Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (including a review of TA140 and TA262): Clinical effectiveness systematic review and economic model. Addendum 1: Re-analysis including proposed Patient Access Scheme for golimumab

A1. Introduction

A1.1 Context

This addendum provides a re-analysis of the Assessment Group model of infliximab, adalimumab and golimumab for the treatment of patients with moderately to severely active ulcerative colitis (UC) after the failure of conventional therapy, taking into account the proposed Patient Access Scheme (PAS) for golimumab. The proposed PAS involves the manufacturer providing the 100mg golimumab dose at the same price as the 50mg golimumab dose.

A1.2 Impact of the PAS on the per-patient cost of golimumab

Within the Assessment Group model, golimumab is assumed to be given as one dose of 200mg and one dose of 100mg during induction treatment. The incorporation of the PAS would halve the cost of induction therapy for all patients irrespective of body mass. Subsequent maintenance therapy for patients who achieve response or remission at induction is assumed to be given at a dose of 100mg every 4 weeks for patients with body mass greater than or equal to 80kg, or 50mg every 4 weeks for patients with body mass less than 80kg. The incorporation of the PAS would halve the cost of maintenance therapy for patients with a body mass greater than 80kg, but would not affect the cost of golimumab in patients with a body mass less than 80kg. Overall, the incorporation of the proposed PAS would mean that golimumab will cost the same for all patients irrespective of body mass.

A2. Methods for incorporating the PAS into the Assessment Group model

In order to reflect the impact of the proposed PAS within the Assessment Group's health economic analysis, the model was amended as follows:

Induction therapy

- The cost of 100mg golimumab was set equal to £762.97 (the same price as 50mg golimumab)
- The number of units of golimumab required during induction was changed to 3 x 100mg
- The relevant price parameter for golimumab was changed to 100mg golimumab

Maintenance therapy

- The number of units of golimumab required per 6-months of maintenance therapy changed to 6.52 x 100mg
- The relevant price parameter for 100mg golimumab was changed to 100mg golimumab.

All other model parameters remain as per the base case described in the full Assessment Report. It should be noted that golimumab is not licensed for paediatric patients hence the re-analysis presented here relates only to the adult UC population.

A3. Health economic results incorporating the proposed PAS

A3.1 Central estimates of cost-effectiveness (base case analysis - adults)

Table 1 presents the base case results generated using the probabilistic version of the model within an adult population in whom colectomy is an acceptable option. The base case analysis of the model suggests that colectomy is expected to produce 14.72 QALYs at a cost of approximately £41,900 over the patient's remaining lifetime. All medical options are expected to produce substantially fewer QALYs at a greater cost than colectomy, hence colectomy is expected to dominate infliximab, adalimumab, golimumab and conventional non-biologic treatments. Whilst the proposed PAS for golimumab reduces the expected cost of this option (from £88,108 to £82,625 over the patient's lifetime), golimumab remains dominated, hence the overall conclusions of the analysis are unaffected.

Table 1: Probabilistic cost-effectiveness results, base case analysis, adult patients in whom colectomy is an option (medical and surgical treatments), including proposed PAS for golimumab

Option	QALYs	Costs	Incremental QALYs	Incremental cost	ICER
Colectomy	14.72	£41,920.71	-	-	dominating
Adalimumab	10.83	£89,288.61	-	-	dominated
Infliximab	10.82	£94,664.81	-	-	dominated
Golimumab	10.65	£82,625.32	-	-	dominated
Conventional treatment	10.48	£71,592.46	-	-	dominated

Figure 1 presents cost-effectiveness acceptability curves (CEACs) for infliximab, adalimumab, golimumab, conventional treatment and colectomy for the adult UC population. Assuming a willingness to pay (WTP) threshold of £20,000 per QALY gained, the probability that colectomy produces the greatest amount of expected net benefit is approximately 0.97. The probability that any of the biologic treatments produce the greatest amount of expected net benefit at this threshold is approximately zero. Assuming a WTP threshold of £30,000 per QALY gained, the probability that colectomy produces the greatest amount of expected net benefit is approximately 0.96. The probability that any of the biologic treatments produce the greatest amount of expected net benefit at this threshold is approximately zero.

Figure 1: CEACs, base case analysis, adult patients in whom colectomy is an option (medical and surgical treatments), including proposed PAS for golimumab

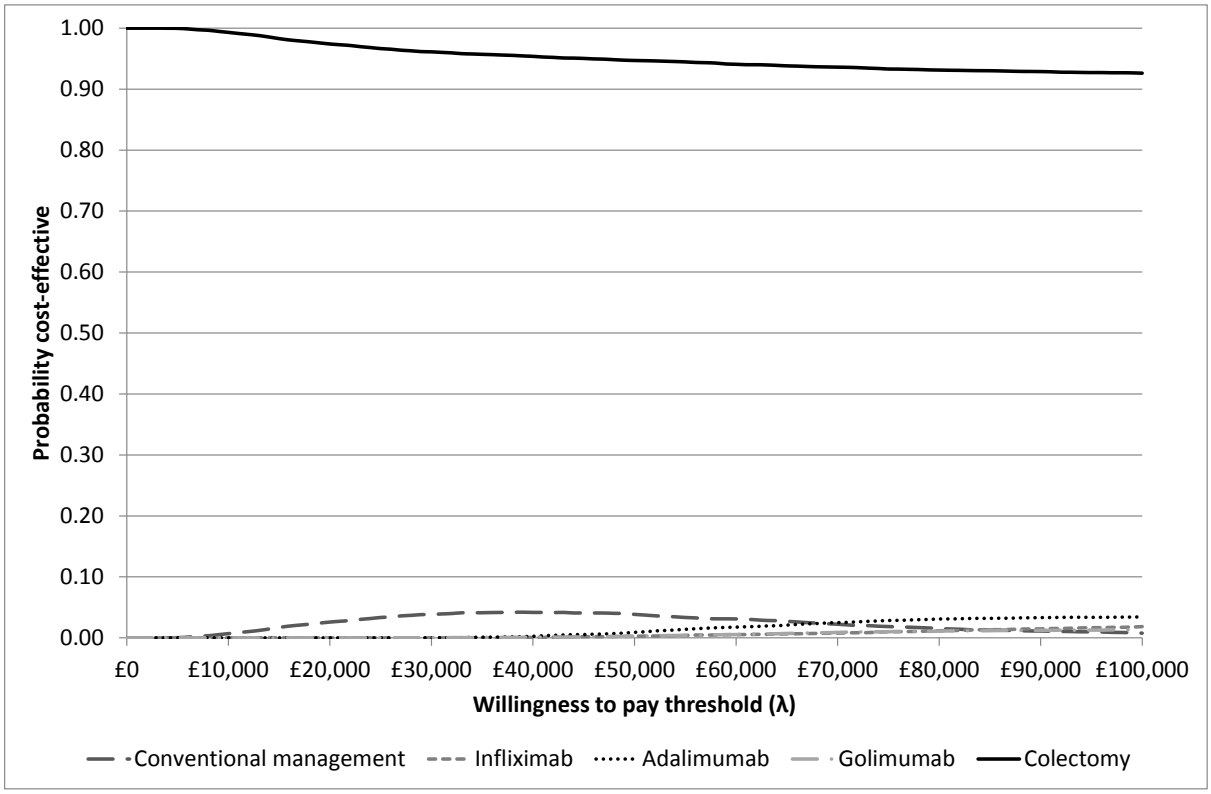


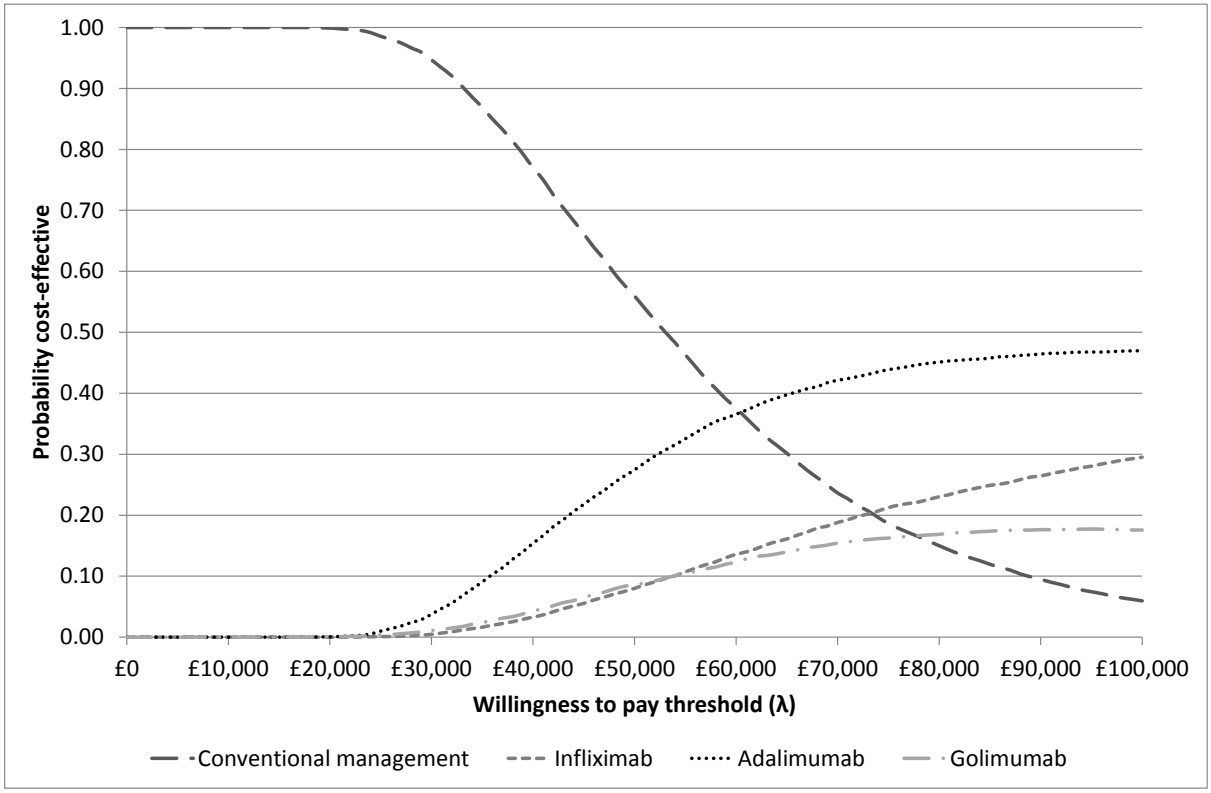
Table 2 presents the probabilistic base case model results within an adult population in whom colectomy is not an acceptable option, thus relevant treatment options are restricted to medical treatments only (infliximab, adalimumab, golimumab and conventional non-biologic treatments). The model results suggest that within this population infliximab is expected to be dominated by adalimumab, whilst golimumab is expected to remain ruled out due to extended dominance. The incremental cost-effectiveness of adalimumab versus conventional treatment is expected to be £50,624 per QALY gained. The proposed PAS reduces the expected cost of golimumab yet this option remains extendedly dominated, hence the conclusions of the analysis are unaffected.

Table 2: Probabilistic cost-effectiveness results, base case analysis, adult patients in whom colectomy is not an option (medical treatments only) , including proposed PAS for golimumab

Option	QALYs	Costs	Incremental QALYs	Incremental cost	ICER
Adalimumab	10.83	£89,288.61	0.35	£17,696.15	£50,623.66
Infliximab	10.82	£94,664.81	-	-	dominated
Golimumab	10.65	£82,625.32	-	-	ext dom
Conventional treatment	10.48	£71,592.46	-	-	-

Figure 2 presents CEACs for infliximab, adalimumab, golimumab and conventional treatment within a population in whom colectomy is not an option. Assuming a WTP threshold of £20,000 per QALY gained, the probability that conventional non-biologic treatment produces the greatest expected net benefit is approximately 1.0. Assuming a WTP threshold of £30,000 per QALY gained, the probability that conventional management produces the greatest expected net benefit is approximately 0.95.

Figure 2: CEACs, base case analysis, adult patients in whom colectomy is not an option (medical treatments only), including proposed PAS for golimumab



A3.2 Sensitivity analysis incorporating the proposed PAS for golimumab

Table 3 summarises the results of the economic analysis for the adult UC population based on the three alternative sensitivity analyses whereby different studies are included in, or excluded from, the network meta-analyses (NMA).

Table 3: Results of probabilistic NMA sensitivity analyses, including proposed PAS for golimumab

	Colectomy	Infliximab	Adalimumab	Golimumab	Conventional management
Adult population in whom colectomy is an option					
NMA sensitivity analysis #1 – ULTRA2 ITT population, excluding Suzuki et al					
ICER	dominating	dominated	dominated	dominated	dominated
P(optimal £20,000/QALY)	0.97	0.00	0.00	0.00	0.03
P(optimal £30,000/QALY)	0.96	0.00	0.00	0.00	0.04
NMA sensitivity analysis #2 - ULTRA2 anti-TNF-α naïve subgroup, including Suzuki et al					
ICER	dominating	dominated	dominated	dominated	dominated
P(optimal £20,000/QALY)	0.96	0.00	0.00	0.00	0.04
P(optimal £30,000/QALY)	0.94	0.00	0.00	0.00	0.06
NMA sensitivity analysis #3 – ULTRA2 ITT population, including Suzuki et al					
ICER	dominating	dominated	dominated	dominated	dominated
P(optimal £20,000/QALY)	0.95	0.00	0.00	0.00	0.05
P(optimal £30,000/QALY)	0.93	0.00	0.00	0.00	0.07
Adult population in whom colectomy is an not option					
NMA sensitivity analysis #1 – ULTRA2 ITT population, excluding Suzuki et al					
ICER	n/a	£251,121 [1]	£54,309 [2]	ext dom [3]	- [4]
P(optimal £20,000/QALY)	n/a	0.00	0.00	0.00	1.00
P(optimal £30,000/QALY)	n/a	0.00	0.02	0.01	0.98
NMA sensitivity analysis #2 - ULTRA2 anti-TNF-α naïve subgroup, including Suzuki et al					
ICER	n/a	£525,806 [1]	£56,656 [2]	ext dom [3]	- [4]
P(optimal £20,000/QALY)	n/a	0.00	0.00	0.00	1.00
P(optimal £30,000/QALY)	n/a	0.00	0.01	0.00	0.98
NMA sensitivity analysis #3 – ULTRA2 ITT population, including Suzuki et al					
ICER	n/a	dominated [2]	£56,013.52 [1]	ext dom [3]	- [4]
P(optimal £20,000/QALY)	n/a	0.00	0.00	0.00	1.00
P(optimal £30,000/QALY)	n/a	0.00	0.02	0.01	0.97

Ext dom – extendedly dominated; n/a – not applicable
Where different to the base case analysis, the QALY rank is shown in parentheses [ ]

In the circumstances whereby colectomy is an option, the three NMA sensitivity analyses produce very similar results to the base case analysis. In all three analyses, colectomy is consistently expected to dominate all medical treatment options, despite the inclusion of the proposed PAS for golimumab. Assuming a willingness to pay (WTP) threshold of £20,000 per QALY gained, the probability that colectomy produces the greatest amount of net benefit is expected to be between 0.95 and 0.97. Assuming a WTP threshold of £30,000 per QALY gained, the probability that colectomy produces the greatest amount of net benefit is expected to be between 0.93 and 0.96. Where colectomy is not an acceptable option, the results are influenced by which studies are included in the NMA, as the difference in effectiveness between adalimumab and infliximab is very small. In sensitivity analyses 1 and 2, infliximab is expected to produce slightly more QALYs than adalimumab, however the ICER for infliximab versus adalimumab is expected to be greater than £251,000 per QALY gained. In these sensitivity analyses, the ICER for adalimumab versus conventional non-biologic treatment is expected to be greater than £54,000 per QALY gained. In sensitivity analysis 3, infliximab is expected to be

ruled out due to simple dominance; the ICER for adalimumab versus conventional non-biologic treatments is expected to be approximately £56,000 per QALY gained. Despite the inclusion of the proposed PAS, golimumab is consistently expected to be ruled out of the analysis due to extended dominance.

Table 4 presents the results of a head-to-head analysis of golimumab, conventional treatments and colectomy.

Table 4: Head-to-head analysis – adult population, golimumab versus conventional management, including proposed PAS for golimumab

Option	QALYs	Costs	Incremental QALYs	Incremental cost	ICER
Golimumab versus conventional management and colectomy					
Colectomy	14.69	£41,962.22	-	-	dominating
Golimumab	10.16	£83,885.11	-	-	dominated
Conventional treatment	9.99	£73,321.49	-	-	dominated

The head-to-head analysis indicates that colectomy is expected to dominate golimumab and conventional non-biologic treatments. Within a population in whom colectomy is not an acceptable option, the incorporation of the proposed PAS for golimumab leads to an expected ICER for golimumab versus conventional treatment of £60,244 per QALY gained.

Table 5 presents the results of the other simple sensitivity analysis. The incorporation of the proposed PAS has no impact upon the results of these analyses.

Table 5: Other deterministic sensitivity analyses, including proposed PAS for golimumab

	Incremental cost per QALY gained				
Sensitivity analysis	Infliximab	Adalimumab	Golimumab	Conventional management	Colectomy
SA5: Base case using point estimates of parameters	dominated	dominated	dominated	dominated	dominating
SA6: Time horizon=20 years	dominated	dominated	dominated	dominated	dominating
SA7: Time horizon=10 years	dominated	dominated	dominated	dominated	dominating
SA8: Time horizon=5 years	dominated	dominated	dominated	-	£1,554
SA9: All utilities except post-surgical complications drawn from Swinburn *et al*†	£179,374 [1]	£80,315 [2]	ext dom [3]	ext dom [4]	-
SA10: Utilities of response/remission drawn from ACT1 trial (0.88, 0.82 for remission and response respectively)	dominated	dominated	dominated	dominated	dominating

Sensitivity analysis	Incremental cost per QALY gained				
	Infliximab	Adalimumab	Golimumab	Conventional management	Colectomy
SA11: Utilities of response/remission drawn from PURSUIT-Maintenance trial (0.89, 0.80 for remission and response respectively)	dominated	dominated	dominated	dominated	dominating
SA12: Relative risk of hospitalisation for golimumab vs conventional treatment assumed to be 1.0	dominated	dominated	dominated	dominated	dominating
SA13: UC health state resource use doubled	dominated	dominated	dominated	dominated	dominating
SA14: UC health state resource use halved	dominated	dominated	dominated	dominated	dominating
SA15: Probability of chronic pouchitis doubled	dominated	dominated	dominated	dominated	dominating
SA16: Probability of chronic pouchitis halved	dominated	dominated	dominated	dominated	dominating
SA17: Cost of surgery doubled	dominated	dominated	dominated	dominated	dominating
SA18: Cost of surgery halved	dominated	dominated	dominated	dominated	dominating
SA19: Probability of undergoing surgery in drug groups halved	dominated	dominated	dominated	dominated	dominating

Ext dom – extendedly dominated
** Excluded as adalimumab and golimumab have marketing authorisation in adult populations only*
† QALY rank shown in parentheses [ ]

A4. Summary

The proposed PAS for golimumab does not have an impact upon the expected cost-effectiveness of golimumab within the base case analysis as golimumab is ruled out due to dominance. Similarly, within most of the sensitivity analyses, the incorporation of the proposed PAS has no impact upon the cost-effectiveness of golimumab. Within the head-to-head analysis, the incremental cost-effectiveness of golimumab versus conventional treatment is reduced from £90,720 per QALY gained to £60,244 per QALY gained.