Common Drug Review

Pharmacoeconomic Review Report

January 2014

Drug	somatropin (Genotropin) (0.15 mg to 0.3 mg per day)
Indication	Replacement of endogenous growth hormone in adults with growth hormone deficiency
Listing request	List in the same manner as other currently listed somatropin products
Manufacturer	Pfizer Canada Inc.

This report was prepared by the Canadian Agency for Drugs and Technologies in Health (CADTH). Through the Common Drug Review (CDR) process, CADTH undertakes reviews of drug submissions, resubmissions, and requests for advice, and provides formulary listing recommendations to all Canadian publicly funded federal, provincial, and territorial drug plans, with the exception of Quebec.

The report contains an evidence-based clinical and/or pharmacoeconomic drug review, based on published and unpublished material, including manufacturer submissions; studies identified through independent, systematic literature searches; and patient-group submissions. In accordance with *CDR Update — Issue 87*, manufacturers may request that confidential information be redacted from the CDR Clinical and Pharmacoeconomic Review Reports.

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ABBREVIATIONS

CDR	Common Drug Review
GHD	growth hormone deficiency

SUMMARY

Somatropin (Genotropin) is available as an injection with 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 who fail to achieve catch-up growth by two to four years or later, short stature associated with Turner syndrome in patients whose epiphyses are not closed, idiopathic short stature, and adults with GHD of adult or childhood-onset. The manufacturer is requesting listing for reimbursement for its use in adult patients with GHD. 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 drugs. Based on the Common Drug Review calculations using a confidential price of $[redacted] per milligram, the daily cost of the maximum dose of Genotropin ($[redacted]; 0.15 mg to 1.33 mg per day) is less than that of Humatrope ($49; 0.006 mg/kg to 0.0125 mg/kg per day), Nutropin ($82; 0.042 mg/kg to 0.175 mg/kg per week), and Omnitrope ($41; 0.15 mg to 1.33 mg per day), but higher than that of Saizen ($38; 0.005 mg/kg to 0.01 mg/kg per day).

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 and who fail to achieve catch-up growth by two to four years or later, short stature associated with Turner syndrome in patients whose epiphyses are not closed, idiopathic short stature, and adults with GHD of adult- or childhood-onset. This Common Drug Review (CDR) pharmacoeconomic report will review its use in adults with GHD. The recommended dose of Genotropin in adults is 0.15 mg to 0.3 mg per day up to a maximum of 1.33 mg per day. The manufacturer submitted a confidential price of $[redacted] per milligram.

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 ADULT GROWTH HORMONE DEFICIENCY

Drug/ Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Daily Drug Cost[a] ($)	Average Annual Drug Cost ($)
Genotropin[b]	**5.3 mg 12 mg**	**Pen**	[redacted]	**Initial: 0.15 mg to 0.30 mg per day Max: 1.33 mg per day**	**Initial: [redacted] – [redacted] Max: [redacted]**	**[redacted] – [redacted] Max: [redacted]**
	0.6 mg 0.8 mg 1.0 mg 1.2 mg 1.4 mg 1.6 mg 1.8 mg 2.0 mg	**Syringe**	[redacted]		**Max: [redacted]**	**Max: [redacted]**
Humatrope	5 mg 24 mg	Vial	233.35 999.99	0.006 mg/kg to 0.0125 mg/kg per day titrated to adverse effects and to maintain IGF-1 less than upper limit for age and gender	21 to 49	7,665 to 17,886
	6 mg 12 mg	Cartridge	280.02 560.04		24 to 49	8,585 to 17,886
Nutropin	10 mg	Vial	389.44	0.042 mg/kg to 0.175 mg/kg per week for patients younger than 35 years; maximum 0.0875 mg/kg per week for those older than 35 years	20 to 82	7,164 to 29,851
Nutropin AQ	10 mg	Cartridge	392.55		20 to 82	7,221 to 30,089
Drug/ Comparator	**Strength**	**Dosage Form**	**Price ($)**	**Recommended Dose**	**Average Daily Drug Cost[a] ($)**	**Average Annual Drug Cost ($)**
Omnitrope	5 mg 10 mg	Vial	155.80 311.60	Initial: 0.15 mg to 0.30 mg per day Max: 1.33 mg per day	Initial: 5 to 9 Max: 41	Initial: 1,706 to 3,412 Max: 15,126
Saizen	3.33 mg 5 mg 8.8 mg	Vial	149.25 224.05 358.47	0.005 mg/kg to 0.01 mg/kg per day	17 to 38	6,245 to 13,742
	6 mg 12 mg 20 mg	Cartridge	268.83 537.66 896.10		18 to 38	6,869 to 13,737

IGF-1 = insulin-like growth factor-1.
Prices are from the Saskatchewan Formulary (accessed August 23, 2013), unless otherwise indicated, and do not include dispensing fees.
[a]Weight-based doses use the average adult weight of 84 kg reported by Kreitschmann-Andermahr et al. 2012.[2]
[b]Manufacturer's confidential submitted price.

2. SUMMARY OF PHARMACOECONOMIC SUBMISSION

The manufacturer submitted a cost-minimization analysis[3] comparing Genotropin to the other somatropin drugs available in Canada: Humatrope, Saizen, Nutropin, and Omnitrope. Norditropin, an additional somatropin available in Canada, was not included in the analysis since 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, as 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,[4] the results of which suggest that there is similar efficacy among the different somatropin drugs (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 of Genotropin 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 used 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 based on the minimum and maximum dosage reported in each of the 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 that of Humatrope ($43), Nutropin ($41), [redacted] Omnitrope ($37), and higher than that of Saizen ($33). At maximum doses, Genotropin would be cost-neutral or would produce cost savings versus Humatrope, Nutropin, and Omnitrope, but would incur additional costs of $[redacted] per patient per year compared with Saizen (Table 3).

TABLE 3: COST COMPARISON BASED ON MAXIMUM DOSES FOR THE TREATMENT OF ADULT GROWTH HORMONE DEFICIENCY

Product	Genotropin	Humatrope	Nutropin	Saizen	Omnitrope
Maximum dose (mg per day[a])	1.33	1.05	1.05	0.84	1.33
Daily cost	$[redacted]	$43.46	$40.89	$33.22	$37.11
Annual	$[redacted]	$15,863	$14,924	$12,126	$13,544
Incremental annual cost (savings) compared with Genotropin		**$2,319**	**$1,380**	**($1,418)**	[redacted]

Adapted from Genotropin Manufacturer Pharmacoeconomic Submission (Tables 4 and 8, pages 19 and 22).[1]
[a] Dosages for Humatrope, Saizen, and Nutropin are based on an average adult weight of 84 kg.[2]

The manufacturer conducted a sensitivity analysis using a maximum dose of 1.0 mg per day in accordance with the Canadian guidelines for the management of adult GHD.[5] The results suggested that the annual cost of Genotropin is lower than that of Humatrope, Nutropin, and Saizen, and [redacted] that of Omnitrope (Table 4).

TABLE 4: MANUFACTURER-SUBMITTED SENSITIVITY ANALYSIS RESULTS FOR THE TREATMENT OF ADULT GROWTH HORMONE DEFICIENCY

Product	Genotropin	Humatrope	Nutropin	Saizen	Omnitrope
Average annual cost per patient[a]	$[redacted]	$15,107	$14,213	$14,436	$10,184

[a] Based on the maximum daily dose (1.0 mg per day) recommended by Ur et al. 2006.[6]

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.[4] However, there are no data to support this assumption in adult GHD patients. No indirect comparisons for Genotropin versus other somatropin drugs 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 adult patients with GHD. Somatropin, available through other brand names and products, is indicated for additional conditions such as idiopathic short stature and short stature homeobox-containing gene deficiency, for children born small for gestational age and for 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 of off-label use is not unique to Genotropin and applies to the other somatropin products on the market in Canada.

A CDR analysis of potential utilization in adult GHD patients in Canada (APPENDIX 1: UTILIZATION ANALYSIS) suggested that Genotropin could be associated with cost savings of up to $1,317,168 per year for public plans.

5. CONCLUSIONS

Based on CDR calculations using a confidential price of $[redacted] per milligram, the daily cost of the maximum dose of Genotropin ($[redacted]; 0.15 mg to 1.33 mg per day) is less than that of Humatrope ($49; 0.006 mg/kg to 0.0125 mg/kg per day), Nutropin ($82; 0.042 mg/kg to 0.175 mg/kg per week), and Omnitrope ($41; 0.15 mg to 1.33 mg per day), but higher than that of Saizen ($38; 0.005 mg/kg to 0.01 mg/kg per day).

APPENDIX 1: UTILIZATION ANALYSIS

The submitted price for Genotropin ($[redacted] per milligram) is lower than that of Humatrope ($41.39 per milligram), 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 in which Genotropin was assumed to replace Humatrope. Based on available prevalence data[5,6] and Canadian population estimates by age and gender for 2012,[7] this scenario analysis assumed that 78.66% of all units reimbursed for Humatrope were used by adult patients with GHD. 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 prices per milligram were used. The results in Table 5 indicate the potential annual cost savings to the drug plan if Genotropin replaced Humatrope.

TABLE 5: CDR ANALYSIS OF 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]	$921,346	$1,317,168

[a] Manufacturer-submitted confidential price.
[b] Does not include markup or dispensing fees.
[c] Savings per year based on provincial and manufacturer-submitted drug prices.
[d] Based on somatropin comparator with most units covered by the ODB in 2012, IMS Brogan PharmaStat.
[e] Assumes that 78.66% of patients receiving Humatrope were adults with GHD.

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