Cost-effectiveness of once-daily somatropin from Sandoz versus once-weekly somatrogon for the treatment of growth hormone deficiency in children and adolescents

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Background

- Growth hormone deficiency (GHD) is a rare disease with prevalence ranging from 1/4,000 to 1/30,000 in children according to the German diagnostic guidelines for GHD. This prevalence is similar but with a wider range than reported in a NICE guidance (1/3,500-4,000).[1-3]
- For the treatment of GHD, GH replacement therapies are recommended. Once-daily recombinant human GH (rhGH) replacement therapy has been approved for treating severe childhood GHD since 1985.[4]
- Recently, there were EMA approval of once-weekly rhGH medicines: somatrogon (rhGH fusion proteins) and lonapegsomatropin (prodrug releasing unmodified rhGH) for the treatment of paediatric GHD.[5]
- In the context of these approvals there is need to assess the economic impact of the new once-weekly somatrogon compared to established once-daily somatropin using cost-effective analysis in paediatric GHD.
- For this analysis, the most economic once-daily somatropin, i.e., somatropin by Sandoz, was selected as a comparator in Germany and the United Kingdom (UK).

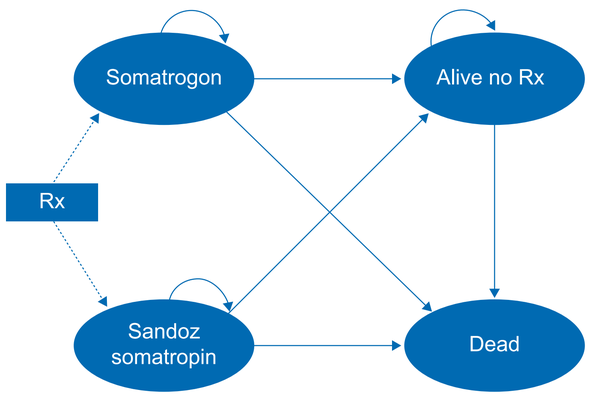
Objective

- This research aims to determine the cost-effectiveness of weekly somatrogon compared to daily somatropin from Sandoz for the treatment of paediatric GHD, from a payer perspective in Germany and the UK.

Methods

- A three-state Markov model was developed to analyse the cost-effectiveness of treatment for GHD with somatrogon versus somatropin.

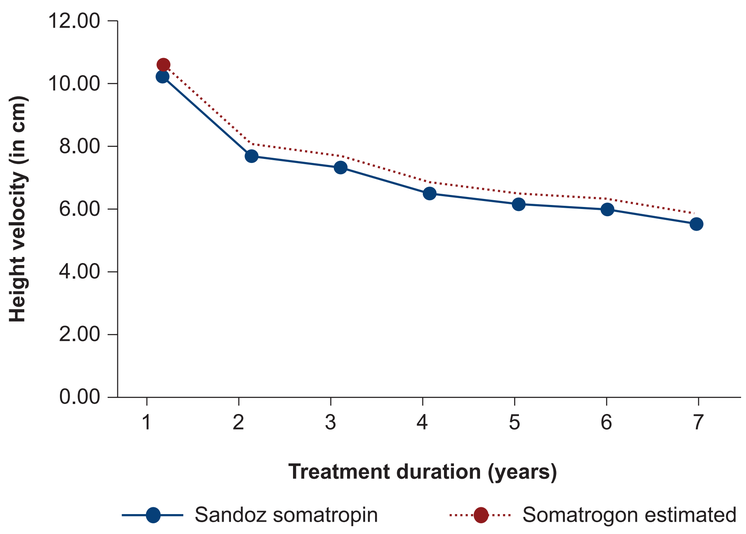
Figure 1. Model structure



Rx: Treatment

- We assumed that the modelled patient commenced treatment at age 8 and continued treatment for seven years until the age of 15, after which growth would revert to untreated GHD levels until the age of 18, after which no further growth was assumed (i.e., Height velocity, HV=0).
- The treatment duration of seven years was selected for the analysis because this was the duration of real-world treatment data available from the PATRO registry.
- HV is the primary efficacy measure of treatment for GHD. Data from the PATRO registry was utilized to model the efficacy of somatropin and to extrapolate the treatment effects of somatrogon beyond 1 year (**Figure 2**).
  - For Sandoz somatropin:
    - ≤7 years of treatment: HV data from the AQ (Phase III) study
- For somatrogon:
  - ≤1-year HV: Data from CP-4-006 (Phase III) study
  - HV decrement derived from Sandoz somatropin modelling was applied from year 2 onwards (i.e., assumed that somatrogon growth rate would moderate over time to the same growth rate as Sandoz somatropin)
- HV of GHD patients, after discontinuing treatment at 15 years of age, was modelled using percentage change in HV observed for off-treatment subjects from the AQ study till 18 years of age.

Figure 2. Graph representing the height velocity extrapolations



- Health utility was mapped to height standard deviation score (HSDS), reported in Christensen et al. 2010, which assessed the relationship between short stature and health related quality of life (HRQoL).[6]
- Data on the disutility associated with daily versus weekly injection was obtained from Abramson et al. 2019, which compared the disutility of weekly and daily semaglutide (in diabetes patients) due to the absence of data on utility differences in a GHD population.[7]

Model Inputs (Table 1)

- Data on the 1-year efficacy of somatrogon was obtained from published literature on CP-4-006 trial.
- Drug costs were calculated from published ex-manufacturer prices of somatrogon and Sandoz somatropin.
- Other treatment costs were assumed to be equal for both treatments and were not included in this analysis.
- The base case comparison was between somatrogon 0.66 mg/kg/week versus Sandoz somatropin 0.03 mg/kg/day as per phase 3 CP-4-006 trial and phase 3 AQ study dosing, respectively.
- Scenario analysis was also performed to analyse cost-effectiveness of somatrogon 0.66 mg/kg/week versus 0.035 mg/kg/day as reported in the CP-4-006 trial and 0.025 mg/kg/day representing lowest recommended dosage. For the scenario analysis we assumed that the higher dose of somatropin would only increase the cost of somatropin and had no effect on efficacy.

Table 1. Base-case model inputs

Parameters	Inputs for Germany	Inputs for UK
Intervention	Somatrogon (**0.66mg/kg/week**), Cost: €25.91 per mg	Somatrogon (**0.66mg/kg/week**), Cost: £7.90 per mg
Comparator	Sandoz somatropin (**0.03mg/kg/day**), Cost: €48.68 per mg	Sandoz somatropin (**0.03mg/kg/day**), Cost: £14.75 per mg
Perspective	Payer	Payer
Discount rates – Costs and Effectiveness (%)	3.0%[8]	3.5%[9]
Willingness to pay threshold	€20,000 per incremental QALY*	£20,000 per incremental QALY[9]
Time horizon	Lifetime	Lifetime
Age at baseline**	8 years	8 years
Gender (male %)**	69.4%	69.4%
Average height of patients at baseline**	111.7 cm	111.7 cm
Average weight of patients at baseline**	20.3 Kg	20.3 Kg
Treatment duration	7 years	7 years
General population height for age by sex	Hesse et al.1997[12] and Hesse et al.1999[13]	British Growth Reference 1990[14]
Weight for age while under treatment by sex	PATRO registry	PATRO registry
Utility measure[7]	Banded HSDS	Banded HSDS
Treatment discontinuation	0% for both treatments, treatment ends after 7 years for entire cohort	0% for both treatments, treatment ends after 7 years for entire cohort

*Based on conservative approach by considering lowest WTP threshold in the UK; Source: **Midpoints from AQ study[10] and CP-4-006 trial[11]; Abramsom 2019[7]; ISPOR 2009[8]; NICE 2020[9]; HSDS: Height Standard Deviation Score; QALY: Quality Adjusted Life Years; WTP: Willingness-to-Pay; UK: United Kingdom; All countries comprise of Belgium, Czech Republic, France, Germany (Hesse/Reinken), Italy, Poland, Spain, Sweden, UK.

Results for Germany

- The summary results from the model for Germany are presented in **Table 2**.

Table 2. Summary results for Germany

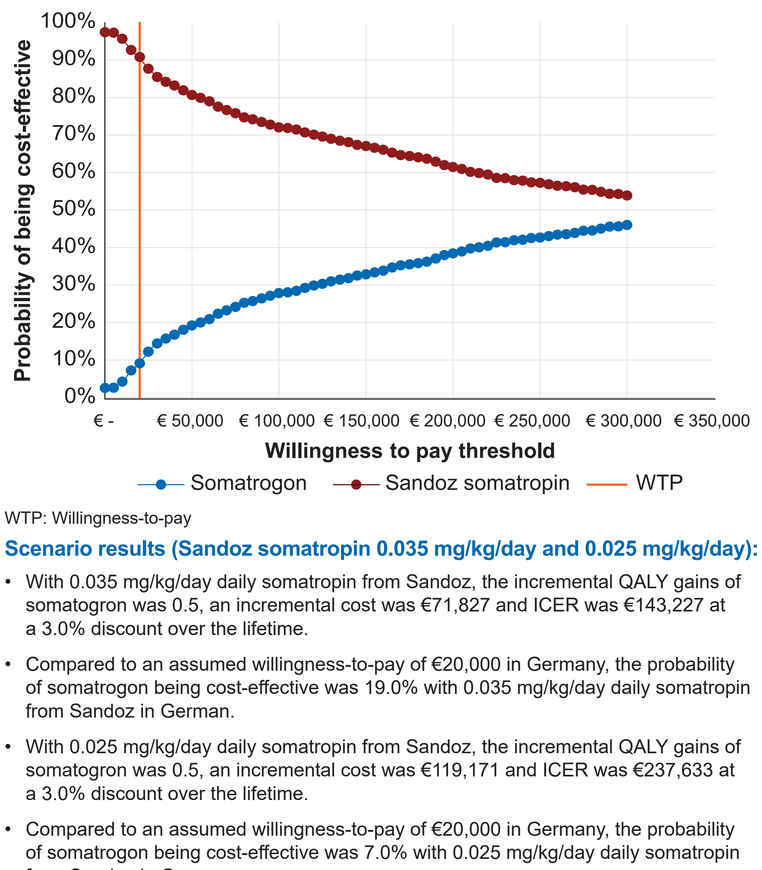
Treatment	Costs	Life Years	QALYs	Δ Costs	Δ QALYs	ICER	NMB
Somatrogon 0.66 mg/kg/week	€237,529	28.93	23.84	-	-	-	-
Sandoz somatropin 0.03 mg/kg/day	€142,030	28.93	23.33	€95,499	0.50	€190,430	-€85,469
Sandoz somatropin 0.035 mg/kg/day*	€165,702	28.93	23.33	€71,827	0.50	€143,227	-€61,797
Sandoz somatropin 0.025 mg/kg/ day*	€118,358	28.93	23.33	€119,171	0.50	€237,633	-€109,141

*Scenario analysis; HSDS: Height Standard Deviation Score; NMB: Net Monetary Benefit; QALY: Quality Adjusted Life Years

Base-case results (Sandoz somatropin 0.03 mg/kg/day):

- In Germany, 7 years of treatment with weekly somatrogon compared with daily somatropin from Sandoz, resulted in incremental QALY gains of 0.5, an incremental cost of €95,499 and an incremental cost-effectiveness ratio (ICER) of €190,430 at a 3.0% discount over the lifetime.
- Compared to an assumed willingness-to-pay of €20,000 in Germany, the probability of somatrogon being cost-effective was 9.0% in Germany (**Figure 3**).

Figure 3. Cost Effectiveness Acceptability Curve for Germany



WTP: Willingness-to-pay

Scenario results (Sandoz somatropin 0.035 mg/kg/day and 0.025 mg/kg/day):

- With 0.035 mg/kg/day daily somatropin from Sandoz, the incremental QALY gains of somatogron was 0.5, an incremental cost was €71,827 and ICER was €143,227 at a 3.0% discount over the lifetime.
- Compared to an assumed willingness-to-pay of €20,000 in Germany, the probability of somatrogon being cost-effective was 19.0% with 0.035 mg/kg/day daily somatropin from Sandoz in German.
- With 0.025 mg/kg/day daily somatropin from Sandoz, the incremental QALY gains of somatogron was 0.5, an incremental cost was €119,171 and ICER was €237,633 at a 3.0% discount over the lifetime.
- Compared to an assumed willingness-to-pay of €20,000 in Germany, the probability of somatrogon being cost-effective was 7.0% with 0.025 mg/kg/day daily somatropin from Sandoz in German.

Results for the United Kingdom

- The summary results from the model for United Kingdom are presented in **Table 3**.

Base-case results (Sandoz somatropin 0.03 mg/kg/day):

- In UK, 7 years of treatment with weekly somatrogon compared with daily somatropin from Sandoz, resulted in incremental QALY gains of 0.54 QALY with an incremental cost of £27,991 and an ICER of £51,957 at a 3.5% discount over the lifetime.

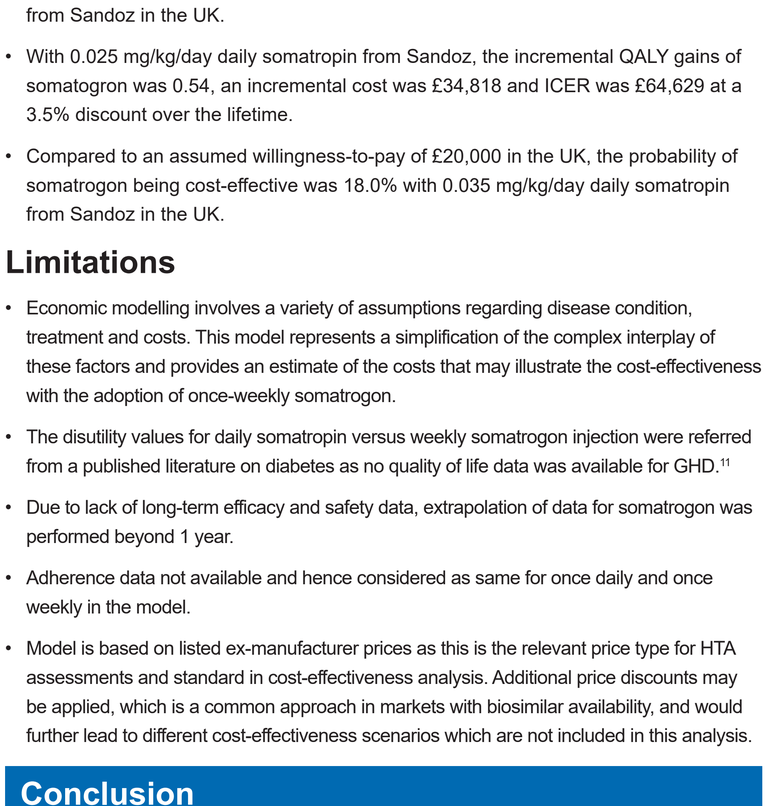
Table 3. Summary results for the United Kingdom

Treatment	Costs	Life Years	QALYs	Δ Costs	Δ QALYs	ICER	NMB
Somatrogon 0.66 mg/kg/week	£68,954	25.83	21.69	-	-	-	-
Sandoz somatropin 0.03 mg/kg/day	£40,963	25.83	21.15	£27,991	0.54	£51,957	-£17,217
Sandoz somatropin 0.035 mg/kg/day*	£47,790	25.83	21.15	£21,164	0.54	£39,285	-£10,389
Sandoz somatropin 0.025mg/kg/day*	£34,136	25.83	21.15	£34,818	0.54	£64,629	-£24,044

*Scenario analysis; HSDS: Height Standard Deviation Score; NMB: Net Monetary Benefit; QALY: Quality Adjusted Life Years

- Compared to an assumed willingness-to-pay £20,000 in the UK, the probability of somatrogon being cost-effective was 23.0% in the UK (**Figure 4**).

Figure 4. Cost Effectiveness Acceptability Curve for the UK



UK: United Kingdom; WTP: Willingness-to-pay

Scenario results (Sandoz somatropin 0.035 mg/kg/day and 0.025 mg/kg/day):

- With 0.035 mg/kg/day daily somatropin from Sandoz, the incremental QALY gains of somatogron was 0.54, an incremental cost was £21,164 and ICER was £39,285 at a 3.5% discount over the lifetime.
- Compared to an assumed willingness-to-pay of £20,000 in the UK, the probability of somatrogon being cost-effective was 33.0% with 0.035 mg/kg/day daily somatropin from Sandoz in the UK.
- With 0.025 mg/kg/day daily somatropin from Sandoz, the incremental QALY gains of somatogron was 0.54, an incremental cost was £34,818 and ICER was £64,629 at a 3.5% discount over the lifetime.
- Compared to an assumed willingness-to-pay of £20,000 in the UK, the probability of somatrogon being cost-effective was 18.0% with 0.035 mg/kg/day daily somatropin from Sandoz in the UK.

Limitations

- Economic modelling involves a variety of assumptions regarding disease condition, treatment and costs. This model represents a simplification of the complex interplay of these factors and provides an estimate of the costs that may illustrate the cost-effectiveness with the adoption of once-weekly somatrogon.
- The disutility values for daily somatropin versus weekly somatrogon injection were referred from a published literature on diabetes as no quality of life data was available for GHD.[11]
- Due to lack of long-term efficacy and safety data, extrapolation of data for somatrogon was performed beyond 1 year.
- Adherence data not available and hence considered as same for once daily and once weekly in the model.
- Model is based on listed ex-manufacturer prices as this is the relevant price type for HTA assessments and standard in cost-effectiveness analysis. Additional price discounts may be applied, which is a common approach in markets with biosimilar availability, and would further lead to different cost-effectiveness scenarios which are not included in this analysis.

Conclusion

- **From a German payer perspective**, once-weekly somatrogon for the treatment of paediatric GHD, compared to somatropin from Sandoz, was unlikely to be cost-effective. Seven years of treatment with weekly somatrogon compared with daily somatropin (0.03 mg/kg/day) from Sandoz, resulted in incremental QALY gains of 0.5, an incremental cost of €95,499 and an ICER of €190,430 at a 3.0% discount over the lifetime. Compared to an assumed willingness-to-pay of €20,000 in Germany, the probability of somatrogon being cost-effective was 9.0% in Germany.
- Likewise, **from the UK payer perspective**, once-weekly somatrogon for the treatment of paediatric GHD, compared to somatropin from Sandoz, was unlikely to be cost-effective. Seven years of treatment with weekly somatrogon compared with daily somatropin (0.03 mg/kg/day) from Sandoz, resulted in incremental QALY gains of 0.54 QALY with an incremental cost of £27,991 and an ICER of £51,957 at a 3.5% discount over the lifetime. Compared to an assumed willingness-to-pay £20,000 in the UK, the probability of somatrogon being cost-effective was 23.0% in the UK.

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