Setmelanotide for treating obesity caused by LEPR or POMC deficiency [ID3764]

A Highly Specialised Technology Appraisal

Appendix #1

Summary of results of commercially-sensitive patient access scheme discounts, undiscounted quality-adjusted life-year weightings and probabilistic base cases

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Produced by

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1. INTRODUCTION

The purpose of this separate appendix is threefold, with the intention to:

- provide additional economic results to those in the ERG report, to include recently confirmed commercially-sensitive patient access scheme (PAS) discounts;
- present undiscounted quality-adjusted life-year (QALY) gains for the company and ERG base cases and scenario analyses, as these will determine the cost-effectiveness of the ICER and enable an assessment of whether QALY weighting can be considered in this appraisal; and
- present probabilistic incremental cost-effectiveness ratios (ICERs) for the ERG base cases.

2. METHODS

A number of additional tables have been generated by the inclusion of the recently confirmed PAS discount, as well as the reporting of undiscounted QALY gains and probabilistic ICERs. These are summarised in Table 1:

Table 1: Relevant tables included in appendix

Description	Location in appendix
Table 2: Company base case results with PAS discount applied (Overall population)	3.1.1.1
Table 3: Company scenario results with PAS discount applied	3.1.1.2
Table 4: ERG base case results with PAS discount applied (POMC paediatric)	3.1.1.3
Table 5: ERG base case results with PAS discount applied (POMC adult)	3.1.1.3
Table 6: ERG base case results with PAS discount applied (LEPR paediatric)	3.1.1.3
Table 7: ERG base case results with PAS discount applied (LEPR adult)	3.1.1.3
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Key: ERG, Evidence Review Group; LEPR, leptin receptor; PAS, patient access scheme; POMC, proopiomelanocortin; QALY, quality-adjusted life-year

3. RESULTS

This section contains the results from the company and ERG analyses incorporating the PAS discount, undiscounted QALY gains and probabilistic ERG base cases. As such, these Tables correspond to NICE Questions 4, 6 and 7. Please note, for completeness the ERG opted to provide incremental undiscounted QALY gains for all company and ERG scenarios (as opposed to the 4 most optimistic scenarios.

3.1.1. Company and ERG analyses including PAS discounts

3.1.1.1. Company base case results

As noted below, setmelanotide plus best supportive care (BSC) resulted in an undiscounted QALY gain of [redacted] compared to BSC alone. Based on the probabilistic analysis, the undiscounted QALY gain was similar at [redacted].

Table 2: Company base case results with PAS discount applied (Overall population)

	Total Costs	Total QALYs (Discounted)	Total QALYs (Undiscounted)	Total LYG	Incremental costs	Incremental QALYs (Discounted)	Incremental QALYs (Undiscounted)	Incremental LYG	Cost per QALY gained
	Company deterministic base case								
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£141,550 (Weighted average of POMC and LEPR)
BSC	£30,451	3.94	4.53	15.26	-	-		-	-
	Company probabilistic base case								
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£142,191

	Total Costs	Total QALYs (Discounted)	Total QALYs (Undiscounted)	Total LYG	Incremental costs	Incremental QALYs (Discounted)	Incremental QALYs (Undiscounted)	Incremental LYG	Cost per QALY gained
									(Weighted average of POMC and LEPR)
BSC	£30,388	3.95	4.57	15.30	-	-		-	-

Key: BSC, best supportive care; ERG, Evidence Review Group; LEPR, leptin receptor; LYG, life-year gain; PAS, patient access scheme; POMC, proopiomelanocortin; QALY, quality-adjusted life-year

3.1.1.2. Company scenario results

Setmelanotide plus BSC resulted in an undiscounted incremental QALY gain of [redacted] compared to BSC alone, in scenarios outlined in Table 3 . It should be noted that in the company's model, settings/inputs were not provided for certain scenario analyses and therefore the ERG were unable to ascertain undiscounted QALYs for these.

Table 3: Company scenario results with PAS discount applied

Scenario	Incremental LYs	Incremental QALYs (Discounted)	Incremental QALYs (Undiscounted)	Incremental Costs (£)	Cost per (discounted) QALY gained
Scenario 1: Uniform baseline BMI distribution	[redacted]	[redacted]	Settings/inputs not provided for these scenarios in company submission/ model	[redacted]	£139,095
Scenario 2: Distribution of POMC and LEPR based on trial population	[redacted]	[redacted]		[redacted]	£143,990
Scenario 3: Distribution of paediatric and adults based on trial population	[redacted]	[redacted]		[redacted]	£143,018

Scenario	Incremental LYs	Incremental QALYs (Discounted)	Incremental QALYs (Undiscounted)	Incremental Costs (£)	Cost per (discounted) QALY gained
Scenario 4: All responders have 1 level improvement in hyperphagia	[redacted]	[redacted]		[redacted]	£153,471
Scenario 5: Inclusion of only comorbidities that are prevalent in paediatric subjects	[redacted]	[redacted]	[redacted]	[redacted]	£141,369
Scenario 6: Incremental cost of BSC by BMI	[redacted]	[redacted]	[redacted]	[redacted]	£141,362
Scenario 7: Response rate stratified by age group based on trial	[redacted]	[redacted]	[redacted]	[redacted]	£141,631
Scenario 8: Hyperphagia mapping based on worst hunger score	[redacted]	[redacted]	Settings/inputs not provided for this scenario in company submission/ model	[redacted]	£179,686
Scenario 9: Increased comorbidity disutility by 50%	[redacted]	[redacted]	[redacted]	[redacted]	£141,728
Scenario 10: Account for acute cost of CV events	[redacted]	[redacted]	Settings/inputs not provided for this scenario in company submission/model	[redacted]	£141,567
Scenario 11: Utility scores decreased by 0.05 for BMI ≥ 50	[redacted]	[redacted]	[redacted]	[redacted]	£141,386

Key: BMI, body mass index; BSC, best supportive care; CV, cardiovascular; LEPR, leptin receptor; LYG, life-year gain; PAS, patient access scheme; POMC, proopiomelanocortin; QALY, quality-adjusted life-year

3.1.1.3. ERG base case results

In the POMC paediatric subgroup, setmelanotide plus BSC resulted in an undiscounted incremental QALY gain of [redacted] compared to BSC alone. Based on the probabilistic analysis, the undiscounted incremental QALY gain was broadly similar at [redacted].

Table 4: ERG base case results with PAS discount applied (POMC paediatric)

	Total Costs	Total QALYs (Discounted)	Total QALYs (Undiscounted)	Total LYG (Discounted)	Incremental costs	Incremental QALYs (Discounted)	Incremental QALYs (Undiscounted)	Incremental LYG	Cost per QALY gained
	ERG deterministic base case								
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£218,390
BSC	£41,504	4.85	8.54	17.34	-	-		-	
	ERG probabilistic base case								
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£218,878
BSC	£41,602	4.84	8.51	17.34	-	-		-	-

Key: BSC, best supportive care; LYG, life-year gain; PAS, patient access scheme; POMC, proopiomelanocortin; QALY, quality-adjusted life-year

In the POMC adult subgroup, setmelanotide plus BSC resulted in an undiscounted incremental QALY gain of [redacted] compared to BSC alone. Based on the probabilistic analysis, the undiscounted incremental QALY gain was similar at [redacted].

Table 5: ERG base case results with PAS discount applied (POMC adult)

	Total Costs	Total QALYs (Discounted)	Total QALYs (Undiscounted)	Total LYG (Discounted)	Incremental costs	Incremental QALYs (Discounted)	Incremental QALYs (Undiscounted)	Incremental LYG	Cost per QALY gained
	ERG deterministic base case								
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£242,240
BSC	£38,619	3.87	6.09	14.49	-	-		-	-
	ERG probabilistic base case								

	Total Costs	Total QALYs (Discounted)	Total QALYs (Undiscounted)	Total LYG (Discounted)	Incremental costs	Incremental QALYs (Discounted)	Incremental QALYs (Undiscounted)	Incremental LYG	Cost per QALY gained
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£242,966
BSC	£41,602	4.84	6.07	17.34	-	-		-	-

Key: BSC, best supportive care; LYG, life-year gain; PAS, patient access scheme; POMC, proopiomelanocortin; QALY, quality-adjusted life-year

In the LEPR paediatric subgroup, setmelanotide plus BSC resulted in an undiscounted incremental QALY gain of [redacted] compared to BSC alone. Based on the probabilistic analysis, the undiscounted incremental QALY gain was slightly lower at [redacted]

Table 6: ERG base case results with PAS discount applied (LEPR paediatric)

	Total Costs	Total QALYs (Discounted)	Total QALYs (Undiscounted)	Total LYG (Discounted)	Incremental costs	Incremental QALYs (Discounted)	Incremental QALYs (Undiscounted)	Incremental LYG	Cost per QALY gained
	ERG deterministic base case								
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£298,476
BSC	£27,166	2.51	3.63	11.39	-	-		-	-
	ERG probabilistic base case								
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£301,661
BSC	£27,202	2.52	3.63	11.39	-	-		-	-

Key: BSC, best supportive care; LEPR, leptin receptor; LYG, life-year gain; PAS, patient access scheme; QALY, quality-adjusted life-year

In the LEPR adult subgroup, setmelanotide plus BSC resulted in an undiscounted incremental QALY gain of [redacted] compared to BSC alone. Based on the probabilistic analysis, the undiscounted incremental QALY gain was similar at [redacted].

Table 7: ERG base case results with PAS discount applied (LEPR adult)

	Total Costs	Total QALYs (Discounted)	Total QALYs (Undiscounted)	Total LYG	Incremental costs	Incremental QALYs (Discounted)	Incremental QALYs (Undiscounted)	Incremental LYG	Cost per QALY gained
	ERG deterministic base case								
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£326,123
BSC	£21,396	1.22	1.54	6.52	-	-		-	-
	ERG probabilistic base case								
Setmelanotide + BSC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	£329,080
BSC	£21,413	1.22	1.53	6.52	-	-		-	-

Key: BSC, best supportive care; LEPR, leptin receptor; LYG, life-year gain; PAS, patient access scheme; QALY, quality-adjusted life-year

3.1.1.4. ERG scenario results

Based on exploratory analysis undertaken by the ERG in the POMC paediatric subgroup, Setmelanotide plus BSC resulted in an undiscounted incremental QALY gain of between [redacted] and [redacted] compared to BSC alone. The ERG noted that the scenario analysis which produces an undiscounted incremental QALY gain of [redacted] (reducing the time horizon to 20 years), is not considered to be particularly plausible and was conducted for exploratory purposes only.

Table 8: Exploratory analyses undertaken by the ERG – PAS applied (POMC paediatric)

Preferred assumption	Incremental costs	Incremental QALYs (undiscounted)	Incremental QALYs (Discounted)	ICER £/QALY (discounted)	% Change from ERG corrected company base case
ERG corrected company base-case	[redacted]	[redacted]	[redacted]	£154,265	-
Scenario 1: Modelled treatment effectiveness	[redacted]				
Alternative treatment efficacy assumption after trial duration (BMI regain)	[redacted]	[redacted]	[redacted]	£196,679	27%
Alternative treatment efficacy assumption after trial duration (BMI maintenance)	[redacted]	[redacted]	[redacted]	£154,366	0%
Treatment response rates and during trial efficacy based on BMI class	[redacted]	[redacted]	[redacted]	£155,019	0%
Reduced setmelanotide efficacy during trial period (BMI drops by [redacted] for POMC)	[redacted]	[redacted]	[redacted]	£156,699	2%
Scenario 2: 1% discontinuation rate per year throughout the lifetime horizon	[redacted]	[redacted]	[redacted]	£160,949	4%
Scenario 3: 3.5% discount rate for health outcomes	[redacted]	[redacted]	[redacted]	£270,333	75%
Scenario 4: Mortality	[redacted]				
No mortality benefit for responders	[redacted]	[redacted]	[redacted]	£195,000	26%
Non-responder and BSC life expectancy converted to equivalent HR multiplier	[redacted]	[redacted]	[redacted]	£153,710	0%
Company's base case mortality multiplier for non-responders and BSC decreased by 10%	[redacted]	[redacted]	[redacted]	£155,263	1%

Preferred assumption	Incremental costs	Incremental QALYs (undiscounted)	Incremental QALYs (Discounted)	ICER £/QALY (discounted)	% Change from ERG corrected company base case
Increased mean and maximum age life expectancy for non-responders and BSC (based on clinical opinion to ERG)	[redacted]	[redacted]	[redacted]	£154,802	0%
Scenario 5: Combined Hyperphagia scenario					
Alternative baseline distribution + transition probability (Severe to mild: 33.3% + disutility based on metreleptin appraisal (equivalent utility multiplier)	[redacted]	[redacted]	[redacted]	£244,166	58%
Scenario 6: 20-year time horizon	[redacted]	[redacted]	[redacted]	£259,792	68%
Scenario 7: Co-morbidity prevalence rates and disutility reduced					
Prevalence rates and disutilities decreased by 10%	[redacted]	[redacted]	[redacted]	£154,877	0%
Paediatric patients assumed to have 10% lower prevalence rates and disutility compared to adults.	[redacted]	[redacted]	[redacted]	£155,082	1%
Scenario 8: Setmelanotide dosing separately for paediatric and adults	[redacted]	[redacted]	[redacted]	£127,919	-17%

Key: BMI, body mass index; BSC, best supportive care; ERG, Evidence Review Group; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; LYG, life-year gain; PAS, patient access scheme; POMC, proopiomelanocortin; QALY, quality-adjusted life-year

Based on exploratory analysis undertaken by the ERG in the POMC adult subgroup, Setmelanotide plus BSC resulted in an undiscounted incremental QALY gain of between [redacted] and [redacted] compared to BSC alone. The ERG noted that the scenario analysis which produces an undiscounted incremental QALY gain of [redacted] (reducing the time horizon to 20 years), is not considered to be particularly plausible and was conducted for exploratory purposes only.

Table 9: Exploratory analyses undertaken by the ERG – PAS applied (POMC adult)

Preferred assumption	Incremental costs	Incremental QALYs (undiscounted)	Incremental QALYs (Discounted)	ICER £/QALY (discounted)	% Change from ERG corrected company base case
ERG corrected company base-case	[redacted]	[redacted]	[redacted]	£147,713	-
Scenario 1: Modelled treatment effectiveness					
Alternative treatment efficacy assumption after trial duration (BMI regain)	[redacted]	[redacted]	[redacted]	£189,988	29%
Alternative treatment efficacy assumption after trial duration (BMI maintenance)	[redacted]	[redacted]	[redacted]	£150,179	2%
Treatment response rates and during trial efficacy based on BMI class	[redacted]	[redacted]	[redacted]	£148,432	0%
Reduced setmelanotide efficacy during trial period (BMI drops by [redacted] for POMC)	[redacted]	[redacted]	[redacted]	£150,847	2%
Scenario 2: 1% discontinuation rate per year throughout the lifetime horizon	[redacted]	[redacted]	[redacted]	£160,949	2%
Scenario 3: 3.5% discount rate for health outcomes	[redacted]	[redacted]	[redacted]	£243,013	65%
Scenario 4: Mortality					
No mortality benefit for responders	[redacted]	[redacted]	[redacted]	£196,499	33%
Non-responder and BSC life expectancy converted to equivalent HR multiplier	[redacted]	[redacted]	[redacted]	£153,701	4%
Company's base case mortality multiplier for non-responders and BSC decreased by 10%	[redacted]	[redacted]	[redacted]	£155,174	5%

Preferred assumption	Incremental costs	Incremental QALYs (undiscounted)	Incremental QALYs (Discounted)	ICER £/QALY (discounted)	% Change from ERG corrected company base case
Increased mean and maximum age life expectancy for non-responders and BSC (based on clinical opinion to ERG)	[redacted]	[redacted]	[redacted]	£147,773	0%
Scenario 5: Combined Hyperphagia scenario					
Alternative baseline distribution + transition probability (Severe to mild: 33.3% + disutility based on metreleptin appraisal (equivalent utility multiplier)	[redacted]	[redacted]	[redacted]	£202,411	37%
Scenario 6: 20-year time horizon	[redacted]	[redacted]	[redacted]	£230,195	56%
Scenario 7: Co-morbidity prevalence rates and disutility reduced					
Prevalence rates and disutilities decreased by 10%	[redacted]	[redacted]	[redacted]	£148,842	1%
Paediatric patients assumed to have 10% lower prevalence rates and disutility compared to adults.	[redacted]	[redacted]	[redacted]	£148,432	0%
Scenario 8: Setmelanotide dosing separately for paediatric and adults	[redacted]	[redacted]	[redacted]	£143,156	-3%

Key: BMI, body mass index; BSC, best supportive care; ERG, Evidence Review Group; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; LYG, life-year gain; PAS, patient access scheme; POMC, proopiomelanocortin; QALY, quality-adjusted life-year

Based on exploratory analysis undertaken by the ERG in the LEPR paediatric subgroup, Setmelanotide plus BSC resulted in an undiscounted incremental QALY gain of between [redacted] and [redacted] compared to BSC alone. The ERG noted that the scenario analysis which produces an undiscounted incremental QALY gain of [redacted] (reducing the time horizon to 20 years), is not considered to be particularly plausible and was conducted for exploratory purposes only.

Table 10: Exploratory analyses undertaken by the ERG – PAS applied (LEPR paediatric)

Preferred assumption	Incremental costs	Incremental QALYs (undiscounted)	Incremental QALYs (Discounted)	ICER £/QALY (discounted)	% Change from ERG corrected company base case
ERG corrected company base-case	[redacted]	[redacted]	[redacted]	£133,528	-
Scenario 1: Modelled treatment effectiveness					
Alternative treatment efficacy assumption after trial duration (BMI regain)	[redacted]	[redacted]	[redacted]	£154,265	16%
Alternative treatment efficacy assumption after trial duration (BMI maintenance)	Not applicable for LEPR				
Treatment response rates and during trial efficacy based on BMI class	[redacted]	[redacted]	[redacted]	£133,528	0%
Reduced setmelanotide efficacy during trial period (BMI drops by [redacted] for LEPR)	[redacted]	[redacted]	[redacted]	£139,594	5%
Scenario 2: 1% discontinuation rate per year throughout the lifetime horizon	[redacted]	[redacted]	[redacted]	£144,810	8%
Scenario 3: 3.5% discount rate for health outcomes	[redacted]	[redacted]	[redacted]	£232,090	74%
Scenario 4: Mortality					
No mortality benefit for responders	[redacted]	[redacted]	[redacted]	£176,297	32%
Non-responder and BSC life expectancy converted to equivalent HR multiplier	[redacted]	[redacted]	[redacted]	£133,218	0%
Company's base case mortality multiplier for non-responders and BSC decreased by 10%	[redacted]	[redacted]	[redacted]	£134,086	0%

Preferred assumption	Incremental costs	Incremental QALYs (undiscounted)	Incremental QALYs (Discounted)	ICER £/QALY (discounted)	% Change from ERG corrected company base case
Increased mean and maximum age life expectancy for non-responders and BSC (based on clinical opinion to ERG)	[redacted]	[redacted]	[redacted]	£153,172	15%
Scenario 5: Combined Hyperphagia scenario					
Alternative baseline distribution + transition probability (Severe to mild: 33.3% + disutility based on metreleptin appraisal (equivalent utility multiplier)	[redacted]	[redacted]	[redacted]	£172,498	29%
Scenario 6: 20-year time horizon	[redacted]	[redacted]	[redacted]	£213,239	60%
Scenario 7: Co-morbidity prevalence rates and disutility reduced	[redacted]				
Prevalence rates and disutilities decreased by 10%	[redacted]	[redacted]	[redacted]	£133,321	0%
Paediatric patients assumed to have 10% lower prevalence rates and disutility compared to adults.	[redacted]	[redacted]	[redacted]	£133,564	0%
Scenario 8: Setmelanotide dosing separately for paediatric and adults	[redacted]	[redacted]	[redacted]	£172,290	29%

Key: BMI, body mass index; BSC, best supportive care; ERG, Evidence Review Group; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; LEPR, leptin receptor; LYG, life-year gain; PAS, patient access scheme; QALY, quality-adjusted life-year

Based on exploratory analysis undertaken by the ERG in the LEPR adult subgroup, Setmelanotide plus BSC resulted in an undiscounted incremental QALY gain of between [redacted] and [redacted] compared to BSC alone. The ERG noted that the scenario analysis which produces an undiscounted incremental QALY gain of [redacted] (reducing the time horizon to 20 years), is not considered to be particularly plausible and was conducted for exploratory purposes only.

Table 11: Exploratory analyses undertaken by the ERG – PAS applied (LEPR adult)

Preferred assumption	Incremental costs	Incremental QALYs (undiscounted)	Incremental QALYs (Discounted)	ICER £/QALY (discounted)	% Change from ERG corrected company base case
ERG corrected company base-case	[redacted]	[redacted]	[redacted]	£147,245	-
Scenario 1: Modelled treatment effectiveness					
Alternative treatment efficacy assumption after trial duration (BMI regain)	[redacted]	[redacted]	[redacted]	£147,71	0%
Alternative treatment efficacy assumption after trial duration (BMI maintenance)	Not applicable for LEPR				
Treatment response rates and during trial efficacy based on BMI class	[redacted]	[redacted]	[redacted]	£147,245	0%
Reduced setmelanotide efficacy during trial period (BMI drops by [redacted] for LEPR)	[redacted]	[redacted]	[redacted]	£153,408	4%
Scenario 2: 1% discontinuation rate per year throughout the lifetime horizon	[redacted]	[redacted]	[redacted]	£149,513	2%
Scenario 3: 3.5% discount rate for health outcomes	[redacted]	[redacted]	[redacted]	£233,697	59%
Scenario 4: Mortality					
No mortality benefit for responders	[redacted]	[redacted]	[redacted]	£198,546	35%
Non-responder and BSC life expectancy converted to equivalent HR multiplier	[redacted]	[redacted]	[redacted]	£149,612	2%
Company's base case mortality multiplier for non-responders and BSC decreased by 10%	[redacted]	[redacted]	[redacted]	£150,342	2%

Preferred assumption	Incremental costs	Incremental QALYs (undiscounted)	Incremental QALYs (Discounted)	ICER £/QALY (discounted)	% Change from ERG corrected company base case
Increased mean and maximum age life expectancy for non-responders and BSC (based on clinical opinion to ERG)	[redacted]	[redacted]	[redacted]	£166,731	13%
Scenario 5: Combined Hyperphagia scenario					
Alternative baseline distribution + transition probability (Severe to mild: 33.3% + disutility based on metreleptin appraisal (equivalent utility multiplier)	[redacted]	[redacted]	[redacted]	£172,789	17%
Scenario 6: 20-year time horizon	[redacted]	[redacted]	[redacted]	£191,987	30%
Scenario 7: Co-morbidity prevalence rates and disutility reduced					
Prevalence rates and disutilities decreased by 10%	[redacted]	[redacted]	[redacted]	£145,936	-1%
Paediatric patients assumed to have 10% lower prevalence rates and disutility compared to adults.	[redacted]	[redacted]	[redacted]	£147,245	0%
Scenario 8: Setmelanotide dosing separately for paediatric and adults	[redacted]	[redacted]	[redacted]	£203,012	38%

Key: BMI, body mass index; BSC, best supportive care; ERG, Evidence Review Group; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; LEPR, leptin receptor; LYG, life-year gain; PAS, patient access scheme; QALY, quality-adjusted life-year