 64% of patients reported a preference for the disposable Norditropin FlexPro pen over the device they

■ **Figure.** Growth Hormone and Insulin Growth Factor 1 Secretion in Children and Adults<sup>14</sup>



GH indicates growth hormone; IGF-1, insulin growth factor 1.  
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were currently using. Patients' current devices varied, but included Genotropin, Humatrope, Norditropin, Nutropin, and Saizen.<sup>25</sup> At one end of the spectrum, 100% of patients currently using the Genotropin MiniQuick reported a preference for the Norditropin FlexPro pen. At the other end of the spectrum, only 33% of those using a Saizen device, such as the easypod, reported a preference for the Norditropin FlexPro pen, while the remaining 67% were either unsure of their preference or preferred their current Saizen device.<sup>25</sup>

In 2010, results were published from another study that compared ease of use and preference by patients and their caregivers for a disposable Genotropin pen compared with the reusable Genotropin pen they were currently using. Of patients and their caregivers, 59.8% reported that the disposable pen was easier to use, while the remaining 40.2% reported either no difference between the 2 devices or preference for the reusable pen.<sup>28</sup>

In 2010, results were published from a cost analysis study that utilized time-and-motion simulations to evaluate the time it takes to learn how to use a device, and the time and steps required to prepare, administer, and store the device for daily rhGH injections. The researchers then applied a cost minimization analysis to assess costs for caregivers (categorized as wages), nondrug medical supplies, and drug products.<sup>26</sup> They found that time demand had the greatest influence on the overall cost to the user. Of the 4 categories observed, time savings was found to be directly related to the time needed to learn how to use and to prepare the devices ( $P < .05$ ). Times needed to administer the drug and store the device were not significantly different among products. For the devices analyzed in the study, the average

learning times (in minutes) were 15.8 for Norditropin NordiFlex, 16.2 for Norditropin NordiPen, 24.0 for HumatroPen, and 26.0 for Genotropin Pen. Alternately, the preparation times (in minutes) were 1.35 for Norditropin NordiFlex, 2.48 for Norditropin NordiPen, 4.11 for Genotropin Pen, and 8.64 for HumatroPen.<sup>26</sup>

### Adherence and Discontinuation of rhGH Treatment

Skipping medication doses and taking medication "holidays" can adversely affect the efficacy of rhGH therapy.<sup>29</sup> Factors associ-

ated with increased patient adherence to rhGH administration include the reliability of the injection device, ease of use, lack of pain, ease of storage, and fewer steps required for preparation of rhGH for injection.<sup>30</sup> In a study of factors that affected poor adherence to rhGH therapy in children, Kapoor and colleagues found that the most significant variables were longer duration of rhGH therapy ( $P < .005$ ), lack of choice of delivery device ( $P < .005$ ), and short prescription durations ( $P < .005$ ).<sup>31</sup> Predicted lower height velocity was also a significant factor in treatment adherence ( $P < .05$ ).<sup>31</sup>

Discontinuation of rhGH therapy by the patient and caregiver is largely the result of unmet clinical expectations. The expectations of height normalization may not be occurring, which may discourage the patient and parents who had higher expectations for increased height than were realistic, even with optimal growth velocity. This is particularly problematic for children with ISS and SGA, who have a variable response to rhGH therapy. For children who must endure daily injections and parents who must prepare and give injections, the gain in height may not seem worth the effort. These are important issues when counseling patients and parents prior to initiating rhGH therapy. Careful consideration should be given to the expectations of the patient and parents, and if these expectations seem unrealistic, they should be counseled as to what to expect regarding growth velocity and final adult height for the patient.

Clinical decisions about continuation or discontinuation of rhGH therapy were examined in a national census study of pediatric endocrinologists ( $N = 727$ ).<sup>32</sup> The survey included a structured questionnaire; pediatric endocrinologists were asked a series of questions about key factors that influenced

■ **Table 3.** Available Product Delivery Devices<sup>1-7,9,10</sup>

Growth Hormone	Device	Storage Requirements
Genotropin <sup>1</sup>	- Pen 5 and Pen 12 and Mixer for use with cartridges - MiniQuik premixed	Cartridges should be stored at 36°-46° F. Cartridges expire 28 days after reconstitution. MiniQuik may be stored below 77° F for up to 3 months. After reconstitution, MiniQuik should be stored at 36°-46° F for up to 24 hours.
Humatrope <sup>2</sup>	- Pen 6, Pen 12, and Pen 24 for use with cartridges - Vial	Cartridges and vials should be stored at 36°-46° F before and after reconstitution. Cartridges expire 28 days after reconstitution. Vials expire 14 days or 24 hours after reconstitution, depending on diluent.
Norditropin <sup>3</sup>	- FlexPro 5, 10, and 15 prefilled pens - NordiFlex 5, 10, 15, and 30 prefilled pens - NordiPen 5 and 15 for use with cartridges	All products should be stored at 36°-46° F before use. FlexPro and NordiFlex 5- and 10-mg pens and NordiPen 5-mg cartridges can be stored below 77° F for use within 3 weeks or at 36°-46° F for use within 4 weeks. FlexPro 15 and NordiFlex 15- and 30-mg pens and NordiPen 15-mg cartridges should be stored at 36°-46° F for use within 4 weeks.
Nutropin <sup>4</sup> and Nutropin AQ <sup>5</sup>	- AQ NuSpin prefilled pen - AQ Pen for use with cartridges - Nutropin or Nutropin AQ vials	Cartridges, reconstituted vials, and NuSpin pen should be stored at 36°-46° F and expire 28 days after reconstitution. Nutropin AQ is light sensitive and cartridges, vials, and NuSpin pen should be stored in the dark. Nutropin vials should be stored at 36°-46° F before and after reconstitution. After reconstitution, vials should be used within 14 days.
Omnitrope <sup>6</sup>	- Pen 5 and Pen 10 for use with cartridges - Vial	Cartridges and vials should be stored 36°-46° F before and after reconstitution. After reconstitution, cartridges should be used within 28 days. After reconstitution, vials should be used within 21 days.
Saizen <sup>7</sup>	- easypod injection device for use with cartridges - cool.click needle-free device - click.easy injection device for use with vial	Cartridges and vials should be stored at 59°-86° F before use. After reconstitution, cartridges and vials should be stored at 36°-46° F for use within 21 days. cool.click device should be stored at 50°-104° F between uses.
Tev-Tropin <sup>9</sup>	- Tjet needle-free device - Tev-Tropin vial	Before reconstitution, store vials at 36°-46° F. After reconstitution, store at 36°-46° F for use within 14 days. Tjet device should be stored at 59°-86° F between uses.
Valtropin <sup>10</sup>	- Prefilled syringe for use with vial	Before reconstitution, store at or below 77° F for up to 3 months. After reconstitution, store at 36°-46° F for up to 21 days.

their decisions to initiate, continue, or discontinue rhGH therapy in children with ISS. Questions were focused on initiation of rhGH therapy and changes to medication during the first year of treatment. The response rate was 90% (n = 656). It is not surprising that most physicians consulted evidence-based guidelines regarding initiation of therapy. For children with the lowest predicted adult height (3 standard deviations less than average), 93% reported that they would initiate rhGH therapy. However, the decision to continue or discontinue treatment reflected the current lack of, or unclear recommendations in, consensus guidelines on best practices for discontinuing therapy.<sup>32</sup>

Most physicians did not discontinue treatment when there was a low response to treatment; 60.3% increased the rhGH dose and 13.8% kept the rhGH dose the same. Twenty-six

percent recommended discontinuing rhGH therapy. This survey also showed that nonphysiologic factors affected decisions to continue or discontinue treatment. For example, more than 28% of physicians believed that rhGH therapy has a positive effect on a child with ISS, despite evidence that the child's adult height would not be significantly affected by treatment. The survey also showed that 88% fully agreed or somewhat agreed that a patient's response to treatment during a trial phase should be the primary determinant for continuation of therapy. However, 31% of physicians stated that they never or seldom discontinue rhGH therapy when it is ineffective. Managed care professionals need to identify opportunities to intervene on continuation decisions; this can be facilitated through use of evidence-based criteria on growth outcomes.

**Table 4.** Support Provided From Pharmaceutical Manufacturers<sup>17-22,33</sup>

Growth Hormone	Web Site Training	Live Nurse Training	Patient Support	Insurance Coverage/Prior Authorization Assistance	Financial Assistance
Genotropin <sup>17</sup>	Video and text	Yes, in person	Patient care consultant, nurse on call	Bridge Program	Copay assistance
Humatrope <sup>18</sup>	Video and text	Yes, via phone or in person	Case manager, Lilly Answer Center	Patient Assistance Program	Lilly Cares
Norditropin <sup>19</sup>	Text	Yes, via phone, Internet, or in person	Case manager, pharmacist on call	NordiCare	JumpStart and Patient Access Program; Nordi-Sure copay assistance
Nutropin and Nutropin AQ <sup>20</sup>	Video and text	Yes, in person	Case manager, nurse hotline	Nutropin GPS	Nutropin GPS, Genentech Access to Care Foundation
Omnitrope <sup>33</sup>	Video and text	Yes, in person	OmniSource support specialist, nurse on call	OmniSource	Sandoz Patient Assistance Program
Saizen <sup>21</sup>	Video and text	Yes, in person	Connections for Growth case manager, nurse on call	Connections for Growth	Saizen Savings Program
Tev-Tropin <sup>22</sup>	Video and text	Yes, via phone or in person	Growth Solutions, nurse on call	Growth Solutions	Tev-Tropin Patient Assistance Program

**Patient Support in rhGH Therapy**

A critical factor for successful treatment outcomes and adherence to rhGH therapy is the availability of a support system for patients and caregivers. Pharmaceutical companies that manufacture rhGH all offer various levels of support for patients. All companies offer support on their Web sites and most offer in-person training from a nurse when recommended by a physician (Table 4).<sup>17-22,33</sup> In addition, many companies have case managers available to assist patients, and almost all companies have programs to provide financial assistance to those who qualify. Several other organizations offer support and education to patients, including how to manage their condition and therapy. The Magic Foundation, the Human Growth Foundation, the Pituitary Network Association, and the Prader-Willi Syndrome Association are some of the advocacy groups for patients and families of those with GH deficiency and other conditions which affect growth. In addition, the Pediatric Endocrinology Nursing Society provides important information, including an rhGH product guide that summarizes key information, such as dosing and correct storage and handling of rhGH in current delivery systems.<sup>34</sup>

**Managed Care: Economic and Purchasing Considerations**

As providers of rhGH therapy, MCOs have the challenge of providing needed medications, while also considering the most economical solutions for delivering this

service. Streamlining the delivery process was improved with the establishment of specialty pharmacy providers.<sup>35</sup> This rapidly growing healthcare approach can provide MCOs with technology-driven databases that improve claims tracking and can stock biotechnology products that retail pharmacies may find difficult to provide. Many MCOs also have delivery programs that assist patients and caregivers by expediting prescription refills. These companies are also improving the costs of medication management, with some estimates at 18% less than the average wholesale cost.

As reimbursements decrease, treatment costs increase, and the patient population for rhGH therapy expands, finding economic solutions with drug manufacturers and pharmaceutical providers is a key consideration for MCOs. One strategy for lowering costs is to have contracts with companies that manufacture these drugs. The downside of this practice is that it reduces the choice of rhGH products and delivery devices. Patient involvement in treatment options has been shown to be an important factor in adherence to rhGH therapy, and this should be considered when making formulary decisions.<sup>31</sup>

As discussed in the article by Nickman and Dunn in this supplement,<sup>36</sup> the overall pharmacoeconomic considerations for treating patients with rhGH have been explored by Joshi and colleagues.<sup>37</sup> However, there are few published studies on this topic. It is clear that for more controversial indications, such as ISS and SGA (without catch-up growth in 1 to 2

years), pharmacoeconomic value will derive from patients who have a good response to treatment and are predicted to experience significant increases in height.

## Conclusions

Numerous conditions are now indicated for rhGH therapy in children and adults. With the increase in FDA-approved indications and new products and delivery devices, MCOs must evaluate the cost benefits of rhGH therapy. Patient adherence to treatment is a key issue for optimizing outcomes in children and adults. Therapy in children is subject to poor adherence, and unrealistic expectations from patients and their families can result in discontinuation of treatment. Pediatric endocrinologists and support groups should advise patients and families that rhGH treatment response varies, and not all children will achieve normalized height profiles as adults. MCOs can maintain an appropriate cost-benefit ratio for patients by using specialty pharmacies to streamline refills and delivery of rhGH, establishing contracts with manufacturers, and applying evidence-based coverage criteria.

**Author affiliations:** SelectHealth, Inc, Salt Lake City, Utah (JDD); Department of Pharmacotherapy and Pharmacotherapy Outcomes Research, University of Utah, Salt Lake City, UT (NAN).

**Funding source:** This activity is supported by an educational grant from Novo Nordisk, Inc.

**Author disclosures:** Dr Dunn reports consultancy/advisory board membership with Novo Nordisk, Inc. Dr Nickman reports grants/research support from Novartis Pharmaceuticals.

**Authorship information:** Concept and design (JDD, NAN); acquisition of data (NAN); analysis and interpretation of data (JDD, NAN); drafting of the manuscript (JDD, NAN); critical revision of the manuscript for important intellectual content (JDD, NAN); statistical analysis (NAN); and supervision (NAN).

**Address correspondence to:** Jeffrey D. Dunn, PharmD, MBA, SelectHealth, Inc, 5381 Green St, Murray, UT 84123. E-mail: jeffrey.dunn@selecthealth.org.

## REFERENCES

1. Genotropin [package insert]. New York, NY: Pfizer, Inc; March 2011.
2. Humatrope [package insert]. Indianapolis, IN: Eli Lilly and Company; February 2011.
3. Norditropin [package insert]. Princeton, NJ: Novo Nordisk Health Care AG; June 2011.
4. Nutropin [package insert]. South San Francisco, CA: Genentech Inc; June 2006.
5. Nutropin AQ [package insert]. South San Francisco, CA: Genentech Inc; January 2008.
6. Omnitrope [package insert]. Princeton, NJ: Sandoz Inc; July 2011.
7. Saizen [package insert]. Rockland, MA: EMD Serono, Inc; September 2007.
8. Serostim [package insert]. Rockland, MA: EMD Serono, Inc; September 2007.
9. Tev-Tropin [package insert]. Sellersville, PA: Gate Pharmaceuticals; October 2009.
10. Valtropin [package insert]. Waltham, MA: LG Life Sciences, Ltd; April 2007.
11. Zorbtive [package insert]. Rockland, MA: Serono, Inc; November 2003.
12. *ICD-9-CM International Classification of Diseases, 9th revision; Clinical Modification, 6th ed.* Los Angeles, CA: Practice Management Information Corporation; 2007.
13. Brabant G, von zur Mühlen A, Wüster C, et al. Serum insulin-like growth factor I reference values for an automated chemiluminescence immunoassay system: results from a multicenter study. *Horm Res.* 2003;60:53-60.
14. Tzeel A, Fine MJ. Plan and pharmacy perspectives: growth hormone therapy, formulary, and benefit authorization. *Manag Care.* 2009;18(8)(suppl 6):17-19.
15. Cook DM, Yuen KC, Biller BM, Kemp SF, Vance ML; American Association of Clinical Endocrinologists. American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in growth hormone-deficient adults and transition patients - 2009 update. *Endocr Pract.* 2009;15(suppl 2):1-29.
16. August GP, Lippe BM, Blethen SL, et al. Growth hormone treatment in the United States: demographic and diagnostic features of 2331 children. *J Pediatr.* 1990;116:899-903.
17. Genotropin Web site. <http://www.genotropin.com>. Accessed November 2, 2011.
18. Humatrope Web site. <http://www.humatrope.com>. Accessed November 2, 2011.
19. Norditropin Web site. <http://www.norditropin-us.com/>. Accessed November 2, 2011.
20. Nutropin Web site. <http://www.nutropin.com>. Accessed November 2, 2011.
21. Saizen Web site. <http://www.saizenus.com>. Accessed November 2, 2011.
22. Tev-Tropin Web site. <http://www.tev-tropin.com>. Accessed November 2, 2011.
23. Bazalo GR, Joshi AV, Germak J. Comparison of human growth hormone products' cost in pediatric and adult patients: a budgetary impact model. *Manag Care.* 2007;16:45-51.
24. Medi-Span Database. Indianapolis, IN: Wolters Kluwer Health. <http://www.medi-span.com>. Accessed October 31, 2011.
25. Fuchs GS, Mikkelsen S, Knudsen TK, Kappelgaard AM. Ease of use and acceptability of a new pen device for the administration of growth hormone therapy in pediatric patients: an open-label, uncontrolled usability test. *Clin Ther.* 2009;31:2906-2914.
26. Nickman NA, Haak SW, Kim J. Cost minimization analysis of different growth hormone pen devices based on time-and-motion simulations. *BMC Nurs.* 2010;9:6.
27. Wickramasuriya BP, Casey A, Akhtar S, et al. Factors determining patient choice of device for GH therapy. *Horm Res.* 2006; 65:18-22.
28. Hey-Hadavi J, Pleil A, Deeb LC, et al. Ease of use and preference for a new disposable self-injection pen compared with a reusable pen for administering recombinant human growth hormone: a multicenter, 2-month, single-arm, open-label clinical trial in patient-caregiver dyads. *Clin Ther.* 2010;32:2036-2047.
29. Haverkamp F, Johansson L, Dumas H, et al. Observations of nonadherence to recombinant human growth hormone therapy in clinical practice. *Clin Ther.* 2008;30:307-316.
30. Dumas H, Panayiotopoulos P, Parker D, Pongpairachana V. Understanding and meeting the needs of those using growth hormone injection devices. *BMC Endocrine Disorders.* 2006;6:5.
31. Kapoor RR, Burke SA, Sparrow SE, et al. Monitoring of concordance in growth hormone therapy. *Arch Dis Child.* 2008; 93:147-148.
32. Silvers JB, Marinova D, Mercer MB, Connors A, Cuttler L. A national study of physician recommendations to initiate

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and discontinue growth hormone for short stature. *Pediatrics*. 2010;126:468-476.

33. Omnitrope Web site. <http://www.omnitrope.com>. Accessed November 2, 2011.

34. Pediatric Endocrinology Nursing Society (PENS) Web site. [www.PENS.org](http://www.PENS.org). Accessed November 2, 2011.

35. **Suchanek D**. The rise and role of specialty pharmacy. <http://www.allhealth.org/briefingmaterials/BiotechHealthcareSpecialty>

Pharmacies-416.pdf. Accessed November 2, 2011.

36. **Nickman NA, Dunn JD**. Issues related to recombinant human growth hormone utilization and optimization in a health plan setting. *Am J Manag Care*. 2011;17(18):eS11-eS15.

37. **Joshi AV, Munro V, Russell MW**. Cost-utility of somatropin (rDNA origin) in the treatment of growth hormone deficiency in children. *Curr Med Res Opin*. 2006;22:351-357.