Comparison of Human Growth Hormone Products' Cost in Pediatric and Adult Patients

A Budgetary Impact Model

Payers' drug costs for human growth hormone are related to product waste that is related to the container in which the product is supplied

Gary R. Bazalo, MS[1]; Ashish V. Joshi, PhD[2]; John Germak, MD[2]

[1]Managed Solutions, Conifer, Colo.; [2]Novo Nordisk, Princeton, N.J.

ABSTRACT

We assessed the economic impact to the United States payer of recombinant human growth hormone (rhGH) utilization, comparing the relative dosage efficiency of marketed pen-based and vial-based products in a pediatric and in an adult population. A budgetary impact model calculated drug costs based on product waste and cost. Waste was the difference between prescribed dose, based on patient weight, and actual delivered dose, based on dosing increments and maximum deliverable dose for pens and a fixed-percent waste as derived from the literature for vials.

Annual wholesale acquisition costs were calculated based upon total milligrams delivered, using a daily dose of 0.03 mg/kg for pediatric patients and 0.016 mg/kg for adults. Total annual drug costs were compared for two scenarios: 1) a product mix based on national market share and 2) restricting use to the product with lowest waste.

Based on the literature, waste for each vial product was 23 percent. Among individual pens, waste was highest for Humatrope 24 mg (19.5 percent pediatric, 14.3 percent adult) and lowest for Norditropin NordiFlex 5 mg (1.1 percent pediatric, 1 percent adult). Restricting use to the brand with least waste (Norditropin), compared to national product share mix, resulted in a 10.2 percent reduction in annual pediatric patient cost from $19,026 to $17,089 and an 8 percent reduction in annual adult patient cost from $24,099 to $22,161.

We concluded that pen delivery systems result in less waste than vial and syringe. Considering all approved delivery systems, Norditropin resulted in the least product waste and lower annual patient cost for both pediatric and adult populations.

Corresponding author:

Gary R. Bazalo, MS
Managed Solutions
28154 Belle Meade Drive
Conifer, Colo. 80433
e-mail: gbazalo@wispertel.net

Gary R. Bazalo, MS, discloses that he is a consultant to Novo Nordisk.

Ashish V. Joshi, PhD, and John Germak, MD, disclose that they are employees of Novo Nordisk.

INTRODUCTION

Human growth hormone prepared by recombinant DNA technology (rhGH) is used to treat children with congenital or acquired growth disorders of various origins, including growth hormone deficiency (GHD), Turner syndrome, chronic renal insufficiency, short children born small for gestational age (SGA), Prader-Willi syndrome and idiopathic short stature (ISS) (Joshi, 2006).

Although rhGH has recently been approved for adults with HIV lipodystrophy and short bowel syndrome, it is most often prescribed for adult patients with documented GHD. Treatment with rhGH may continue over many years at a significant annual drug acquisition cost. Manufacturer revenues from growth hormone are estimated to be just over $1 billion in 2006 (Frost and Sullivan, 2006). The bulk of this cost is often borne by insurers, including managed care plans. As of April 2006, there were six manufacturers of rhGH in the United States. Since the chemical entity of growth hormone (somatropin) is the same for all manufacturers, product differentiation is based upon uniqueness of delivery devices, net price per milligram of active substance, and patient support services offered by each manufacturer.

With respect to delivery systems, rhGH is generally administered to pediatric and adult patients based on the weight of the individual via traditional vial and syringe or via pen-based injection systems of various types. Although the pen systems differ in ease of use and discomfort to patients, from an economic point of view the pen characteristics of interest are the dosing increments provided by the pen dosing dial and the maximum dose that can be delivered by the pen (Joshi,2005; Bazalo, 2005).

The dosing increment determines how closely the pen can deliver the calculated dosage based on patient weight. The maximum deliverable dose determines the range of patient

weights that the pen can accommodate. Dosing accuracy increases with finer dosing increments, and results in less product waste and consequently saves dollars. For products delivered by vial and syringe, the governing economic factor is the error inherent in drawing up and injecting rhGH (Gnanalingham, 1998; Lteif, 1999). In this study we assess the economic impact of the available drug delivery systems and drug cost per milligram of each manufacturer of rhGH via a budget impact model.

METHODS

Table 1 shows the pen-based delivery and vial packages for all available rhGH products in the United States as of April 2006. The table shows the available milligrams in each package, wholesaler acquisition cost (WAC) per package, WAC per mg, and approximate 2005 United States market share based on a survey conducted in 2006 (Frost and Sullivan, 2006). Market share was available only at the brand level. We assumed equal usage of all devices within each brand. For pen-based delivery systems, the maximum deliverable dosage and the dosing increment are also shown. Tev-Tropin is indicated in pediatric patients only.

We developed a budget impact model to examine the expected product waste for the pen-based and vial/syringe delivery systems of each manufacturer. Waste is defined as the difference between the actual dosage of drug delivered and the calculated dosage based on patient weight. The model calculates the total drug cost for each device and manufacturer brand based on the total milligrams delivered and the cost per milligram for two populations of patients, pediatric and adult, each having a specific weight distribution. Consistent with its label, only pediatric patients are included in the model analysis for Tev-Tropin.

The pediatric population had a flat weight distribution extending from 10 to 55 kilograms. The adult population had a flat weight distribution extending from 55 to 100 kilograms.

Product waste was calculated for each pen device across the patient weight distribution as follows. First, the weight-based daily dosage for a given patient, weight based on a pediatric dosage of 0.030 mg/kg and an adult dosage of 0.016 mg/kg, was calculated. For Tev-Tropin, we used the label dosing of 0.1 mg/kg three times

TABLE 1
Available rhGH packages in the United States

Product / package	Total mg	WAC price per package	WAC price per mg*	Market share**	Max dose (mg)+	Dose increment (mg)+
Norditropin NordiFlex 5 mg	5	$248.37	$49.67	1.6%	1.50	0.025
Norditropin NordiFlex 10 mg	10	$496.72	$49.67	1.6%	3.00	0.05
Norditropin NordiFlex 15 mg	15	$745.10	$49.67	1.6%	4.50	0.075
Norditropin Nordipen 5 mg	5	$248.37	$49.67	1.6%	1.25	0.05
Norditropin Nordipen 15 mg	15	$745.10	$49.67	1.6%	4.00	0.1
Humatrope pen 6 mg	6	$298.00	$49.67	4.8%	1.20	0.1
Humatrope pen 12 mg	12	$596.00	$49.67	4.8%	2.40	0.2
Humatrope pen 24 mg	24	$1,192.00	$49.67	4.8%	4.80	0.4
Humatrope vial 5 mg	5	$248.35	$49.67	4.8%	NA	NA
Genotropin 5.8 mg***	5	$231.54	$46.31	12.5%	2.00	0.1
Genotropin 13.8 mg***	12	$568.00	$47.33	12.5%	4.00	0.2
Nutropin AQ pen cartridge	10	$496.70	$49.67	9.5%	4.00	0.1
Nutropin AQ vial 10 mg	10	$496.70	$49.67	9.5%	NA	NA
Nutropin vial 5 mg	5	$248.35	$49.67	9.5%	NA	NA
Nutropin vial 10 mg	10	$496.70	$49.67	9.5%	NA	NA
Saizen 5 mg	5	$225.55	$45.11	5.0%	4.00	0.1
Saizen 8.8 mg	8.8	$360.88	$41.01	5.0%	4.00	0.1
Tev-Tropin vial 5 mg	5	$164.50	$32.90	<0.1%	NA	NA

*Source: Price-Check PC, April 2006
**Source: Frost and Sullivan, 2006
***Product available from the Genotropin 5.8 mg and 13.8 mg pens is 5 mg and 12 mg, respectively
+ For pen devices only

a week for pediatric patients. Second, it was determined whether the daily dosage could be accommodated by the maximum dosage of the pen device. If so, the "delivered dosage," defined as the smallest amount of drug that the pen can deliver that is equal to or greater than the weight-based dosage, was calculated.

Waste is defined as the difference between the delivered dosage and the weight-based dosage. For example, if the weight-based dosage is 0.86 mg and the dosage increment is 0.1 mg, then the delivered dosage is 0.9 and the waste is 0.04 milligrams. For the same patient, a dosage increment of 0.025 yields a delivered dosage of 0.875 and waste of 0.015 mg. The waste for a given pen was then calculated as the average waste over all patient weights in the distribution. Daily drug cost was calculated as daily delivered dose multiplied by the cost per milligram averaged over the patient weight distribution. Annual drug cost was calculated as daily drug cost multiplied by 365. Since most patients require multiple pens in a single month, we assumed that unused material in a pen at the end of a month was used in the following month.

Waste for each vial product was based on the literature and was set at 23 percent, including injection error (15 percent), and syringe/needle dead space (8 percent) (Becton Dickinson technical data sheet).

Drug cost per milligram was based on wholesale acquisition cost in Table 1. Product discounts and patient copayments were set to zero.

We calculated the waste for each product pen device and for each

TABLE 2
Product waste

	Pediatric patients		Adult patients	
Product / package	**Max weight (kg)**	**Waste based on ideal dose**	**Max weight (kg)**	**Waste based on ideal dose**
Norditropin		**2.6%**		**2.4%**
Norditropin NordiFlex 5 mg	50	1.1%	93	1.0%
Norditropin NordiFlex 10 mg	55	2.0%	100	1.9%
Norditropin NordiFlex 15 mg	55	3.0%	100	3.0%
Norditropin Nordipen 5 mg	41	2.5%	78	2.2%
Norditropin Nordipen 15 mg	55	4.6%	100	3.8%
Humatrope		**14.5%**		**12.2%**
Humatrope vial 5 mg	55	23.0%	100	23.0%
Humatrope pens		*11.7%*		*8.7%*
Humatrope pen 6 mg	40	5.8%	75	4.4%
Humatrope pen 12 mg	55	9.7%	100	7.3%
Humatrope pen 24 mg	55	19.5%	100	14.3%
Genotropin		**7.1%**		**5.5%**
Genotropin 5.8 mg	55	4.6%	100	3.8%
Genotropin 13.8 mg	55	9.7%	100	7.3%
Nutropin		**18.4%**		**18.2%**
Nutropin AQ vial 10 mg	55	23.0%	100	23.0%
Nutropin vial 5 mg	55	23.0%	100	23.0%
Nutropin vial 10 mg	55	23.0%	100	23.0%
Nutropin pens		*4.6%*		*3.8%*
Nutropin AQ pen cartridge	55	4.6%	100	3.8%
Saizen		**4.6%**		**3.8%**
Saizen 5 mg	55	4.6%	100	3.8%
Saizen 8.8 mg	55	4.6%	100	3.8%
Tev-Tropin		**23%**		**NA**
Tev-Tropin vial 5 mg	55	23%	NA	NA

product vial as a percentage of the required weight-based dosage. In addition, the average waste for each manufacturer's product was calculated by assuming an evenly divided mix of all available pens and vial packages for each manufacturer. We calculated total annual rhGH WAC drug acquisition cost and total rhGH milligrams for 500 pediatric patients and 500 adults, as well as the mean cost and milligrams per patient, based on two scenarios: 1) a product mix based on national market share using the share numbers from Table 1, and 2) restricting use to the product with lowest waste. Because it had low market share in 2005, we did not include Tev-Tropin in the scenario calculations.

RESULTS

Product waste

Table 2 shows the percent waste for each rhGH pen-based and vial package and for each rhGH brand (assuming equal use of each package within brands) for pediatric and adult patients. Percentage waste for Tev-Tropin was calculated for pediatric patients only. For brands that have both pen and vial packages (Humatrope and Nutropin), the average waste is given for pens only and for pens and vials together.

Some of the smaller pens (NordiFlex 5 mg, Nordipen 5 mg and Humatrope 6 mg) are not able to treat patients to the pediatric upper limit of 55 kg and the adult upper limit of 100 kg. The upper weight limit for these pens is noted in Table 2.

Norditropin yielded the least product waste, 2.6 percent for pediatric patients and 2.4 percent for adults. For pediatric patients, the waste was 4.6 percent for Saizen, 7.1 percent for Genotropin, 14.5 percent for Humatrope (11.7 percent for Humatrope pens), 18.4 percent for Nutropin (4.6 percent for the Nutropin pen), and 23 percent for Tev-Tropin. For adult patients, the waste was 3.8 percent for Saizen, 5.5 percent for Genotropin, 12.2 percent for Humatrope (8.7 percent for Humatrope pens), and 18.2 percent for Nutropin (3.8 percent for the Nutropin pen).

Total rhGH delivered

Table 3 shows total annual milligrams per patient for each package and brand. Of the packages that cover the entire modeled weight distribution, Norditropin NordiFlex 10 mg delivered the amount of rhGH closest to weight-based dosage (363 mg for pediatric patients and 461 mg for adults), which was also the least amount, for the entire weight distribution of patients. Using this package as a benchmark, we computed the delivered mgs of rhGH for the other packages as a percentage of the benchmark package. Compared to

TABLE 3
Annual delivered rhGH mgs and comparison to benchmark device

	Annual delivered mgs		Percent of mgs delivered by NordiFlex 10 mg	
Product / package	**Pediatric**	**Adult**	**Pediatric**	**Adult**
NordiFlex 5 mg*	332	437	*	*
NordiFlex 10 mg	363	461	100.0%	100.0%
NordiFlex 15 mg	367	466	101.0%	101.0%
Nordipen 5 mg*	286	397	*	*
Nordipen 15 mg	372	470	102.5%	101.8%
Humatrope pen 6 mg*	290	396	*	*
Humatrope pen 12 mg	390	486	107.5%	105.2%
Humatrope pen 24 mg	425	517	117.2%	112.1%
Humatrope vial 5 mg	438	557	120.6%	120.7%
Genotropin 5.8 mg	372	470	102.5%	101.8%
Genotropin 13.8 mg	390	486	107.5%	105.2%
Nutropin AQ pen cartridge	372	470	102.5%	101.8%
Nutropin AQ vial 10 mg	438	557	120.6%	120.7%
Nutropin vial 5 mg	438	557	120.6%	120.7%
Nutropin vial 10 mg	438	557	120.6%	120.7%
Saizen 5 mg	372	470	102.5%	101.8%
Saizen 8.8 mg	372	470	102.5%	101.8%
Tev-Tropin vial 5 mg	625	NA	172.3%	NA

* Package does not cover entire modeled weight distribution

this benchmark, other rhGH packages delivered 1 percent to over 20 percent more milligrams for the same dosage requirements. The Tev-Tropin delivered amount is much higher due to its label dosage.

Total acquisition cost and rhGH milligrams

Table 4 shows the total annual number of rhGH milligrams delivered by all products under the two scenarios described in the methodology. Exclusive use of Norditropin resulted in an 11.4 percent reduction in total rhGH milligrams delivered. Table 5 shows average annual rhGH milligrams per patient. Average annual pediatric patient usage fell from 393 mg to 344 mg. The average annual adult usage fell from 498 mg to 446 mg.

Table 6 shows total WAC drug acquisition costs for each scenario. Exclusive use of Norditropin resulted in a 9 percent reduction in annual drug acquisition costs. Table 7 shows the mean annual WAC drug acquisition costs per patient. Figure 1 shows the mean annual delivered milligrams of rhGH per patient for each scenario. Figure 2 shows the mean annual WAC drug acquisition costs per patient for each scenario.

DISCUSSION

According to technical data supplied by a large manufacturer of syringes, products delivered by syringe have an inaccuracy of about 23 percent (Becton Dickinson). Two studies measured the accuracy of syringes delivering low doses of insulin (< 5 units) in children, and the mean error was found to be 23 percent and 12.3 percent (Gnanalingham, 1998; Lteif, 1999). The error rate in the first study corresponded to the error rate reported in the syringe technical specifications used in the model (Becton Dickinson). Using the lower error rate of 12.3 percent resulted in a reduction in the annual WAC cost percentage savings in Table 6 from 10.2 percent to 7.1 percent in children, from 8.0 percent to 4.9 percent in adults and from 9.0 percent to 5.9 percent for all patients combined.

Waste in the pen-based delivery systems ranged from 1.1 percent (Norditropin NordiFlex 5 mg) to 19.5 percent (Humatrope pen 24 mg) in pediatric patients and 1.0 percent to 14.3 percent in adults. A 1 percent reduction in rhGH drug product results in average saving of $216 per

TABLE 4
Total annual rhGH milligrams delivered under two scenarios

Patient segment	Product mix based on US market share	Norditropin only	Change
Pediatric	196,727	172,010	–12.6%
Adult	249,137	223,065	–10.5%
All patients	445,864	395,075	–11.4%

TABLE 5
Mean annual per patient rhGH milligrams delivered under two scenarios

Patient segment	Product mix based on market share	Norditropin only	Change
Pediatric	393.5	344.0	–12.6%
Adult	498.3	446.1	–10.5%
All patients	445.9	395.1	–11.4%

TABLE 6
Total WAC costs for two scenarios

Patient segment	Product mix based on market share	Norditropin only	Change
Pediatric	$9,513,163	$8,544,315	–10.2%
Adult	$12,049,703	$11,080,379	–8.0%
Total	$21,562,866	$19,624,694	–9.0%

TABLE 7
Per Patient WAC costs for two scenarios

Patient segment	Product mix based on market share	Norditropin only	Cchange
Pediatric	$19,026	$17,089	–10.2%
Adult	$24,099	$22,161	–8.0%
Total	$21,563	$19,625	–9.0%

FIGURE 1
Mean annual delivered mgs of rhGH per patient for each scenario

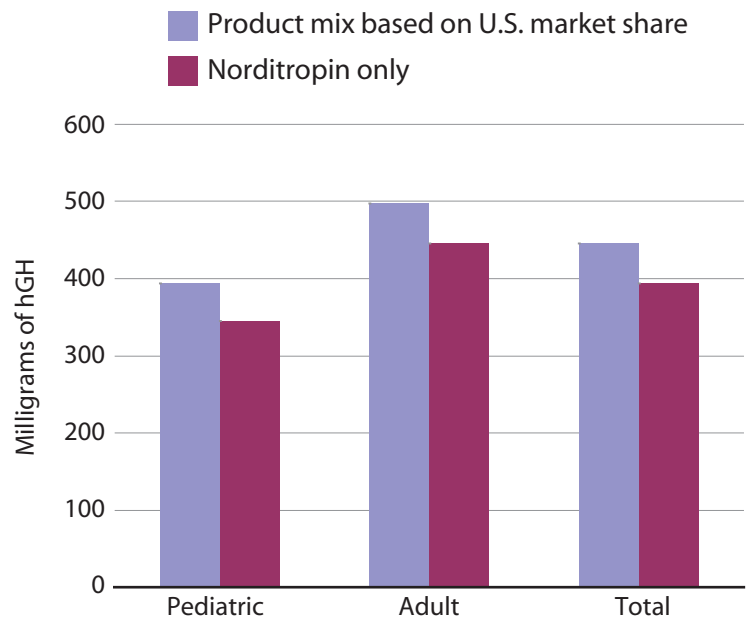
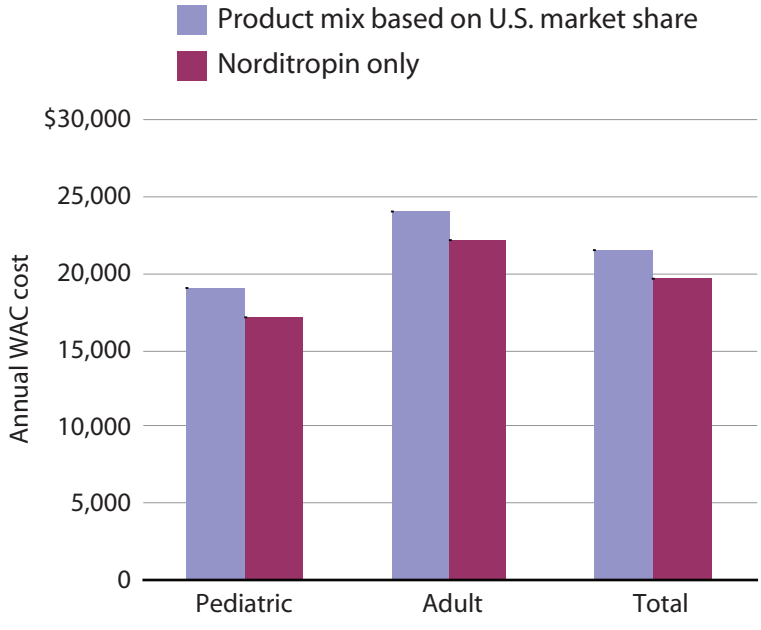


FIGURE 2
Mean annual WAC drug acquisition cost per patient for each scenario



patient annually (1 percent of $21,563) shown in Table 7. Norditropin yielded the least waste. Use of Norditropin compared to a mix of products based on United States market share (see Table 1 for share figures) resulted in 11.4 percent fewer milligrams of rhGH delivered and a 9 percent reduction in costs for adults and pediatric patients combined. This is a reduction in annual costs per patient of $1,938 (from $21,563 to $19,625).

Norditropin NordiFlex pen 10 mg provided the best combination of patient weight coverage and minimum waste. This pen covered the entire modeled weight distribution for pediatric patients and adults with product waste of 2 percent. For pediatric patients under 50 kgs and adults under 93 kgs, Norditropin NordiFlex pen 5 mg provided the least waste, 1.1 percent for pediatric patients and 1 percent for adults.

The key variable in our model is the dosing increment of the pen-based delivery systems. The pens with the finest dosing increments were the Norditropin NordiFlex 5 mg (0.025 mg) followed by the Norditropin NordiFlex 10 mg and NordiPen 5 mg (0.05 mg each). Most other pen products had a dosing increment of 0.1 mg or higher (See Table 1).

WAC price per milligram did not vary greatly among products with the exception of the Tev-Tropin 5 mg vial. However this product is available in a vial package only and its label dose of 0.1 mg/kg body weight three times per week results in the highest product cost, despite the lower WAC cost per milligram, because of the higher milligram usage based on prescribed dose and percentage waste (see Table 3). We did not include Tev-Tropin in the analysis because it had a small share of the market in 2006. However, if we assume a 10 percent market share for Tev-Tropin taken equally from the other GH products, then the costs for the product mix in Table 6 for pediatric patients would rise

from $9,513,163 to $9,631,257, increasing the savings derived from the Norditropin-only scenario for pediatric patients from 10.2 percent to 11.3 percent. (Tev-Tropin is not indicated in adults).

A limitation of this study is that WAC price levels were used for the calculation of all costs. The actual net costs for a health plan or insurer should take into account member copayments or coinsurance as well as manufacturer price discounts. Since these factors vary widely for a given brand among health plans, we made no attempt to model these factors in the study. Manufacturer "value-added" programs may also have an effect on net costs. Again, most manufacturers have these programs and we have no reason to assume that one manufacturer is providing programs of higher value than another.

Health plans may use prior authorization programs to limit the use of non-formulary products. Indeed, this is the primary mechanism plans use to move market share between products in a category. We did not include the effect of prior authorization programs, since any of the GH products could be affected by such a program, primarily through higher copayments.

Another potential limitation of this study lies in its assumptions. This is a theoretical model and is not based on actual patient data from insurers or PBMs. The model assumes that the patients are compliant, that the dose is given accurately according to instructions, and that all dispensed product is used by patients. Nonetheless, the model provides a reasonable estimate of potential product cost savings because of device characteristics such as finer dosing.

Payers should understand the effect of the various delivery systems available from each manufacturer when comparing prices. Dosing efficiency, WAC price, label dosing and product discounts all contribute to the overall economic result for rhGH products. In addition to the economics, patient-support programs and patient comfort should be considered in the selection of preferred rhGH products.

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