New GH costs from BNF September 2009.

New costs for rhGH became available after the report was submitted to NICE on the 28 August 2009 with the publication of the BNF 58 in September 2009. The previous costs and current costs of the rhGH are given in Table A1 below:

Table A1: The previous and current cost of rhGH from the BNF.

	BNF 57	BNF 58
Genotropin	£23.19	£23.19
Humatrope	£22.88	£18.00
Norditropin	£23.18	£21.39
Saizen	£23.18	£23.18
Nutropin	£23.00	£20.70
Zomacton	£20.33	£19.92

The TAR report sent in August to NICE used the cost of £23.18 per mg for rhGH, because two of the manufacturers used this cost and a third manufacturer used a similar cost of £23.19 per mg. This update has taken the average cost of rhGH from the six manufacturers due to a larger spread of prices in the new version of the BNF. The average cost is now £21.06 per mg. This cost was used to update the following sections of the report:

1. The estimates of cost effectiveness for the deterministic results.
2. The one way deterministic sensitivity analyses results.
3. The summary of cost effectiveness.

A further analysis is included that takes into account the 1.9% reduction in costs due to PPRS price cuts in January 2010.

1. Estimation of cost effectiveness using the new BNF cots for rhGH

The basecase deterministic results are shown in Table A2 for each condition. In the base case analysis all conditions, except GHD, used the clinical benefit seen in the best quality RCT for each condition (Section 3). The cost effectiveness of rhGH versus no treatment varied from £23,196 for GHD to £135,311 for PWS per QALY gained. With the exception of PWS, all conditions have an ICER lower than £40,531 per QALY gained.

Table A2. (cf. Table 46) Cost effectiveness results for the base case analysis

Condition		Costs (£)	QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)	cm gain	ICER (£/cm)
GHD	No rhGH treatment	£2,211	16.8					
	rhGH treatment	£38,031	18.4	£35,820	1.54	£23,196	12.80	£2,798
TS	No rhGH treatment	£1,965	15.9					
	rhGH treatment	£62,752	17.4	£60,787	1.54	£39,460	9.30	£6,536
PWS	No rhGH treatment	£2,646	17.6					
	rhGH treatment	£67,794	18.1	£65,148	0.48	£135,311	11.10	£5,869
CRI	No rhGH treatment	£1,876	11.6					
	rhGH treatment	£35,877	12.4	£34,001	0.87	£39,273	9.20	£3,696
SGA	No rhGH treatment	£2,432	17.1					
	rhGH treatment	£34,431	18.1	£31,999	0.97	£33,079	3.30	£9,697
SHOX-D	No rhGH treatment	£2,646	16.8					
	rhGH treatment	£53,434	18.1	£50,788	1.25	£40,531	6.30	£8,062

Inc.= incremental

A further analysis was undertaken to see the effect of continuation of rhGH treatment into adulthood for 34% of the original cohort until the age of 25. The incremental cost per QALY was £28,244 (Table A3).

Table A3. (cf.. Table 47) Cost effectiveness results for continuation of rhGH treatment into adulthood for GHD patients

Condition		Costs (£)	QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)	cm gain	ICER (£/cm)
GHD continuers	No rhGH treatment	£2,211	16.8					
	rhGH treatment	£45,826	18.4	£43,615	1.54	£28,244	12.80	£3,407

Inc.=incremental

2. Cost effectiveness of rhGH treatment – deterministic sensitivity analysis using the new BNF cost for rhGH.

The results of the KIGs clinical benefit are given in Table A4. The ICER of rhGH versus no treatment varied from an ICER of £18,980 per QALY gained for SGA to £144,050 per QALY gained for PWS. Results remain at a similar magnitude to the updated base case results with the exception of the SGA analyses. The ICER for SGA is much lower in this analysis because the incremental clinical height gain is lower in the RCT effectiveness data compared to the KIGS effectiveness data.

Table A4. (cf.. Table 48) Cost effectiveness results with clinical benefit from KIGS database

		Height			Incremental	Incremental	ICER
Condition		(HtSDS)	Costs (£)	QALYs	costs (£)	QALYs	(£/QALY)
TS	No treatment	-3.18	£1,965	15.8			
	rhGH treatment	-2.24	£62,752	17.1	£60,787	1.28	£47,553
PWS	No treatment	-2.22	£2,646	17.4			
	rhGH treatment	-1.36	£67,794	17.9	£65,148	0.45	£144,050
CRI	No treatment	-2.99	£1,876	11.5			
	rhGH treatment	-2.17	£35,877	12.2	£34,001	0.74	£46,245
SGA	No treatment	-3.23	£2,432	16.8			
	rhGH treatment	-2.01	£34,431	18.4	£31,999	1.69	£18,980
SHOX-D	No treatment	-3.18	£2,646	16.6			
	rhGH treatment	-2.24	£53,434	17.9	£50,788	1.31	£40,531

The discount rates from the previous published HTA report (i.e. costs 6% and benefits 1.5%) were used. For all conditions, except PWS, the ICER reduced to less than £30,000 per QALY. See Table A5.

Table A5. (cf. Table 49) Cost effectiveness results with alternative discount rates

Condition	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)	cm gain	ICER (£/cm)
GHD	£32,407	2.49	£12,999	12.80	£2,532
TS	£55,753	2.49	£22,358	9.30	£5,995
PWS	£58,075	0.79	£73,836	11.10	£5,232

CRI	£31,609	1.22	£25,804	9.20	£3,436
SGA	£29,362	1.57	£18,690	3.30	£8,898
SHOX-D	£45,937	2.05	£22,436	6.30	£7,292

One-way deterministic sensitivity analyses were performed, in which model parameters were systematically and independently varied, using a realistic minimum and maximum value. See section 4.6.1 for details. The costs effectiveness results remain fairly sensitive to the variation in parameters included in the deterministic sensitivity analysis. For all the conditions, the model results remain most sensitive to treatment start age and length, compliance and utility gain. The sensitivity analysis for the cost was rerun between £18.00 and £23.18 to reflect the new prices given in the BNF 58. Tables A6-A11 report the results of the updated deterministic sensitivity analyses for the conditions for the most influential parameters.

The deterministic sensitivity results for GHD are shown in Table A6. The results were most sensitive to dosage and varied between £21,379 and £35,917 per QALY gained.

Table A6. (cf. Table 50) Deterministic sensitivity analyses for GHD

Parameter	Baseline	Upper value	Lower value	Upper value ICER, (£/QALY)	Lower value ICER, (£/QALY)	Range
Dosage, mg/kg	0.025	0.039	0.023	£35,917	£21,379	£14,538
Utility gain per HtSDS	0.061	0.073	0.049	£19,776	£28,047	£8,271
Compliance	85%	100%	70%	£27,205	£19,187	£8,018
Treatment age, years	9 – 16	11 – 16	7 – 16	£19,279	£25,659	£6,380
Cost of rhGH treatment £/mg	£21.06	£23.18	£18.00	£25,483	£19,895	£5,588
Utility benefit spread over	2 years	1 year	7 years	£22,732	£25,638	£2,906
Standard mortality rate	2.4	2.4	1	£23,196	£22,184	£1,012

The deterministic sensitivity results for TS are shown in Table A7. The results were most sensitive to utility gain and varied between £33,131 and £48,778 per QALY gained.

Table A7 (cf. Table 51) Deterministic sensitivity analyses for TS

Parameter	Baseline	Upper value	Lower value	Upper value ICER, (£/QALY)	Lower value ICER, (£/QALY)	Range
Utility gain per HtSDS	0.061	0.073	0.049	£33,131	£48,778	£15,647
Treatment age, years	10 – 16	12 – 16	8 – 16	£30,505	£45,105	£14,600
Compliance	85%	100%	70%	£46,376	£32,544	£13,832

Dosage, mg/kg	0.045	0.05	0.4	£43,815	£35,106	£8,709
Utility benefit spread over	2 years	1 year	6 years	£38,672	£42,753	£4,081
Standard mortality rate	2.4	2.4	1	£39,460	£37,308	£2,152
Cost of rhGH treatment £/mg	£21.06	£23.18	£18.00	£43,405	£33,766	£9,639

The deterministic sensitivity results for PWS are shown in Table A8. The results were most sensitive to compliance and varied between £111,560 and £159,062 per QALY gained.

Table A8 (cf. Table 52) Deterministic sensitivity analyses for PWS

Parameter	Baseline	Upper value	Lower value	Upper value ICER, (£/QALY)	Lower value ICER, (£/QALY)	Range
Compliance	85%	100%	70%	£159,062	£111,560	£47,502
Cost of rhGH treatment £/mg	£21.06	£23.18	£18.00	£148,860	£115,755	£33,105
Treatment age, years	7 – 15	9 – 15	5 – 15	£119,036	£144,159	£25,123
Utility benefit spread over	2 years	1 year	8 years	£132,645	£152,275	£19,630
Dosage, mg/kg	0.035	0.035	0.03	£135,311	£116,084	£19,227
Utility gain per HtSDS	0.061	0.073	0.049	£128,030	£143,471	£15,441
Standard mortality rate	2.4	2.4	1	£135,311	£129,640	£5,671

The deterministic sensitivity results for CRI are shown in Table A9. The results were most sensitive to the treatment start age and length of treatment and varied between £28,080 and £46,477 per QALY gained.

Table A9 (cf. Table 53) Deterministic sensitivity analyses for CRI

Parameter	Baseline	Upper value	Lower value	Upper value ICER, (£/QALY)	Lower value ICER, (£/QALY)	Range
Treatment age, years	9 – 14	11 – 14	7 – 14	£28,080	£46,477	£18,397
Utility benefit spread over	2 years	1 year	5 years	£38,253	£54,105	£15,852
Utility gain per HtSDS	0.061	0.073	0.049	£33,188	£48,091	£14,903
Compliance	85%	100%	70%	£46,181	£32,365	£13,816
Standard mortality rate	21	21	1	£39,273	£28,820	£10,453
Cost of rhGH treatment £/mg	£21.06	£23.18	£18.00	£43,214	£33,585	£9,629
Dosage, mg/kg	0.045	0.05	0.04	£43,623	£34,923	£8,700

The deterministic sensitivity results for SGA are shown in Table A10. The deterministic sensitivity results were most sensitive to utility gain and varied between £27,641 and £41,180 per QALY gained.

Table A10. (cf. Table 54) Deterministic sensitivity analyses for SGA

Parameter	Baseline	Upper value	Lower value	Upper value ICER, (£/QALY)	Lower value ICER, (£/QALY)	Range
Utility gain per HtSDS	0.061	0.073	0.049	£27,641	£41,180	£13,539
Treatment age, years	8 – 14	10 – 14	6 – 14	£25,675	£37,921	£12,246
Compliance	85%	100%	70%	£38,888	£27,270	£11,618
Cost of rhGH treatment £/mg	£21.06	£23.18	£18.00	£36,392	£28,296	£8,096
Dosage, mg/kg	0.035	0.04	0.035	£37,781	£33,079	£4,702
Utility benefit spread over	2 years	1 year	6 years	£32,422	£35,818	£3,396
Standard mortality rate	2.4	2.4	1	£33,079	£31,657	£1,422

The deterministic sensitivity results for SHOX-D are shown in Table A11. The deterministic sensitivity results were most sensitive to utility gain and varied between £33,868 and £50,457 per QALY gained.

Table A11. (cf. Table 55) Deterministic sensitivity analyses for SHOX-D

Parameter	Baseline	Upper value	Lower value	Upper value ICER, (£/QALY)	Lower value ICER, (£/QALY)	Range
Utility gain per HtSDS	0.061	0.073	0.049	£33,868	£50,457	£16,589
Compliance	85%	100%	70%	£47,657	£33,406	£14,251
Treatment age, years	7 – 14	9 – 14	5 – 14	£33,787	£44,666	£10,879
Cost of rhGH treatment £/mg	£21.06	£23.18	£18.00	£44,596	£34,664	£9,932
Dosage, mg/kg	0.045	0.04	0.05	£36,045	£45,018	£8,973
Utility benefit spread over	2 years	1 year	7 years	£39,733	£44,729	£4,996
Standard mortality rate	2.4	2.4	1	£40,531	£38,822	£1,709

An additional scenario was undertaken for PWS cohort to take into account a possible reduction in BMI from rhGH. See section 4.6.1 of the main report for more details. The cost effectiveness of PWS would be £54,800 per QALY gained if the maximum reduction of BMI from the RCTs is used.

Probabilistic sensitivity analysis results:

For an updated willingness to pay at the price of £21.06 for all conditions, rhGH treatment had the probability of being cost effective at willingness to pay thresholds of £20,000, £30,000 and £50,000 per QALY as: 22%, 95% and 100% for GHD, 2%, 19% and 78% for

TS, 0%, 1% and 8% for PWS, 2%, 16% and 80% for CRI, 4%, 38% and 90% for SGA, and 1%, 15% and 74% for SHOX-D, respectively.

Table A12. Probabilistic results for the base case analysis

				Incremental	Incremental	ICERs
Condition		QALYs	Costs (£)	QALYs	Costs (£)	(£/QALY)
GHD	rhGH treatment	18.36	£37,719	1.543	35517	£23,019
	No treatment	16.81	£2,277			
TS	rhGH treatment	17.43	£62,128	1.546	60176	£38,931
	No treatment	15.89	£1,952			
PWS	rhGH treatment	18.19	£67,716	0.576	65076	£113,075
	No treatment	17.61	£2,639			
CRI	rhGH treatment	12.44	£35,702	0.868	33828	£38,951
	No treatment	11.57	£1,874			
SGA	rhGH treatment	18.06	£34,283	0.966	31854	£32,963
	No treatment	17.09	£2,429			
SHOX-D	rhGH treatment	18.07	£53,027	1.267	50394	£39,781
	No treatment	16.80	£2,633			

At the price of £18.00 for SHOXs, rhGH treatment had the probability of being cost effective at willingness to pay thresholds of £20,000, £30,000 and £50,000 per QALY as: 3%, 28% and 85% for SHOX-D, respectively.

PPRS price cut in 2010

A further 1.9% fall in the price of rhGH in 2010 is expected, due to a further round of PPRS price cuts in early 2010. If this price cut is taken into account then the average cost per drug for 6 manufacturers will be £20.66. Table A13 presents the base case cost effectiveness results as a result of this price decrease.

Table A13 Cost effectiveness results for the base case analysis at rhGH at a costs of £20.66

Condition		Costs (£)	QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)	cm gain	ICER (£/cm)
GHD	No rhGH treatment	£2,211	16.8					
	rhGH treatment	£37,365	18.4	£35,153	1.54	£22,764	12.80	£2,746
TS	No rhGH	£1,965	15.9					

	treatment							
	rhGH treatment	£61,605	17.4	£59,640	1.54	£38,716	9.30	£6,413
PWS	No rhGH treatment	£2,646	17.6					
	rhGH treatment	£66,563	18.1	£63,917	0.48	£132,755	11.10	£5,758
CRI	No rhGH treatment	£1,876	11.6					
	rhGH treatment	£35,234	12.4	£33,357	0.87	£38,530	9.20	£3,626
SGA	No rhGH treatment	£2,432	17.1					
	rhGH treatment	£33,826	18.1	£31,394	0.97	£32,454	3.30	£9,513
SHOX-D	No rhGH treatment	£2,646	16.8					
	rhGH treatment	£52,473	18.1	£49,827	1.25	£39,764	6.30	£7,909

Inc.= incremental

3. Summary of cost effectiveness: update

- From this independent model, the incremental cost per QALY estimates of rhGH compared to no treatment were: £23,196 for GHD, £39,460 for TS, £135,311 for PWS, £39,273 for CRI, £33,079 for SGA and £40,531 for SHOX-D. A further analysis was run for PWS which included a lifelong improvement of body composition of 1.8 kg/m^2 BMI and an associated additional utility of 0.031. Under these assumptions, the cost effectiveness of PWS reduced to £54,800 per QALY gained.
- The effect of a range of parameter values in the economic model were evaluated in sensitivity analyses. The model results were found to be most sensitive to the discount rate used. When the previous NICE discount rate of 6% for costs and 1.5% for benefits was used, all conditions were cost effective for a willingness to pay threshold of £30,000 per QALY apart from PWS. The model results are also sensitive to treatment start age and length, compliance and utility gain.
- A further reduction of 1.9% from the PPRS price cuts would reduce the incremental cost per QALY estimates of rhGH compared to no treatment to: £22,764 for GHD, £38,716 for TS, £132,755 for PWS, £38,530 for CRI, £32,454 for SGA and £39,764 for SHOX-D