Common Drug Review

Pharmacoeconomic Review Report

January 2014

Drug	somatropin (Genotropin)
Indication	The treatment of short stature associated with Turner syndrome in patients whose epiphyses are not closed
Listing request	List in similar manner to other growth hormone products
Manufacturer	Pfizer Canada Inc.

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ABBREVIATIONS

CDR	Common Drug Review
CI	confidence interval
GHD	growth hormone deficiency
ISS	idiopathic short stature
SGA	small for gestational age
SHOX	short stature homeobox-containing gene deficiency
TS	Turner syndrome

SUMMARY

Somatropin (Genotropin) is available as an injection under multiple strengths (0.6 mg, 0.8 mg, 1.0 mg, 1.2 mg, 1.4 mg, 1.6 mg, 1.8 mg, and 2.0 mg syringes, and 5.3 mg and 12 mg pens). It is indicated in Canada for the treatment of children who have growth failure due to an inadequate secretion of endogenous growth hormone (growth hormone deficiency [GHD]), growth failure in short children born small for gestational age (SGA) and who fail to achieve catch-up growth by two to four years or later, short stature associated with Turner syndrome (TS) in patients whose epiphyses are not closed, idiopathic short stature (ISS), and adults with GHD of adult or childhood onset. The manufacturer is requesting reimbursement for its use in patients with TS. Similar clinical effectiveness for Genotropin versus comparators was assumed based on the results of one trial comparing Genotropin to Omnitrope for treatment of GHD in children.[1] There were no published indirect comparisons of these agents. Based on Common Drug Review (CDR) calculations using a confidential price of $[redacted], the daily cost of the maximum dose of Genotropin ($[redacted]; 0.33 mg/kg/week) is less than that of Humatrope ($100; 0.375 mg/kg/week), Nutropin ($84; 0.375 mg/kg/week), and Saizen ($96; 0.320 to 0.375 mg/kg/week).

REVIEW OF THE PHARMACOECONOMIC SUBMISSION

1. INTRODUCTION

Somatropin (Genotropin) is an injectable recombinant human growth hormone indicated in Canada for the treatment of children who have growth failure due to an inadequate secretion of endogenous growth hormone (growth hormone deficiency [GHD]), growth failure in short children born small for gestational age (SGA) and who fail to achieve catch-up growth by two to four years or later, short stature associated with Turner syndrome (TS) in patients whose epiphyses are not closed, idiopathic short stature (ISS), and adults with GHD of adult or childhood onset. This Common Drug Review (CDR) pharmacoeconomic (PE) report will review its use in patients with TS. The maximum recommended dose of Genotropin in patients with TS is 0.33 mg per kg per week. The manufacturer submitted a confidential price of $[redacted] per mg.[1]

1.1 Cost Comparison Table

The comparator treatments presented in the table below have been deemed the appropriate comparators by clinical experts. Comparators may be recommended (appropriate) practice versus actual practice. Comparators are not restricted to drugs, but may be devices or procedures. Costs are manufacturer list prices, unless otherwise specified.

TABLE 1: COST COMPARISON TABLE FOR GENOTROPIN FOR PATIENTS WITH TURNER SYNDROME

Drug/ Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Daily Drug Cost[a] ($)	Average Annual Drug Cost ($)
Genotropin[b]	**5.3 mg** **12 mg**	**Pen**	[redacted]	0.33 mg/kg body weight per week in 6 to 7 doses	[redacted]	[redacted]
	0.6 mg **0.8 mg** **1.0 mg** **1.2 mg** **1.4 mg** **1.6 mg** **1.8 mg** **2.0 mg**	**Syringe**	[redacted]		[redacted]	[redacted]
Humatrope	5 mg 24 mg	Vial	233.35 999.99	Up to 0.375 mg/kg/week	Up to 89	Up to 32,581
	6 mg 12 mg	Cartridge	280.02 560.04		Up to 100	Up to 36,493
Nutropin	10 mg	Vial	389.44	Up to 0.375 mg/kg/week in 3 to 7 doses	Up to 83	Up to 30,452
Nutropin AQ	10 mg	Cartridge	392.55		Up to 84	Up to 30,695
Saizen	3.33 mg 5 mg 8.8 mg	Vial	149.25 224.05 358.47	0.32 to 0.375 mg/kg/week in 3 or 7 doses	74 to 96	27,181 to 35,047
	6 mg 12 mg 20 mg	Cartridge	268.83 537.66 896.10		82 to 96	29,897 to 35,035

Prices are from the Saskatchewan Formulary (accessed Aug 23, 2013), unless otherwise indicated, and do not include dispensing fees.
[a]Weight-based doses use an average weight of 39.99 kg.[1] Assumes daily doses and wastage of excess for single dose syringes.
[b]Manufacturer's confidential submitted price.

2. SUMMARY OF PHARMACOECONOMIC SUBMISSION

The manufacturer submitted a cost-minimization analysis[1] comparing Genotropin with the other somatropins available in Canada: Humatrope, Saizen, and Nutropin. Omnitrope was not included because it is not indicated for use in TS patients in Canada. Norditropin, an additional somatropin available in Canada, was not included in the analysis because the manufacturer was unable to identify any use of this product in both public and private drug plans across the country. Serostim, another somatropin, was not included because its sole indication in Canada is for treatment of HIV wasting associated with catabolism, weight loss, or cachexia.

Similar clinical effectiveness of Genotropin with comparators was assumed by the manufacturer, based on the results of one trial comparing Genotropin to Omnitrope for treatment of GHD in children,[2] the results of which suggest that there is similar efficacy among the different somatropins (Table 2).No indirect comparisons were identified in the literature search. The analysis was conducted from the Canadian public-payer perspective.

TABLE 2: TRIAL RESULTS FOR OMNITROPE VERSUS GENOTROPIN IN PEDIATRIC GROWTH HORMONE-DEFICIENT PATIENTS

	Omnitrope	Genotropin	95% CI
Number of patients	44	45	
Height baseline, cm	113.3	109.3	
Height at 9 months, cm	121.9	117.7	–0.59 to 1.06

CI = confidence interval.
Source: Genotropin Manufacturer Pharmacoeconomic Submission (Table 1, page 16).[1]

Only drug acquisition costs were considered and these were obtained from the IMS Delta PA database.[1] The manufacturer assumed similar health care resource utilization among all somatropin products. For the drug costs, the manufacturer utilized the lowest cost per milligram for each product regardless of the variation in drug formulation or administration system. For the base-case analysis, the products were compared on adult daily dosage based on the minimum and maximum dosage reported in each comparator's respective product monograph (Table 3). The manufacturer reported that the average daily cost of the maximum dose of Genotropin ($[redacted]) is lower than Humatrope ($89), Nutropin ($83), and Saizen ($85). At maximum doses, Genotropin would be cost-saving versus Humatrope, Nutropin, and Saizen (Table 3).

TABLE 3: COST COMPARISON BASED ON MAXIMUM DOSES FOR THE TREATMENT OF TURNER SYNDROME

Product[a]	Genotropin	Humatrope	Nutropin	Saizen
Maximum dose (mg/kg/day)[b]	0.047	0.054	0.054	0.054
Daily cost	$[redacted]	$88.67	$83.42	$84.73
Annual cost	$[redacted]	$32,364.80	$30,449.03	$30,926.02
Incremental annual cost (savings) compared with Genotropin		**$13,166**	**$11,251**	**$11,728**

Adapted from Genotropin Manufacturer Pharmacoeconomic Submission (Tables 5 & 9, pages 20 & 23).[1]
[a]Omnitrope excluded as it is not indicated for Turner syndrome in Canada.
[b]Dosages for Humatrope, Saizen, and Nutropin are based on an average pediatric weight of 39.99 kg.[3]

The manufacturer conducted a sensitivity analysis using a dose of 0.025 mg/kg per day, which is based on the clinical study by Takeda et al.[3] The results suggested that the annual cost of Genotropin is lower than that of Humatrope, Nutropin, and Saizen (Table 4).

TABLE 4: MANUFACTURER-SUBMITTED SENSITIVITY ANALYSIS RESULTS FOR TREATMENT OF PATIENTS WITH TURNER SYNDROME

Product	Genotropin	Humatrope	Nutropin	Saizen	Omnitrope
Average annual cost per patient[a]					
	$[redacted]	$27,186.43	$25,577.18	$25,977.85	Not applicable

[a]Based on the mean daily dose (0.045 mg/kg/day) included in the analysis by Takeda et al. 2010.[3]

3. INTERPRETATIONS AND KEY LIMITATIONS

3.1 Lack of Evidence to Support Equivalent Efficacy and Safety

Equivalent efficacy was assumed based on a single head-to-head trial comparing Genotropin to Omnitrope in pediatric patients with GHD.[2] However, there are no data to support this assumption in patients with TS compared, nor are there any head-to-head trials against any active comparator in patients with TS. In addition, no indirect comparisons were identified in a literature search carried out by CDR.

4. ISSUES FOR CONSIDERATION

The manufacturer is requesting that Genotropin be listed for use in patients with TS. Somatropin, available through other brand names and products, is indicated for additional conditions like ISS, short stature homeobox-containing gene (SHOX) deficiency, SGA, and in children with growth failure due to chronic renal failure. The potential for off-label use of Genotropin can be associated with considerable costs to the drug plans. However, it should be noted that this possibility for off-label use is not unique to Genotropin and is applicable to the other available somatropin products on the market in Canada.

A CDR analysis of potential utilization in TS patients in Canada (see APPENDIX 1: UTILIZATION ANALYSIS) suggested that Genotropin could potentially be associated with cost savings of up to $140,745 per year for public plans.

5. CONCLUSIONS

Based on CDR calculations using a confidential price of $[redacted] per mg, the daily cost of the maximum dose of Genotropin ($[redacted]; 0.33 mg/kg/week) is less than that of Humatrope ($100; 0.375 mg/kg/week), Nutropin ($84; 0.375 mg/kg/week), and Saizen ($96; 0.320 to 0.375 mg/kg/week).

APPENDIX 1: UTILIZATION ANALYSIS

The submitted price for Genotropin ($[redacted] per mg) is lower than that of Humatrope ($41.39 per mg), which is the most widely reimbursed somatropin in Canada (based on public plan data), with an approximate market share of 58% in 2012. A scenario analysis was conducted whereby Genotropin was assumed to replace Humatrope. Based on available prevalence data[4,5] and Canadian population estimates by age and gender for 2012,[6] this scenario analysis assumed that 8.4% of all units reimbursed for Humatrope were used by patients with Turner syndrome. This analysis is based on public coverage of Humatrope (no private plans are included). For product costs, both available provincial drug prices and manufacturer-submitted average per milligram prices were used. The results in Table 5 indicate the potential annual cost savings to the drug plan had Genotropin replaced Humatrope.

TABLE 5: COMMON DRUG REVIEW ANALYSIS ON UTILIZATION FOR GENOTROPIN

Current Price[a] ($/mg)	Scenario	Minimum Savings[b,c]	Maximum Savings[b,c]
$[redacted]	Genotropin replaces the most widely used somatropin (Humatrope).[d,e]	$98,450	$140,745

[a]Manufacturer submitted confidential price.
[b]Does not include markup or dispensing fees.
[c]Savings per year — based on using provincial and manufacturer-submitted drug prices.
[d]Based on somatropin comparator with most units covered by the Ontario Drug Benefit (ODB) Plan in 2012, IMS Brogan PharmaStat.
[e]Assumes that 8.4% of patients receiving Humatrope were patients with Turner syndrome.

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