Translating Clinical Guidelines Into Practice: The Effective and Appropriate Use of Human Growth Hormone

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In a recent roundtable discussion, the contemporary medical utilization of recombinant human growth hormone (rhGH) and its managed care implications were discussed by a panel of clinicians (Peter A. Lee, MD, PhD, professor of pediatrics, Penn State College of Medicine, Hershey, PA; and Robert Rapaport, MD, Emma Elizabeth Sullivan Professor of Pediatric Endocrinology and Diabetes, and director, Division of Pediatric Endocrinology and Diabetes, Icahn School of Medicine at Mount Sinai/Kravis Children's Hospital, New York, NY) and managed care professionals (Gary M. Owens, MD, president, Gary Owens Associates, Ocean View, DE; and Jeffrey D. Dunn, PharmD, MBA, senior vice president, VRx, Salt Lake City, UT). The panel was moderated by Robert Navarro, PharmD, clinical professor, Department of Pharmaceutical Outcomes and Policy, College of Pharmacy, University of Florida, Gainesville, FL.

In a climate of healthcare reform, the panel's discussion was intended to educate and inform managed care practitioners about the importance of balancing treatment accessibility with the responsible administration of rhGH among appropriate patients to optimize clinical outcomes.

Why Is Recombinant Human Growth Hormone Needed?

Treatment with rhGH is used in most cases to increase low levels of growth hormone (GH), an essential pituitary hormone and endogenous growth factor. GH acts directly on growth plates and the liver to stimulate the production of insulin-like growth factor I (IGF-I), which, along with GH, promotes normal body growth.[1-4] The secretion of GH is controlled by many factors, including growth hormone–releasing hormone, somatostatin, and ghrelin.[3] Numerous identifiable and unidentified factors can lead to GH deficiency or an attenuation of GH effectiveness, with the net result being a shorter-than-expected stature and possible metabolic imbalances.

Random measurement of GH blood levels is not a reliable means of measuring GH levels because GH is secreted in a pulsatile fashion. A better method of measuring the function of the GH system is to measure serum insulin-like growth factor-1 (IGF-I) and insulin-like growth factor binding protein-3 (IGF-BP3) levels, because their daily levels are less variable.[3] GH provocative testing

Abstract

There are 9 recombinant human growth hormone (rhGH) products currently available for 10 US Food and Drug Administration–approved indications; each rhGH product is approved for 1 or more indications. Adult and pediatric patients with the various conditions for which rhGH is indicated, from idiopathic short stature (ISS) and growth hormone (GH) deficiency to short bowel syndrome and HIV/AIDS wasting, may benefit from rhGH treatment. In clinical practice, pediatric patients with GH deficiency or ISS make up the majority of the population receiving treatment with rhGH.

Most rhGH products are provided through specialty pharmacies that often have to balance the needs of the patient, their own utilization objectives, and the availability of the rhGH on formulary from a particular payer. Often, a payer will prefer only 2 or 3 rhGH products to cover all 10 indications. As such, managed care professionals need to be more informed about the options available and should be familiar with the different indications to help educate patients about treatment. Additionally, healthcare providers should endeavor to identify and manage the care of appropriate patients who would potentially benefit from rhGH therapy, and should be aware of formulary options. Because many of the patients are children and young adults, adherence to treatment is a concern; patient education on the importance of treatment adherence should be ongoing. Various mechanisms are in place (eg, prior authorization requirements and case manager follow-up) to help ensure that rhGH products are used, and used appropriately.

This publication includes highlights from a roundtable discussion by key opinion leaders (clinicians and managed care professionals) on how managed care policies and clinical guidelines on appropriate use of rhGH translate into real-world practice. Also discussed are the efficacy and safety of rhGH therapy for its pediatric indications, and the role of specialty pharmacies in managing patient access to therapy.

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For author information and disclosures, see end of text.

Sidebar 1: Healthcare reform

As the healthcare and managed care landscapes continue to evolve amid reforms, there are varying opinions regarding the impact on growth hormone therapies and utilization. While the healthcare system itself may undergo some vast changes, it may be difficult to predict the future for coverage of growth hormone treatments. Dunn noted that current criteria for coverage and preferred products are already available, and as a consequence, a dramatic shift in disease management is unlikely to occur. Further, relative to managed care structures, accountable care organizations (ACOs) will assume a heavy burden of risks, and as such, according to Owens, strategies for growth hormone therapies will be similar to current managed care approaches: to seek the less expensive but equally efficacious and safe drug products. The concept of tiered benefit structures for insurance plans may also result in substantial out-of-pocket costs for patients who are members of a lower-level exchange-based plan.

can also be performed by administering agents that stimulate GH secretion (eg, L-dopa, clonidine, arginine, insulin, or glucagon) and measuring serial GH levels (eg, every 15 minutes for 1 hour). Because of the difficulty in differentiating normal and abnormal responses, these tests are not precise. However, their results, along with knowledge of the patient's height, growth velocity, physical examination, screening test results, and IGF-I and IGF-BP3 levels, can provide enough evidence to diagnose or rule out GH deficiency.[3] There is no single test that is diagnostic of GH deficiency, and clinicians are strongly encouraged to collect as much clinical information as feasible before making a diagnosis.

The list of conditions that may be appropriate for rhGH treatment is shown in the **Table**.[5-16] In clinical practice, pediatric patients with GH deficiency or idiopathic short stature (ISS) make up the majority of the population receiving treatment with rhGH; thus the focus of the roundtable discussion was the use of rhGH in these pediatric patients.[17]

In pediatric patients with GH deficiency or ISS, rhGH treatment is used to attain an adult height within the genetically expected range based upon parental heights. Appropriate dosing with rhGH will not allow patients to be taller than their genetic potential; however, rhGH can allow patients to reach their genetically determined adult height.

Because rhGH is an expensive treatment option, and because it is being administered for conditions that may not be life threatening, it can be difficult to balance the needs of the patient with the economic realities of the healthcare system. Payers may focus on the short-term costs of rhGH therapy, as the long-term benefits may be difficult to directly quantify. While the primary benefits are taller stature for age and adult height within the normal range within genetic expectations, there may be other long-term benefits associated with rhGH therapy. For example, a recent study by Chaplin et al (2011) indicated that long-term treatment with rhGH in children with GH deficiency or ISS improved self-esteem as well as stability and mood outcome measures.[18]

Table. FDA-Approved Indications for Recombinant Human Growth Hormone and Currently Available Products[5-16]

	FDA-Approved Indications[5-16]									
Product	**GH deficiency**	**Growth failure due to CRI**	**HIV/AIDS wasting/ cachexia**	**ISS**	**NS**	**PWS**	**SBS**	**SGA**	**SHOX-D**	**TS**
Genotropin	X			X		X		X		X
Humatrope	X			X				X	X	X
Norditropin	X				X			X		X
Nutropin AQ	X	X		X						X
Omnitrope	X			X		X		X		X
Saizen	X									
Serostim			X							
Tev-Tropin	X (ped)									
Zorbtive							X			

CRI indicates chronic renal insufficiency; FDA, US Food and Drug Administration; GH, growth hormone; ISS, idiopathic short stature; NS, Noonan syndrome; ped, pediatric; PWS, Prader-Willi syndrome; SBS, short bowel syndrome; SGA, small-for-gestational-age infants who fail to catch up to normal growth percentiles; SHOX-D, short stature homeobox-containing gene deficiency; TS, Turner syndrome.

Sidebar 2: What are patient expectations of growth hormone treatment?

Patient expectations for treatment are impacted by a number of factors, including socioeconomic status and the relative sophistication and attitudes of patients' parents. Consequently, there is a great deal of variation, stated Lee. Whereas some families are willing to pursue GH therapy regardless of coverage or out-of-pocket costs, other families are not, perhaps due to medical expenses or concerns regarding the administration of GH. However, both Rapaport and Lee emphasized that judicious treatment with GH is given with the goal of promoting growth so children will attain their genetic height potential.

Sidebar 3: Selecting a treatment product

Currently, there are a number of GH products on the market in the United States. Although some products share approved indications for use, differences in dosing schedules between products may mean that certain products are better suited for use among different patient populations. Choosing the appropriate GH product is contingent upon many factors, including coverage status, patient preference, administration device, and inert ingredients (eg, excipients). Formulation excipients vary by brand of GH product and should be taken into consideration when selecting a product for a patient with hypersensitivity to particular excipients.[8-16]

Ultimately, the panelists agreed that "Growth hormone products are clinically identical," without differences in efficacy and safety. The variations are in how the GH product is stored, dosed, and administered by device. While clinicians may advise the families of patients to select a product that best suits the patient's lifestyle and coverage, pricing is a large component of the decision-making process for managed care, admitted Dunn. There exists, however, a partnership between providers and families to deliver the best care, and in an effort to do so, preferences of the patient population and the input of key opinion leaders are frequently taken into consideration.

The Advent of the Specialty Pharmacy

The Orphan Drug Act of 1983 was designed to encourage the development of treatments for rare diseases.[19] Several drugs approved under the Orphan Drug Act are different formulations of rhGH. A 2011 survey of health plan pharmacy directors and medical directors revealed that 92% of plans classified treatment for GH disorders with rhGH as a specialty pharmaceutical.[20] In addition, the directors surveyed stated that most rhGH products (83%) required prior authorization (PA). The main reasons for a PA were to verify an indication (60%) or to drive utilization of a preferred product (28%).[20]

All current rhGH products have the same mechanism of action, but have different FDA-approved indications. Commonly, rhGH products are used interchangeably for the different indications. As previously discussed, pediatric patients with GH deficiency or ISS make up the majority of the population receiving treatment with rhGH.[17] Clinical guidelines for the use of GH in children state that there are no observable differences in the outcomes of therapy among the different products, though there may be patient and parent preferences for particular injection devices.[21] Health plans may restrict the number of rhGH products to 2 or 3 "preferred" products. This means that specialty pharmacists and clinicians must be familiar with dosing recommendations for the different indications to help ensure adherence to the correct dosing.

Current Indications for Recombinant Human Growth Hormone

Growth hormone deficiency

GH deficiency occurs when the body does not produce enough GH. The etiology may be congenital or acquired, but in the majority of pediatric cases it is unknown (ie, idiopathic). Congenital GH deficiency can be the result of a number of gene mutations involved in the GH-pituitary-hypothalamic axis. Anatomic abnormalities (anencephaly or prosencephaly, optic nerve hypoplasia/septo-optic dysplasia, or vascular malformations) may also lead to GH deficiency. Acquired GH deficiency may result from neoplasms, cysts, inflammatory or infiltrative processes, head trauma, surgery, radiation, or chemotherapy. Even though the preceding is an expansive list, in many cases, the cause of GH deficiency in most children is unknown. Severe GH deficiency is characterized by short stature, slow growth, and delayed skeletal maturation, with reduced secretion of GH in response to provocative stimulation.[6]

Dosing of rhGH is adjusted based upon response, with the goal of allowing pediatric patients to attain their genetically estimated adult height. With the exception of Serostim and

Sidebar 4: Describe the type of patients you treat with growth hormone therapy

Although patients with other manifestations of growth failure, such as ISS, Turner syndrome, and Noonan syndrome, are certainly seen and treated in clinical practice, pediatric patients with GH deficiency constitute the majority of cases that Rapaport encounters. For these young patients, treatment is generally initiated following appropriate diagnosis, and continues until bone fusion, when patients are retested to determine whether they will require GH therapy as an adult.

Despite the education that is available for GH deficiency, Rapaport contended that treatment could be initiated even earlier, noting that "If one looks at large national databases, the age at which children are started on treatment has really not changed very much, even though we do emphasize that earlier treatment is better, initiating treatment at a younger age is better."

Lee added that he sees a wide variety of patients and patient families, from those demanding the best and most recent treatment to make their child taller, to those who are quite content to let nature do as nature does. However, Lee suspects that there is a trend toward patients who expect and want more treatment.

Zorbtive, all rhGH medications are approved to treat GH deficiency.[8-13,15]

Growth failure due to chronic renal insufficiency

Children with chronic kidney disease may develop severe growth failure. The combination of energy malnutrition, water and electrolyte disturbances, metabolic acidosis, anemia, and hormonal disturbances affecting the somatotropic and gonadotropic hormone axes may all be involved in the etiology of growth failure.[6]

Carefully monitored, timely treatment with rhGH allows these pediatric patients the opportunity to catch up to normal height levels, and a majority of these patients achieve normal adult height.[11,22]

HIV/AIDS-related wasting and/or cachexia

HIV/AIDS-related wasting often has a multifactorial etiology, including abnormalities of the GH–IGF-I axis.[6]

Treatment with GH may be of benefit to some patients by counteracting the wasting that is part of the progression of this condition.[14]

Idiopathic short stature

By definition, an individual is classified as having ISS if their height is 2.25 standard deviations (or more) below the mean height for a given age, sex, and population group in the absence of systemic, endocrine, nutritional, or chromosomal abnormalities.[6]

Treatment with rhGH increases height and growth velocity in children with ISS.[8,9,11,12]

Sidebar 5: Why is idiopathic short stature excluded in some plans?

Managed care organizations recognize that ISS is a valid medical condition; however, it can be difficult to balance the needs of the patient with the economic realities of the healthcare system. Because it may be challenging to directly measure the long-term benefits of rhGH therapy, payers may focus on the short-term costs. As such, some plans and employer groups have excluded ISS from coverage. While, arguably, only a minority of highly managed employers practice this exclusion, it can be frustrating for patients who desire pharmacologic intervention and for the clinicians who want to help.

From a clinician's perspective, this exclusion can also be frustrating. Lee stated, "I have had patients denied for idiopathic short stature who are very dramatically short. You know, I'm talking about a 7-year-old that is not the size of a 5½-year-old, but is the size of a 3-year-old. I sort of wish there could be some different criteria for idiopathic short stature based on statistics somehow, if they are more than [a given number of] standard deviations below normal for age and sex, rather than just a low-normal."

Noonan syndrome

Noonan syndrome is a genetic condition that afflicts 1 in 1000 to 2500 live births.[23] It is characterized by proportionate postnatal short stature (among some but not all), dysmorphic facial features, chest deformities, and congenital heart disease

(most commonly pulmonary valve stenosis and hypertrophic cardiomyopathy). Some children may also develop mild mental retardation, cryptorchidism, and clotting disorders. Mutations of the tyrosine phosphatase nonreceptor type 11 gene have been observed in some patients, but how these mutations result in short stature remains unclear.[6]

Treatment with rhGH can increase the patient's height, but not all patients with Noonan syndrome have short stature and some will reach normal adult height without treatment.[10] As with other indications, better outcomes may occur with earlier initiation and longer duration of GH treatment.[3]

Prader-Willi syndrome

Prader-Willi syndrome is a rare genetic condition. Those affected have an uncontrollable craving for food that leads to obesity and retarded growth that may result in short stature. Other hormonal balances are also present.[6]

Patients with Prader-Willi syndrome show increased growth rates when given rhGH.[8,12]

Short bowel syndrome

Short bowel syndrome is a rare condition in which the patient has lost approximately two-thirds or more of his or her small intestine, usually as a result of trauma, cancer, thrombosis, radiation, or other cause. These patients are generally dependent on parenteral means to receive their nutrition.[6]

Treatment with rhGH is designed to increase transmucosal transport of water, electrolytes, and nutrients and thereby decrease parenteral nutrition requirements.[16] At present, only 1 rhGH product (Zorbtive) is approved for short bowel syndrome. With rhGH therapy, reduced weekly parenteral nutrition requirements have been observed.[16]

Small-for-gestational-age infants

Small for gestational age (SGA) occurs in about 3% of infants at birth. By the age of 2 years, most infants will experience sufficient growth to normalize their height, but it is estimated that approximately 8% of SGA infants will remain short throughout childhood and as adults.[3,6]

Although most of these pediatric patients do not show evidence of decreased GH secretion, rhGH treatment results in catch-up growth among the 8% who have not caught up spontaneously, commonly to within the normal height range for age, and results in adult height within the normal range for sex.[8-10,12]

Short stature homeobox-containing gene deficiency

Short stature homeobox (SHOX)-containing gene deficiency results in short stature. Absence of the SHOX gene may occur with Turner syndrome or as a separate condition. During fetal development, the SHOX gene appears to be involved in the regulation of bone growth, and under normal circumstances, individuals have 2 copies of the SHOX gene.[3,6]

Children with SHOX gene deficiency may have short stature and develop mesomelic disproportion of the limbs and Madelung deformity.[24] Patients with SHOX gene deficiency do not have low GH levels, but treatment with rhGH can increase their height.[9]

Turner syndrome

Turner syndrome is a disorder in females defined by the complete or partial absence of the second X chromosome.[23]

Sidebar 6: How important are treatment guidelines for growth hormone therapy? The clinician's perspective

While treatment guidelines do function well as rough management tools, Rapaport emphasized that individualized and tailored therapies are able to target the idiosyncratic nuances and fine points that generalized treatment guidelines cannot. While guidelines are undoubtedly beneficial and serve useful purposes, to clinical practitioners, guidelines are "simply *guidelines*."

Sidebar 7: Why aren't all the growth hormone products covered?

Managed care views GH therapy as a high-cost category that should be aggressively managed. Managed care strategies are implemented in an effort to address the needs of an entire patient population. Therefore, on occasion, those efforts may not satisfy the needs of some individual cases. GH products, due to their similarities in efficacy and safety, are often viewed as a single commodity rather than as unique products, and as a consequence, the number of products that are available and offered under a plan may be limited. These limited selections may inconvenience some patients, admittedly, but that is the "economic reality" of these expensive therapies.

Although most (≥90%) of Turner syndrome conceptions are aborted spontaneously, they do account for about 1 in 2000 to 2500 live female births. A common feature of Turner syndrome is severe short stature during both childhood and adulthood. The average height of untreated women with Turner syndrome is 4 feet, 8 inches.[3,6]

Treatment with rhGH does increase the height of these patients,[8-12] and most can reach normal height with proper treatment.[10] Norditropin is the only rhGH product with an approved dose of up to 67 mcg/kg/day in patients with Turner syndrome.[10]

Implementing Utilization Management of Recombinant Human Growth Hormone: Balancing Access and Appropriate Use

There are several guidelines issued by professional societies regarding the diagnosis and management of the various conditions that may benefit from rhGH treatment,[21,25-28] with more in development (eg, MCG, formerly the Milliman Care Guidelines).[29] Historically, treatment guidelines published by clinical organizations have heavily emphasized the clinical aspect of optimal disease management. As the sector of specialty pharmacy continues to grow amid a climate of rising healthcare expenditures, managed care authorities have turned to stringent cost-containment strategies that balance rhGH treatment accessibility with responsible administration among the most appropriate patients and treatment candidates to maximize patient outcomes while moderating the use of limited resources. Many payers will limit the number of rhGH products available to 2 or 3 products because of financial arrangements, as all products have the same mechanism of action. In other words, because these drugs are thought to be clinically equivalent, this is an instance in which the indications of a particular medication are not relevant to which drug is preferred by the plan and subsequently prescribed. In a survey of managed care providers, 77% stated that they have preferred products to treat GH disorders.[20] Specialty care pharmacists, along with clinicians, need to balance the

Sidebar 8: How important are treatment guidelines for growth hormone therapy? The managed care perspective

Owens and Dunn explained that clinicians and managed care both consider treatment guidelines for GH therapy, but whereas clinicians use those guidelines as a "rough" tool for directing treatment, managed care uses them to help steer medical policies, which are population-based. Policy decisions are based on numerous components, and while guidelines do not dictate which drug product to prescribe and thus do not contribute to formulary decisions, they remain useful as resources for determining the policies regarding the use and coverage of laboratory tests, diagnostic tools, and GH products. Although these policies are designed to benefit the entire patient population eligible for GH, problems can arise for certain individual cases. Appeal processes and peer-to-peer discussions have been implemented in an effort to resolve these issues.

According to Owens, "Because therapy is expensive, these processes and peer-to-peer discussions are important. We certainly want every patient who has an appropriate need to get appropriate therapy."

Sidebar 9: Can guidelines occasionally be a deterrent?

Some specialty pharmacies that are less experienced with these rare conditions may adhere to the guidelines too closely. Because these conditions are rare, the patient population is smaller, and variance is the norm and not the exception. Rapaport noted that adhering too closely to the guidelines does not allow a clinician the ability to use his or her expertise in prescribing.

Another concern with the guidelines that was expressed by Lee is that they are often in need of updating based on more recent information. Some guidelines are more than 5 years old; the Lawson Wilkins Pediatric Endocrinology Society guidelines are 10 years old.[21]

Sidebar 10: Drug wastage

As some devices and medication dosages may result in the wastage of expensive GH products, clinicians often devise creative methods to minimize that waste and optimize appropriate drug utilization, such as adjusting doses to maximize the use of GH in a cartridge, or using the remainder of one cartridge of GH toward the next dose with the new cartridge.

needs of the patient with the rhGH products available from that patient's provider.

Patient-centric factors must also be considered to further drive optimal medication utilization. For example, patients who travel frequently will likely benefit from a product that does not require refrigeration. Ease of use may also improve patient adherence.

A 2010 study that assessed the potential time involvement, required weekly administration steps, and utilization costs of daily rhGH administration found that pen devices with a greater time demand were associated with increased opportunity costs and net expenditures.[30] Another economic study examined the amount of waste that accumulates when using different products and found that the waste ranged from 14.3% to 19.5% with vial or syringe delivery products compared with 1.0% to 1.1% with pen delivery systems.[31]

Another concern with rhGH treatment is patient adherence. Because most patients taking rhGH are children and young adults, adherence can be an issue for some patients. Studies have observed that poor adherence to rhGH may impede the benefits of treatment.[32] Efforts to regularly educate patients on the importance of compliance with treatment should be encouraged by all parties (see sidebars).

Sidebar 11: Adherence to treatment—clinician's perspective

Overall, adherence to GH therapy is relatively high, but there are certainly critical challenges to treatment adherence, such as a lack of motivation on the part of the patient. As GH therapy is a long-term treatment, the key to maintaining a high rate of adherence is to utilize realistic approaches and seize opportunities to emphasize that regular, daily administration of the GH product is necessary for an efficacious and optimal response until growth is complete.

A concern for physicians is when a patient or family switches plans. This may necessitate a change in treatment because of differences in plan coverage. Rapaport said, "That's always a difficult transition because they need to be reeducated [regarding] a new device. There is no reason why that should happen, according to the families, and I certainly understand that. It interrupts therapy possibly; the different product hopefully should be identical, but it can be a concern." It was also noted that this reeducation is time consuming for both the physician and the staff, and generally not reimbursed.

Sidebar 12: Adherence to treatment—managed care perspective

Dunn noted that his company uses an endocrine delivery network that usually involves their home care agency. As a result, people are tracking the utilization of the product. However, the adherence/compliance data that the company collects are used more for managerial decisions and less for reminding patients to take their medicine. However, that dynamic may change, and the company does have case managers and some programs in place to help with compliance issues.

Owens added that he and his colleagues monitor drug consumption through their specialty pharmacy. "It's a loose monitoring because you're really depending on when the patient refills the prescription, and you use that to determine whether or not the patient is taking the medication. Of course, what we don't know is do they have it in the house and [are they] maybe not taking it? In other words, is there a refrigerator full of products somewhere that are not being taken? We have no way of getting at that, but if we do find those people who don't refill the medicine, they do get reminders, and we have units in the specialty pharmacy that work to help manage compliance."

Inappropriate use of recombinant human growth hormone

Owing to its anabolic and lipolytic properties, rhGH has also been used inappropriately for athletic performance enhancement and "anti-aging" purposes. In the managed care setting, the inappropriate use of rhGH is generally very rare and most often will lead to reimbursement being discontinued.

If there is some suspicion that the patient is obtaining rhGH for nonmedical use or with the intention of providing the product to another person, medical professionals are encouraged to provide information about the risks associated with the use of rhGH in normal adults. Persons known to take GH (or anabolic steroids) include military personnel, police officers, firefighters, students, body builders, wrestlers, athletes, and anti-aging customers. The inappropriate use of these drugs in normal adults may increase their risk of

cancer, diabetes, hypertension, arthralgia, edema, carpal tunnel–like syndrome, and psuedotumor cerebri.[33]

Sidebar 13: Off-label use of growth hormone

While GH therapies have substantial benefits for patients who need them the most, the misappropriation and off-label use of GH products (eg, GH misuse for enhancing aesthetics and athletic performance) is a constant concern. Managed care bodies have implemented various tools, such as prior authorizations, to combat and prevent off-label use of rhGH. Panelists felt that these measures have prevented most (and most obvious) misuse.

Owens stated, "We don't have employers asking are you going to be covering this for aging clinics or body-building, or any of the other off-label uses. That's one of the reasons they want a prior authorization on growth hormone, to make sure we're not paying for that."

Conclusion

Specialty pharmacies are the most common means of dispensing rhGH. Given that all 9 rhGH products contain the same active molecule and managed care professionals generally consider the products therapeutically interchangeable, to reduce costs, most payers limit the number of preferred rhGH formulations to only a few that cover all of the indications for which rhGH can be prescribed. It can be difficult to balance the needs of the patient with the economic realities of the healthcare system. Payers may focus on the short-term costs of rhGH therapy, as the long-term benefits may be difficult to directly quantify. While the primary benefits are taller stature for age and adult height within the normal range within genetic expectations, there may be other long-term benefits associated with rhGH therapy. Thus, when rhGH treatment is appropriate, it is imperative that specialty pharmacists and clinicians help patients understand the importance of adhering to treatment, and work with payers to choose a treatment regimen that is suitable for the lifestyle of the patient and covered by managed care policies. In other words, specialty care pharmacists and clinicians need to balance the needs of the patient with managed care considerations. In situations where rhGH therapy is not deemed necessary by payers, there are methods in place for clinicians to seek clarification and/or reconsideration. Moving forward, these treatments may come under further scrutiny as payers make efforts to limit the costs while still providing care to those who really need it.

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