

Addendum to the “Comments on the Patient Access Scheme, and responses to the ERG report and Appraisal committee document” produced by the ERG

This document provides additional details for the sensitivity analyses presented in Tables 5 and 6 of the ERG’s ‘Comments’ document. This document also provides additional sensitivity analyses produced in response to requests made during the lead team meeting held on the 27th October 2010. During this meeting a request was made for additional information to explore the impact of the Manufacturer’s assumptions about the extrapolation of short-term data on the duration of response to estimate the mean duration of response to romiplostim over the remainder of a patient’s lifetime.

Additional details on sensitivity analyses conducted: Impact of changes when conducted as one-way sensitivity analyses rather than multi-way sensitivity analyses.

Non-splenectomised patients

a) Base case analysis

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████			
QALYs	██████	██████	£37,561	1.51	£24,795

	With romiplostim	Without romiplostim	Difference
Life years	22.91	20.10	2.81
rescue meds used	69.24	89.59	-20.35
Times IVI g used	40.6	52.6	-11.95

b) Increased use of comparator treatments by 25%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£39,803	1.46	£27,254
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.11	20.38	2.73
rescue meds used	67.94	88.33	-20.39
Times IVI g used	39.9	51.9	-11.97

c) Increasing response time by 50%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£41,196	1.45	£28,495
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.15	20.44	2.71
rescue meds used	67.06	87.28	-20.22
Times IVI g used	39.4	51.2	-11.87

d) Increasing response rates by 25%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£38,919	1.48	£26,228
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.02	20.25	2.77
rescue meds used	68.43	88.78	-20.35
Times IVI g used	40.2	52.1	-11.95

e) Use of rescue medications reduced to 80% of base case

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£55,418	1.57	£35,248
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	22.76	19.84	2.92
rescue meds used	57.29	73.94	-16.65
Times IVI g used	33.6	43.4	-9.77

f) Use of alternative utility values

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£37,561	1.47	£25,565
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	22.91	20.10	2.81
rescue meds used	69.24	89.59	-20.35
Times IVI g used	40.6	52.6	-11.95

g) Worst case scenario: All those who withdraw before end of trial follow-up cease to respond to romiplostim

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£11,929	0.38	£31,601
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	20.77	20.10	0.67
rescue meds used	86.83	89.59	-2.77
Times IVI g used	51.0	52.6	-1.62

Splenectomised Patients

a) Base case analysis

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£4,743	1.03	£4,615
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.88	21.96	1.92
rescue meds used	140.12	178.27	-38.15
Times IVI g used	89.6	114.0	-24.40

b) Increased use of comparator treatments by 25%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£8,597	0.99	£8,654
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	24.03	22.16	1.87
rescue meds used	136.92	174.94	-38.02
Times IVI g used	87.6	111.9	-24.32

c) Increasing response time by 50%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£10,534	0.98	£10,784
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	24.09	22.25	1.85
rescue meds used	135.16	172.89	-37.73
Times IVI g used	86.4	110.6	-24.13

d) Increasing response rates by 25%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	████████	████████	£6,992	1.00	£6,969
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.99	22.10	1.89
rescue meds used	138.19	176.27	-38.08
Times IVI g used	88.4	112.7	-24.35

e) Use of rescue medications reduced to 80% of base case

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	████████	████████	£37,309	1.16	£32,190
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.37	21.21	2.16
rescue meds used	110.71	140.09	-29.38
Times IVI g used	70.8	89.6	-18.79

f) Use of alternative utility values

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	████████	████████	£4,743	1.00	£4,757
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.88	21.96	1.92
rescue meds used	140.12	178.27	-38.15
Times IVI g used	89.6	114.0	-24.40

g) Worst case scenario: All those who withdraw before end of trial follow-up cease to respond to romiplostim

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs QALYs	██████	██████	£4,542	0.24	£18,647

	With romiplostim	Without romiplostim	Difference
Life years	22.39	21.96	0.43
rescue meds used	172.37	178.27	-5.90
Times IVI g used	110.2	114.0	-3.77

Additional data on life years and use of rescue medications for multi-way sensitivity analyses conducted

Non-splenectomised

a) Base case analysis

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs QALYs	██████	██████	£37,561	1.51	£24,795

	With romiplostim	Without romiplostim	Difference
Life years	22.91	20.10	2.81
rescue meds used	69.24	89.59	-20.35
Times IVI g used	40.6	52.6	-11.95

b) Increased use of comparator treatments by 25% & response time by 50%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£44,321	1.38	£32,198
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.40	20.79	2.61
rescue meds used	65.24	85.43	-20.19
Times IVI g used	38.3	50.1	-11.85

c) As above and also increasing response rates by 25%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£46,885	1.32	£35,413
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.58	21.05	2.53
rescue meds used	63.72	83.84	-20.11
Times IVI g used	37.4	49.2	-11.81

e) As above and the use of rescue medications reduced to 80% of base case

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£63,304	1.37	£46,213
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.45	20.83	2.62
rescue meds used	52.80	69.27	-16.47
Times IVI g used	31.0	40.7	-9.67

f) As above and use of alternative utility values

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£63,304	1.33	£47,591
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.45	20.83	2.62
rescue meds used	52.80	69.27	-16.47
Times IVI g used	31.0	40.7	-9.67

g) As above and all those who withdraw before end of trial follow-up cease to respond to romiplostim

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£17,834	0.32	£55,470
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	21.46	20.83	0.63
rescue meds used	67.01	69.27	-2.26
Times IVI g used	39.3	40.7	-1.33

Splenectomised

a) Base case analysis

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£4,743	1.03	£4,615
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	23.88	21.96	1.92
rescue meds used	140.12	178.27	-38.15
Times IVI g used	89.6	114.0	-24.40

b) Increased use of comparator treatments by 25% & response time by 50%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£15,774	0.93	£16,934
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	24.29	22.52	1.78
rescue meds used	130.78	168.24	-37.45
Times IVI g used	83.6	107.6	-23.95

c) As above and also increasing response rates by 25%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£19,960	0.89	£22,409
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	24.46	22.75	1.72
rescue meds used	127.22	164.41	-37.19
Times IVI g used	81.4	105.2	-23.79

e) As above and the use of rescue medications reduced to 80% of base case

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£49,347	1.00	£49,226
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	24.02	22.09	1.93
rescue meds used	100.79	129.53	-28.75
Times IVI g used	64.5	82.8	-18.39

f) As above and use of alternative utility values

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£49,347	0.97	£50,690
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	24.02	22.09	1.93
rescue meds used	100.79	129.53	-28.75
Times IVI g used	64.5	82.8	-18.39

g) As above and all those who withdraw before end of trial follow-up cease to respond to romiplostim

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£14,707	0.23	£64,646
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	22.53	22.09	0.44
rescue meds used	125.14	129.53	-4.39
Times IVI g used	80.0	82.8	-2.81

Additional sensitivity analyses to explore the impact of reducing the duration of response to romiplostim

As noted above the manufacturer has extrapolated the duration of response from relatively short-term follow-up data. This has been accomplished by fitting a weibull curve to the proportion of people responding at each follow-up period in the trials contributing data. However, the longer the follow-up period then the fewer study participants contributed to data. Consequently, at the longer follow-up period the proportions used to fit the model are based on a very small number of people and are imprecise. This imprecision has not been reflected in the estimation of mean duration of response.

In the sensitivity analyses reported below an exploratory analysis has been conducted to explore the impact of small to moderate (up to 30%) reductions in duration of response. These analyses have been repeated for both those who have not received a splenectomy and those that have had a splenectomy.

Non-splenectomised patients

a) Base case

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	£37,561	1.51	£24,795
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	22.91	20.10	2.81
rescue meds used	69.24	89.59	-20.35
Times IVI g used	40.6	52.6	-11.95

b) Reducing mean duration of response of romiplostim by 10%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	██████	██████	£24,938
QALYs	██████	██████			

	With romiplostim	Without romiplostim	Difference
Life years	22.73	20.10	2.63
rescue meds used	71.13	89.59	-18.46
Times IVI g used	41.8	52.6	-10.84

c) Reducing mean duration of response of romiplostim by 20%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs QALYs	████████	████████	████████	████████	£25,122

	With romiplostim	Without romiplostim	Difference
Life years	22.53	20.10	2.43
rescue meds used	73.10	89.59	-16.49
Times IVI g used	42.9	52.6	-9.68

d) Reducing mean duration of response of romiplostim by 30%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs QALYs	████████	████████	████████	████████	£25,363

	With romiplostim	Without romiplostim	Difference
Life years	22.31	20.10	2.21
rescue meds used	75.14	89.59	-14.45
Times IVI g used	44.1	52.6	-8.48

Splenectomised patients

a) Base case

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs QALYs	■	■	£4,743	1.03	£4,615

	With romiplostim	Without romiplostim	Difference
Life years	23.88	21.96	1.92
rescue meds used	140.12	178.27	-38.15
Times IVI g used	89.6	114.0	-24.40

b) Reducing mean duration of response of romiplostim by 10%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs QALYs	■	■	■	■	£5,026

	With romiplostim	Without romiplostim	Difference
Life years	23.75	21.96	1.79
rescue meds used	143.51	178.27	-34.76
Times IVI g used	91.8	114.0	-22.23

c) Reducing mean duration of response of romiplostim by 20%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs QALYs	■	■	■	■	£5,523

	With romiplostim	Without romiplostim	Difference
Life years	23.62	21.96	1.65
rescue meds used	147.06	178.27	-31.21
Times IVI g used	94.1	114.0	-19.96

d) Reducing mean duration of response of romiplostim by 30%

	With romiplostim	Without romiplostim	Marginal Costs	Marginal QALYs	ICER
Costs	██████	██████	██████	██████	£6,138
QALYs	██████	██████	██████	██████	

	With romiplostim	Without romiplostim	Difference
Life years	23.46	21.96	1.50
rescue meds used	150.74	178.27	-27.53
Times IVI g used	96.4	114.0	-17.61