

ADDENDUM
Evidence Review Group's Report
Certolizumab pegol for treating moderate to severe plaque
psoriasis

**Amended clinical evidence provided by the company following
the FAC and updated cost-effectiveness results**

1 ERG commentary on the amended network meta-analysis

As part of the factual inaccuracy (FAC) pro-forma response to the ERG report, the company provided further exploration into the discrepancies in the PASI response rates for guselkumab predicted in their network meta-analysis and what was reported in the clinical trials for guselkumab. The revised NMA resulted in an increase in the estimated PASI 75 responder rate for guselkumab from [REDACTED] to [REDACTED] which is aligned with the PASI 75 responder rate observed in the clinical trials for guselkumab.

The company provided the corrected WinBugs code and data input (Table 3 in the FAC document). The ERG had identified several problems with the previous WinBugs code the company provided in the company submission and in the points for clarification response. The code did not appear to be correct and so the ERG was unable to reproduce the results reported in the company submission.

The ERG assessed the new WinBugs code, however there was still an essential part of the code missing (initial values and the centering constant), which were requested and provided a few days later. The ERG made some revisions to the updated WinBugs code. The duplicate line defining $\theta_{[i,k,j]}$ with no regression was deleted and a redundant final bracket was removed. The duplicate line defining $\theta_{[i,k,j]}$ with no regression was deleted and a correction to the definition of z in the linear predictor was made to conform with the TSU code corrected in September 2016 (now $z[C[i,j+1]-1]$). A correction for extreme values of the probabilities when zero events are observed was also added. In addition, a redundant final bracket was removed. The results obtained by running the corrected code are different to those reported in Figure 19, 20 and 22 of the CS, with slightly lower predicted absolute PASI responses for both doses of certolizumab and higher predicted absolute PASI responses for all other treatments. Therefore, the treatment ranking has changed from the original ranking presented in the CS. Ixekimumab, guselkumab, brodalumab, secukinumab (300 mg) and infliximab now have a higher PASI 75 response rate than certolizumab (200mg) and certolizumab (400 mg).

The company also provided revised WinBugs data as part of the pro-forma response (Table 4 in the FAC document), which the company state resolves the discrepancy of the lower guselkumab PASI 75 response rate reported in the submission compared to published guselkumab results. The revised WinBugs data includes only VOYAGE 1 and VOYAGE 2 trials for guselkumab. Whereas, previously the NMA also included the X-PLORE phase II RCT, which was not included in the guselkumab submission. The company also said the revised WinBugs data includes PASI 50 response estimates for guselkumab from VOYAGE 1 and VOYAGE 2 as identified in the guselkumab company submission. Whereas, previously the PASI 50 estimates for guselkumab from these studies were imputed as the data was not publically available. The company state that this revised data results in higher estimated PASI 75 response rates for guselkumab that are in line with the published estimates. However, the VOYAGE 1 and VOYAGE 2 PASI 50 input data provided in the factual inaccuracy

pro-forma response is identical to the original data, indicating that there has not been an update to the PASI 50 data. Nevertheless, the results obtained using the original data for guselkumab produced a PASI 75 response rate that was higher than the PASI 75 response rate presented in the CS (██████ vs ██████, respectively). The updated guselkumab estimates are now in line with previously published estimates and are consistent with the clinical trial data for guselkumab.

Figure 1 Updated NMA: PASI 50 responder rates

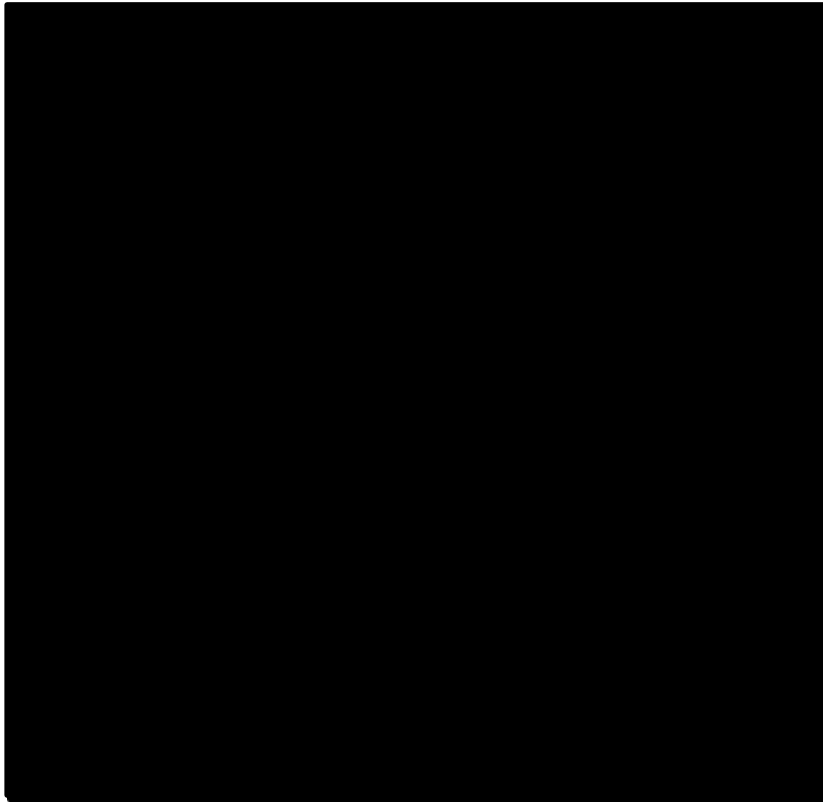


Figure 2 Updated NMA: PASI 75 responder rates

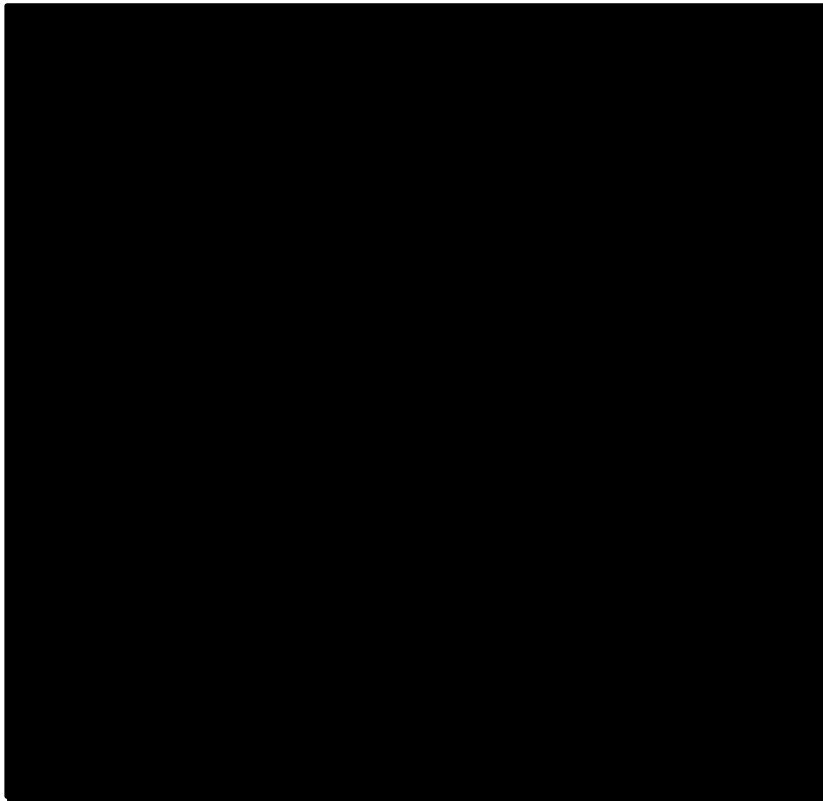
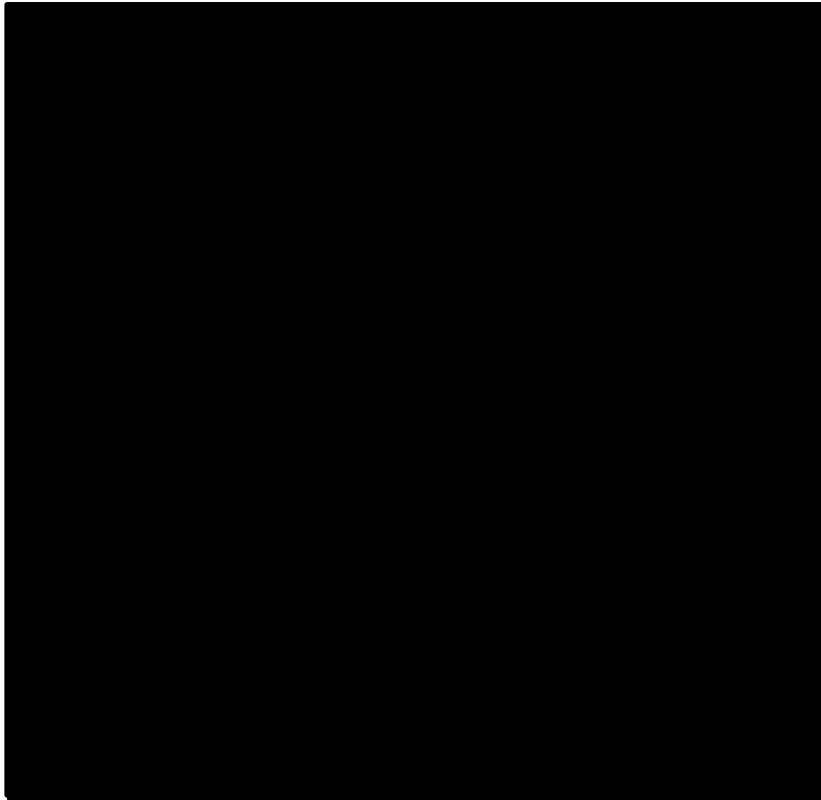


Figure 3 Updated NMA: PASI 90 responder rates



2 Impact on the ICER of additional clinical and economic analyses undertaken by the ERG

Following the updated NMA provided by the company in their Factual Accuracy Check document, the ERG incorporated the results of the NMA provided by the company into the ERG-corrected model. This section presents the updated results reflecting the impact of this new information.

The results included in this document supersede those presented in Section 6 of the original ERG report. Note that the results presented here include only the complex PAS discount for certolizumab. A confidential appendix to this addendum presents the results with the confidential PAS applied for the comparator treatments (brodalumab, guselkumab, ixekizumab and secukinumab).

The sections of this addendum are as follows:

- Section 3 Corrections and adjustments to the company's base case model
- Section 4.1 Treatment sequencing and net-monetary benefit analysis
- Section 4.2 Cost-effectiveness of BSC
- Section 4.3 Alternative time-horizons
- Section 4.4 Alternative HRQoL data sources
- Section 4.5 Biosimilar costs and uptake
- Section 4.6 Certolizumab pegol PASI response
- Section 4.7 Dose escalation scenario
- Section 4.8 Alternative positioning of biologics in treatment pathway
- Section 5.1 ERG alternative base-case – candidates for systemic biologic therapy
- Section 5.2 Dose escalation strategy
- Section 5.3 Candidates for systemic non-biologic therapy

In the majority of scenarios, the rankings are very similar to those of the original analysis, the only difference being the rankings for secukinumab and guselkumab are inverted.

3 ERG corrections and adjustments to the company's base case model

Table 1 presents the results of the ERG-corrected company base-case, updating the results of Table 35 in the original ERG report. The largest differences in the results following the updates were to secukinumab, guselkumab, brodalumab and ixekizumab. The ICER for these treatments was lower in the updated analysis and guselkumab was no longer dominated by certolizumab, due to the higher number of QALYs generated by these sequences as a result of the higher PASI response rates predicted by the new NMA for these comparators (Figure 1 to Figure 3).

The results of the scenario for candidates for systemic non-biologics (Table 3) are the same as were presented in the ERG report, as this scenario was based on clinical data observed in the CZP trials and not the NMA.

Table 1 Company base-case and ERG corrected results (ERG Report Table 35)

First line therapy	Subsequent sequence	Total		Incremental		ICER vs BSC	CZP200 ICER vs comparator
		QALYs	Costs	QALYs	Costs		
Company base-case analysis results							
Best supportive care	BSC, BSC, BSC, BSC	████	██████	-	-	-	£70,086
Certolizumab pegol 200mg	UST 90mg, INF 100mg, BSC, BSC	████	██████	████	██████	£70,086	-
Certolizumab pegol 400mg	UST 90mg, INF 100mg, BSC, BSC	████	██████	████	██████	£100,788	£710,883
Etanercept	UST 90mg, INF 100mg, BSC, BSC	████	██████	████	██████	£83,289	£11,471
Infliximab	UST 90mg, INF 100mg, BSC, BSC	████	██████	████	██████	£83,790	£36,171
Secukinumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	████	██████	£93,317	£598,382
Guselkumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	████	██████	£96,944	Dominant
Adalimumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	████	██████	£80,525	Dominant
Brodalumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	████	██████	£97,027	£720,462
Ustekinumab 90mg	ADA 40mg, INF 100mg, BSC, BSC	████	██████	████	██████	£68,027	Dominant
Ustekinumab 45mg	ADA 40mg, INF 100mg, BSC, BSC	████	██████	████	██████	£67,742	Dominant
Ixekizumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	████	██████	£95,529	£432,904
ERG-corrected company base-case analysis results							
Best supportive care	BSC, BSC, BSC, BSC	████	██████	-	-	-	£90,527

First line therapy	Subsequent sequence	Total		Incremental		ICER vs BSC	CZP200 ICER vs comparator
		QALYs	Costs	QALYs	Costs		
Certolizumab pegol 200mg	UST 90mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	-
Certolizumab pegol 400mg	UST 90mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	£731,555
Etanercept	UST 90mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	£9,943
Infliximab	UST 90mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	£88,926
Secukinumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	£452,740
Guselkumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	£325,428
Adalimumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	Dominant
Brodalumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	£555,547
Ustekinumab 90mg	ADA 40mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	Dominant
Ustekinumab 45mg	ADA 40mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	Dominant
Ixekizumab	UST 90mg, INF 100mg, BSC, BSC	████	██████	██	██████	████	£354,577
Abbreviations: QALY, quality-adjusted life years; ICER, incremental cost-effectiveness ratio; BSC, best supportive care; CZP, certolizumab pegol; ADA, adalimumab; BROD, brodalumab; ETN, etanercept; GUS, guselkumab; IFX, infliximab; IXE, ixekizumab; SEC, secukinumab; UST, ustekinumab							

Table 2 Company base-case (escalation strategy for inadequate responders) and ERG corrections (ERG Report Table 36)

First line therapy	Subsequent sequence	Total		Incremental		ICER vs BSC	ICER
		QALYs	Costs	QALYs	Costs		
Company base-case analysis results (escalation strategy)							
Adalimumab 40mg	ADA80, UST90, INF, BSC	████	██████	-	-	£98,035	-
Certolizumab pegol 200mg	CZP400, UST90, INF, BSC	████	██████	████	██████	£87,125	£36,638
ERG-corrected company base-case analysis results (escalation strategy)							
Adalimumab 40mg	ADA80, UST90, INF, BSC	████	██████	-	-	£110,051	-
Certolizumab pegol 200mg	CZP400, UST90, INF, BSC	████	██████	████	██████	£100,757	£36,036
Abbreviations: ERG, evidence review group; QALY, quality-adjusted life years; ICER, incremental cost-effectiveness ratio; BSC, best supportive care; CZP, certolizumab pegol; ADA, adalimumab; IFX, infliximab; UST, ustekinumab							

Table 3 Company base-case (candidates for systemic non-biologics) and ERG corrections (ERG Report Table 37)

First line therapy	Subsequent sequence	Total		Incremental		ICER
		QALYs	Costs	QALYs	Costs	
Company base-case analysis results (candidates for systemic non-biologics)						
Best supportive care	ADA40, UST90, INF, BSC	████	██████	-	-	-
Certolizumab pegol 200mg	UST90, INF, BSC, BSC	████	██████	████	████	£3,602
ERG-corrected company base-case results (candidates for systemic non-biologics)						
Best supportive care	ADA40, UST90, INF, BSC	████	██████	-	-	-
Certolizumab pegol 200mg	UST90, INF, BSC, BSC	████	██████	████	████	£6,757
Abbreviations: ERG, evidence review group; QALYs, quality-adjusted life years; ICER, incremental cost-effectiveness ratio; BSC, best supportive care; CZP, certolizumab pegol; ADA, adalimumab; IFX, infliximab; UST, ustekinumab						

4 Additional ERG Analyses

4.1 Treatment sequencing and net-monetary benefit analysis

Table 4 presents the results of ERG Scenario 1, where single-line head-to-head comparisons between sequences were implemented. This updates the results of Table 35 in the original ERG report.

In this scenario, the rankings are very similar to those of the original analysis, the only difference being the rankings for secukinumab and guselkumab are inverted.

Table 4 ERG Scenario 1: single lines of therapy using incremental net-benefit and rankings (ERG Report Table 38)

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
ERG Scenario 1: single-line head-to-head comparisons							
Certolizumab pegol 200mg	████	████	£0.00	2	£0.00	1	£45,023
Certolizumab pegol 400mg	████	██████	-£31,110.98	11	-£30,606.75	11	£130,304
Etanercept	████	██████	£964.00	1	-£898.47	2	£77,637
Infliximab	████	██████	-£25,563.60	10	-£24,994.44	10	£112,734
Secukinumab	████	██████	-£21,008.50	6	-£20,473.53	6	£100,732
Guselkumab	████	██████	-£22,023.95	7	-£21,217.60	7	£97,640
Adalimumab	████	██████	-£1,310.60	3	-£2,089.07	3	£59,719
Brodalumab	████	██████	-£24,815.01	9	-£24,304.45	9	£112,149
Ustekinumab 90mg	████	██████	-£2,855.47	5	-£3,053.61	4	£57,002

Ustekinumab 45mg	■■■■	■■■■■■■■	-£2,805.02	4	-£3,171.65	5	£59,181
Ixekizumab	■■■■	■■■■■■■■	-£23,224.93	8	-£22,462.80	8	£101,749
Abbreviations: BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; INB, incremental net monetary benefit							

4.2 Cost-effectiveness of BSC

Table 5 presents the results of ERG Scenario 2, where assumptions regarding quality of life and cost of BSC were assumed to be consistent with those used in a previous NICE appraisal of brodalumab. This updates the results of Table 39 in the original ERG report.

In the updated scenarios, the rankings of certolizumab rankings remain the same. Adalimumab becomes more cost-effective at a £20,000 threshold (becomes the second most cost-effective treatment). Similar to Scenario 1, the rankings for secukinumab and guselkumab are inverted.

Table 5 ERG Scenario 2: TA511 Assumptions applied (ERG Report Table 39)

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
ERG Scenario 2: TA511 assumptions							
Certolizumab pegol 200mg	■■■■	■■■■■■■■	£0.00	1	£0.00	1	£21,287
Certolizumab pegol 400mg	■■■■	■■■■■■■■	-£30,018.87	11	-£29,187.26	11	£75,355
Etanercept	■■■■	■■■■■■■■	-£3,184.08	3	-£6,278.09	5	£43,583
Infliximab	■■■■	■■■■■■■■	-£24,116.95	10	-£23,072.71	10	£63,033
Secukinumab	■■■■	■■■■■■■■	-£19,725.38	6	-£18,778.37	6	£55,997
Guselkumab	■■■■	■■■■■■■■	-£20,329.01	7	-£19,015.33	7	£54,807
Adalimumab	■■■■	■■■■■■■■	-£3,045.61	2	-£4,346.94	4	£30,739
Brodalumab	■■■■	■■■■■■■■	-£23,603.73	9	-£22,702.86	9	£63,218
Ustekinumab 90mg	■■■■	■■■■■■■■	-£3,315.64	4	-£3,651.30	2	£28,981
Ustekinumab 45mg	■■■■	■■■■■■■■	-£3,607.78	5	-£4,216.15	3	£30,294
Ixekizumab	■■■■	■■■■■■■■	-£21,512.93	8	-£20,211.39	8	£56,849
Key: BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; INB, incremental net monetary benefit							

4.3 Alternative time-horizons

Table 6 presents the results of ERG Scenarios 3 to 5, where the time horizon of the analysis was altered. This updates the results of Table 40 in the original ERG report

While there are some small differences to the rankings (the rankings for secukinumab and guselkumab are inverted), the same conclusions can be made from the updated analysis, that the NMB ranking framework is not sensitive to the duration of BSC.

Table 6 ERG Scenarios 3, 4, and 5: alternative time horizons (ERG Report Table 40)

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
ERG Scenario 3: 5 year time horizon							
Certolizumab pegol 200mg	■	■	£0.00	2	£0.00	1	£51,846
Certolizumab pegol 400mg	■	■	-£23,456.43	11	-£23,145.83	11	£153,690
Etanercept	■	■	£738.47	1	-£381.65	2	£88,330
Infliximab	■	■	-£19,859.88	10	-£19,455.19	10	£132,585
Secukinumab	■	■	-£16,704.41	6	-£16,337.84	6	£120,533
Guselkumab	■	■	-£17,330.11	7	-£16,830.78	7	£117,572
Adalimumab	■	■	-£1,478.77	3	-£1,957.32	3	£73,038
Brodalumab	■	■	-£18,894.81	9	-£18,542.31	9	£130,906
Ustekinumab 90mg	■	■	-£2,876.49	5	-£2,996.13	4	£70,189
Ustekinumab 45mg	■	■	-£2,836.38	4	-£3,062.52	5	£73,152
Ixekizumab	■	■	-£18,688.05	8	-£18,177.26	8	£122,751
ERG Scenario 4: 10 year time horizon							
Certolizumab pegol 200mg	■	■	£0.00	2	£0.00	1	£48,512
Certolizumab pegol 400mg	■	■	-£29,091.09	11	-£28,658.22	11	£140,715
Etanercept	■	■	£1,092.31	1	-£494.53	2	£82,780
Infliximab	■	■	-£24,064.03	10	-£23,555.70	10	£121,541
Secukinumab	■	■	-£19,887.32	6	-£19,414.36	6	£109,070
Guselkumab	■	■	-£20,830.52	7	-£20,136.73	7	£105,951
Adalimumab	■	■	-£1,280.41	3	-£1,947.83	3	£65,084
Brodalumab	■	■	-£23,254.14	9	-£22,801.58	9	£120,739
Ustekinumab 90mg	■	■	-£2,840.73	5	-£3,009.57	4	£62,242
Ustekinumab 45mg	■	■	-£2,778.47	4	-£3,093.26	5	£64,680
Ixekizumab	■	■	-£22,059.57	8	-£21,389.29	8	£110,343
ERG Scenario 5: 15 year time horizon							
Certolizumab pegol 200mg	■	■	£0.00	2	£0.00	1	£46,302
Certolizumab pegol 400mg	■	■	-£30,590.33	11	-£30,109.14	11	£133,967
Etanercept	■	■	£1,043.08	1	-£730.14	2	£79,501
Infliximab	■	■	-£25,178.59	10	-£24,629.19	10	£115,835
Secukinumab	■	■	-£20,723.20	6	-£20,208.31	6	£103,627
Guselkumab	■	■	-£21,727.46	7	-£20,957.37	7	£100,518
Adalimumab	■	■	-£1,284.47	3	-£2,026.99	3	£61,564

Brodalumab	■■■	■■■■■	£24,413.15	9	£23,921.34	9	£115,199
Ustekinumab 90mg	■■■	■■■■■	£2,846.72	5	£3,035.35	4	£58,798
Ustekinumab 45mg	■■■	■■■■■	£2,789.60	4	£3,139.47	5	£61,059
Ixekizumab	■■■	■■■■■	£22,932.50	8	£22,199.96	8	£104,710
Key: BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; INB, incremental net monetary benefit							

4.4 Alternative HRQoL data sources

Table 7 presents the results of ERG Scenarios 6 and 7, where alternative assumptions regarding HRQoL were explored. This updates the results of Table 42 in the original ERG report

In this scenario, the rankings are very similar to those of the original analysis, the only difference being the rankings for secukinumab and guselkumab are inverted.

Table 7 ERG Scenarios 6 and 7: Alternative HRQoL assumptions and sources (ERG Report Table 42)

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
ERG Scenario 6: Population limited to DLQI≥10							
Certolizumab pegol 200mg	■■■	■■■	£0.00	1	£0.00	1	£34,111
Certolizumab pegol 400mg	■■■	■■■■■	£30,808.79	11	£30,153.47	11	£98,940
Etanercept	■■■	■■■■■	£181.66	2	£2,616.96	2	£57,929
Infliximab	■■■	■■■■■	£25,236.71	10	£24,504.10	10	£85,750
Secukinumab	■■■	■■■■■	£20,699.76	6	£20,010.42	6	£76,592
Guselkumab	■■■	■■■■■	£21,547.17	7	£20,502.43	7	£74,264
Adalimumab	■■■	■■■■■	£1,781.31	3	£2,795.13	3	£45,034
Brodalumab	■■■	■■■■■	£24,523.47	9	£23,867.14	9	£85,291
Ustekinumab 90mg	■■■	■■■■■	£2,979.23	4	£3,239.26	4	£43,168
Ustekinumab 45mg	■■■	■■■■■	£3,024.86	5	£3,501.43	5	£44,742
Ixekizumab	■■■	■■■■■	£22,787.81	8	£21,807.12	8	£77,482
ERG Scenario 7: Equal utilities applied to biologics and BSC with population limited to DLQI≥10							
Certolizumab pegol 200mg	■■■	■■■	£0.00	2	£0.00	1	£49,928
Certolizumab pegol 400mg	■■■	■■■■■	£31,113.73	11	£30,610.88	11	£142,326
Etanercept	■■■	■■■■■	£1,059.34	1	£755.45	2	£99,227
Infliximab	■■■	■■■■■	£25,461.49	10	£24,841.26	10	£120,989
Secukinumab	■■■	■■■■■	£20,936.46	6	£20,365.48	6	£108,681
Guselkumab	■■■	■■■■■	£22,015.92	7	£21,205.55	7	£105,710
Adalimumab	■■■	■■■■■	£1,302.18	3	£2,076.43	3	£68,706
Brodalumab	■■■	■■■■■	£24,737.61	9	£24,188.35	9	£120,966

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
Ustekinumab 90mg	████	██████	-£2,842.68	5	-£3,034.43	4	£63,540
Ustekinumab 45mg	████	██████	-£2,804.65	4	-£3,171.10	5	£66,635
Ixekizumab	████	██████	-£23,139.60	8	-£22,334.80	8	£109,051
Key: BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; INB, incremental net monetary benefit							

4.5 Biosimilar costs and uptake

Table 8 presents the results of ERG Scenarios 8 to 10, where biosimilar costs for adalimumab, etanercept, and infliximab were applied. This updates the results of Table 43 in the original ERG report

In this scenario, the rankings are very similar to those of the original analysis for the majority of comparator sequences. In these scenarios, secukinumab and infliximab became more cost-effective than guselkumab. Any discount over 20% to the originator list price of adalimumab places it first in the NMB rankings at 20k and 30k. At a discount of 60%, the pairwise ICER of adalimumab versus BSC is £2,229.

Table 8 ERG Scenario 8, 9, and 10: Biosimilar costs applied for adalimumab, etanercept, and infliximab (ERG Report Table 43)

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
ERG Scenario 8: Biosimilar costs for etanercept, infliximab, 20% discount for adalimumab							
Certolizumab pegol 200mg	████	██████	£0.00	3	£0.00	3	£45,023
Certolizumab pegol 400mg	████	██████	-£31,110.98	11	-£30,606.75	11	£130,304
Etanercept	████	██████	£2,102.37	2	£239.90	2	£67,594
Infliximab	████	██████	-£21,124.58	7	-£20,555.41	7	£100,283
Secukinumab	████	██████	-£21,008.50	6	-£20,473.53	6	£100,732
Guselkumab	████	██████	-£22,023.95	8	-£21,217.60	8	£97,640
Adalimumab	████	██████	£2,938.71	1	£2,160.25	1	£40,555
Brodalumab	████	██████	-£24,815.01	10	-£24,304.45	10	£112,149
Ustekinumab 90mg	████	██████	-£2,855.47	5	-£3,053.61	4	£57,002
Ustekinumab 45mg	████	██████	-£2,805.02	4	-£3,171.65	5	£59,181
Ixekizumab	████	██████	-£23,224.93	9	-£22,462.80	9	£101,749
ERG Scenario 9: Biosimilar costs for etanercept, infliximab, 40% discount for adalimumab							
Certolizumab pegol 200mg	████	██████	£0.00	3	£0.00	3	£45,023
Certolizumab pegol 400mg	████	██████	-£31,110.98	11	-£30,606.75	11	£130,304

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
Etanercept	■■■■	■■■■■	£2,102.37	2	£239.90	2	£67,594
Infliximab	■■■	■■■■■	-£21,124.58	7	-£20,555.41	7	£100,283
Secukinumab	■■■	■■■■■	-£21,008.50	6	-£20,473.53	6	£100,732
Guselkumab	■■■	■■■■■	-£22,023.95	8	-£21,217.60	8	£97,640
Adalimumab	■■■■	■■■■■	£7,188.03	1	£6,409.56	1	£21,392
Brodalumab	■■■	■■■■■	-£24,815.01	10	-£24,304.45	10	£112,149
Ustekinumab 90mg	■■■■	■■■■■	-£2,855.47	5	-£3,053.61	4	£57,002
Ustekinumab 45mg	■■■■	■■■■■	-£2,805.02	4	-£3,171.65	5	£59,181
Ixekizumab	■■■	■■■■■	-£23,224.93	9	-£22,462.80	9	£101,749
Key: BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; INB, incremental net monetary benefit							

4.6 Certolizumab pegol PASI response

Table 9 presents the results of ERG Scenarios 11 and 12, where alternative PASI response rates for certolizumab were explored. This updates the results of Table 44 in the original ERG report

In this scenario, the rankings are very similar to those of the original analysis, the only difference being the rankings for secukinumab and guselkumab are inverted.

Table 9 ERG Scenarios 11 and 12: CIMPASI-1 and CIMPASI-2 PASI response rates (ERG Report Table 44)

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
ERG Scenario 11: CIMPASI-1 PASI response rates for certolizumab pegol							
Certolizumab pegol 200mg	■■■■	■■■■■	£0.00	2	£0.00	1	£47,413
Certolizumab pegol 400mg	■■■	■■■■■	-£31,830.98	11	-£30,802.91	11	£130,304
Etanercept	■■■■	■■■■■	£244.00	1	-£1,094.63	2	£77,637
Infliximab	■■■	■■■■■	-£26,283.61	10	-£25,190.60	10	£112,734
Secukinumab	■■■	■■■■■	-£21,728.50	6	-£20,669.69	6	£100,732
Guselkumab	■■■	■■■■■	-£22,743.95	7	-£21,413.76	7	£97,640
Adalimumab	■■■■	■■■■■	-£2,030.61	3	-£2,285.23	3	£59,719
Brodalumab	■■■	■■■■■	-£25,535.01	9	-£24,500.61	9	£112,149
Ustekinumab 90mg	■■■■	■■■■■	-£3,575.47	5	-£3,249.77	4	£57,002
Ustekinumab 45mg	■■■■	■■■■■	-£3,525.02	4	-£3,367.81	5	£59,181
Ixekizumab	■■■	■■■■■	-£23,944.93	8	-£22,658.96	8	£101,749
ERG Scenario 12: CIMPASI-2 PASI response rates for certolizumab pegol							
Certolizumab pegol 200mg	■■■■	■■■■■	£0.00	2	£0.00	1	£42,566

[illegible]

4.7 Dose escalation scenario

Table 10 presents the results of the ERG's dose escalation scenarios. This scenario updates Table 45 in the original ERG report. The results presented in Table 10 are very similar to those in the original analyses, as the PASI responses for certolizumab did not change a great deal after the NMA was amended. It should be noted that this is a comparison of two strategies – switching drug versus dose escalation. In the first strategy, patients are switched to ustekinumab upon partial or non-response on certolizumab 200mg at 16 weeks, this is compared to a strategy where these patients are switched to receive a higher dose (400mg q2w) dose of certolizumab instead.

Table 10 ERG Scenarios 13, 14, and 15: Dose escalation (ERG Report Table 45)

First line therapy	Subsequent sequence	Total		Incremental		ICER
		QALYs	Costs	QALYs	Costs	
ERG Scenario 13: Dose escalation (PASI<75 at 16w)						
Certolizumab pegol 200mg	UST90, BSC, BSC, BSC	████	██████	-	-	-
Certolizumab pegol 200mg	CZP400, BSC, BSC, BSC	████	██████	████	██████	Dominated
ERG Scenario 14: Dose escalation (PASI50-74 at 16w)						
Certolizumab pegol 200mg	UST90, BSC, BSC, BSC	████	██████	-	-	-
Certolizumab pegol 200mg	CZP400, BSC, BSC, BSC	████	██████	████	██████	£491,819
ERG Scenario 15: Dose escalation (PASI50-74 at 16w) and ██████████						

Certolizumab pegol 200mg	UST90, BSC, BSC, BSC	████	████	-	-	-
Certolizumab pegol 200mg	CZP400, BSC, BSC, BSC	████	████	████	████	£20,337
Abbreviations: QALY, quality-adjusted life years; PASI, psoriasis area severity index; BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; UST, ustekinumab.						

4.8 Alternative positioning of biologics in treatment pathway

In this scenario (corresponding to Table 46 in the original ERG report), the results are unchanged from the original analysis, as this scenario did not use clinical data drawn the NMA that was subsequently updated by the company.

Table 11 ERG Scenarios 16 and 17: Candidates for systemic non-biologics (ERG Report Table 46)

First line therapy	Subsequent sequence	Total		Incremental		ICER
		QALYs	Costs	QALYs	Costs	
ERG Scenario 16: Candidates for systemic non-biologics CZP 1 st vs CZP 2 nd line & sequencing						
Best supportive care	CZP200, UST90, INF, BSC	████	████	-	-	-
Certolizumab pegol 200mg	UST90, INF, BSC, BSC	████	████	████	████	£402,644
ERG Scenario 17: Candidates for systemic non-biologics CZP alternate positioning only						
Certolizumab pegol 200mg	BSC, BSC, BSC, BSC	████	████	-	-	-
Best supportive care	CZP200, BSC, BSC, BSC	████	████	████	████	Dominated
Abbreviations: QALY, quality-adjusted life years; BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; UST, ustekinumab; INF, infliximab.						

5 ERG alternative base-case

5.1 Candidates for systemic biologic therapy

The NMB rankings of guselkumab and secukinumab switch following the inclusion of the corrected NMA results. The significant increase in PASI 75 response rates for guselkumab results in a substantial increase in total costs, which outweigh the greater benefits in the updated NMA.

A fully incremental analysis of the company's and ERG's preferred base-cases including all PAS discounts is presented in the accompanying confidential appendix.

Table 12 ERG Alternative base-case (candidates for biologics) (ERG Report Table 47)

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
ERG Alternative base-case: Scenario 1+7+8 (0% adalimumab discount)							
Certolizumab pegol 200mg	■■■	■■■	£0.00	2	£0.00	2	£49,928
Certolizumab pegol 400mg	■■■	■■■■■	-£31,113.73	11	-£30,610.88	11	£142,326
Etanercept	■■■	■■■■■	£2,197.72	1	£382.92	1	£86,390
Infliximab	■■■	■■■■■	-£21,022.46	7	-£20,402.24	7	£107,625
Secukinumab	■■■	■■■■■	-£20,936.46	6	-£20,365.48	6	£108,681
Guselkumab	■■■	■■■■■	-£22,015.92	8	-£21,205.55	8	£105,710
Adalimumab	■■■	■■■■■	-£1,302.18	3	-£2,076.43	3	£68,706
Brodalumab	■■■	■■■■■	-£24,737.61	10	-£24,188.35	10	£120,966
Ustekinumab 90mg	■■■	■■■■■	-£2,842.68	5	-£3,034.43	4	£63,540
Ustekinumab 45mg	■■■	■■■■■	-£2,804.65	4	-£3,171.10	5	£66,635
Ixekizumab	■■■	■■■■■	-£23,139.60	9	-£22,334.80	9	£109,051
Abbreviations: BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; INB, incremental net monetary benefit							

The ERG's alternative base-case 2 as presented in Table 13 shows a similar drop in the ranking of guselkumab due to the aforementioned reasons, with infliximab now placed sixth rather than 8th/7th. The effect of a reduction in the list price of adalimumab between 20-60% is also presented, which again places certolizumab third in the ranking behind adalimumab and etanercept.

Table 13 Exploratory analysis on the ERG alternative base-case (ERG Report Table 48)

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
ERG Alternative base-case 2: Scenario 2 + 8							
Certolizumab pegol 200mg	■■■	■■■	£0.00	2	£0.00	1	£21,287
Certolizumab pegol 400mg	■■■	■■■■■	-£30,018.87	11	-£29,187.26	11	£75,355
Etanercept	■■■	■■■■■	-£2,045.72	3	-£5,139.73	5	£36,497
Infliximab	■■■	■■■■■	-£19,677.97	6	-£18,633.73	6	£55,306
Secukinumab	■■■	■■■■■	-£19,725.38	7	-£18,778.37	7	£55,997
Guselkumab	■■■	■■■■■	-£20,329.01	8	-£19,015.33	8	£54,807
Adalimumab	■■■	■■■■■	£1,203.66	1	-£97.67	2	£18,238
Brodalumab	■■■	■■■■■	-£23,603.73	10	-£22,702.86	10	£63,218
Ustekinumab 90mg	■■■	■■■■■	-£3,315.64	4	-£3,651.30	3	£28,981
Ustekinumab 45mg	■■■	■■■■■	-£3,607.78	5	-£4,216.15	4	£30,294
Ixekizumab	■■■	■■■■■	-£21,512.93	9	-£20,211.39	9	£56,849

Treatment (single line)	Inc. QALYs vs CZP	Inc. costs vs CZP	INB vs CZP at 20k	20k rank	INB vs CZP at 30k	30k rank	Pairwise ICER vs BSC
ERG Alternative base-case 3: Scenario 1+7+8 (20% adalimumab discount)							
Certolizumab pegol 200mg	████	████	£0.00	3	£0.00	3	£49,928
Certolizumab pegol 400mg	████	████	-£31,113.73	11	-£30,610.88	11	£142,326
Etanercept	████	████	£2,197.72	2	£382.92	2	£86,390
Infliximab	████	████	-£21,022.46	7	-£20,402.24	7	£107,625
Secukinumab	████	████	-£20,936.46	6	-£20,365.48	6	£108,681
Guselkumab	████	████	-£22,015.92	8	-£21,205.55	8	£105,710
Adalimumab	████	████	£2,947.14	1	£2,172.88	1	£46,659
Brodalumab	████	████	-£24,737.61	10	-£24,188.35	10	£120,966
Ustekinumab 90mg	████	████	-£2,842.68	5	-£3,034.43	4	£63,540
Ustekinumab 45mg	████	████	-£2,804.65	4	-£3,171.10	5	£66,635
Ixekizumab	████	████	-£23,139.60	9	-£22,334.80	9	£109,051
Abbreviations: BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; INB, incremental net monetary benefit							

5.2 Dose escalation strategy

As the update to the NMA had little effect upon the response rates for ustekinumab and certolizumab, the dose escalation strategy results are largely unchanged from the original ERG report. Table 14 includes an additional scenario that uses the ERG's preferred HRQoL data, and includes

████████████████████████████████████████████████████████████████████████████████

Table 14 ERG Alternative base-case (dose escalation) (ERG Report Table 49)

First line therapy	Subsequent sequence	Total		Incremental		ICER
		QALYs	Costs	QALYs	Costs	
ERG Alternative base-case (dose escalation): ERG Scenario 7 + 14						
Certolizumab pegol 200mg	UST90, BSC, BSC, BSC	████	████	-	-	-
Certolizumab pegol 200mg	CZP400, BSC, BSC, BSC	████	████	████	████	£533,154
ERG Alternative base-case (dose escalation): ERG Scenario 7 + 15 ██████████						
Certolizumab pegol 200mg	UST90, BSC, BSC, BSC	████	████	-	-	-
Certolizumab pegol 200mg	CZP400, BSC, BSC, BSC	████	████	████	████	£22,047
Abbreviations: BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; UST, ustekinumab.						

5.3 Candidates for systemic non-biologic therapy

As this scenario used trial-derived subgroup data for certolizumab pegol, the results are unchanged from those presented in Table 50 of the original ERG report.

Table 15 ERG Alternative base-case (candidates for non-biologics) (ERG Report Table 50)

First line therapy	Subsequent sequence	Total		Incremental		ICER
		QALYs	Costs	QALYs	Costs	
ERG Alternative base-case (candidates for non-biologics): ERG Scenario 7 + 17						
Best supportive care	CZP200, BSC, BSC, BSC	██████	██████	-	-	-
Certolizumab pegol 200mg	BSC, BSC, BSC, BSC	██████	██████	██████	██████	Dominated
Abbreviations: BSC, best supportive care; CZP, certolizumab pegol; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year						