Assessment Group Report

Estimated cost per QALY ratios for bDMARD strategies following the correction of identified errors.

Produced by ScHARR, University of Sheffield

Authors Matt Stevenson, Professor of Health Technology Assessment, ScHARR

Allan Wailoo, Professor of Health Economics, ScHARR

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Background

On the 17th of March 2015 four documents were put on the NICE website.

These were:

- An updated version of the Assessment Group report having taken into consideration comments received on the previous report and executable model. [1]
- A brief summary of the aforementioned Assessment Group report. [2]
- A NICE decision support unit (DSU) report investigating the progression of disease on people with rheumatoid arthritis treated with non-biologic therapies. [3]
- A report indicating the impact on the incremental cost-effectiveness ratios (ICERs) that would be implied by the information provided in the NICE DSU report. [4]

Further comments were received in relation to these four documents and in addition the Assessment Group has identified an error in the method used to simulate HAQ progression whilst on cDMARDs. The purpose of this document is to provide the Appraisal Committee with updated results following correction of the errors. Given the change in the method used for simulating HAQ progression whilst on cDMARDs the base case values have become more favourable to bDMARDs. The base case results follow a discussion of the acknowledged errors. The error relating to the simulated HAQ progression relates only to the non-linear simulated HAQ progression. As such, the results from the linear analyses remain unchanged from that previously reported for populations 2 and 3 in the Assessment report. [1]

All Assessment Group preferred scenarios have been undertaken assuming that HAQ progression for patients on cDMARDs is non-linear as this hypothesis was supported within the recent DSU report.[3] The population has been divided into those patients with severe RA (defined as a DAS score >5.1) and those with moderate to severe RA (a DAS score between 3.2 and 5.1). For brevity those with moderate to severe RA will be referred to as having moderate RA. Only deterministic results are presented as previous evidence did not show a concern with non-linearity. The results from the linear model have been reproduced for completeness.

Note that further exploratory analyses on the assumed duration of HAQ progression, removal of rituximab and tocilizumab from the sequence and the impacts of incorporating biosimilars for infliximab are contained in a separate document.[5]

Acknowledged errors within the model

1) Implementation of the non-linear HAQ progression

In previous versions of the model when using the non-linear HAQ progression a person would have needed to have a predicted HAQ score of ≥ 0.125 in order to be considered for a HAQ increase, as HAQ is a discrete scale (ranging from 0 to 3) with step values of 0.125: where HAQ changes in excess of 0.125 were generated then the probability of moving two HAQ steps was calculated and applied. This method had the limitation that if an increase of 0.125 was not achieved then no HAQ progression was assumed possible, which would not be the case based on average HAQ increases. For example, were a HAQ increase of 0.100 simulated, it would imply that out of 125 identical patients, on average, 100 would have had a HAQ increase and 25 not. To rectify this limitation, the method used has been changed to estimate the change in HAQ in each six month period and calculate a probability that the patient changed HAQ score. This results in more HAQ progressions associated with cDMARD use, allows these progressions to occur sooner and for there to be a greater spread in the individual distributions of HAQ score, which can be important due to the non-linear assumptions of utility and cost with HAQ. In addition to this change, the values in the 15th year of simulated cDMARD use were slightly amended and visual basic for applications code was altered in order to ensure that patients who changed from methotrexate to non-biologic therapy maintained the correct duration on the predicted HAQ progression curve.

This problem has much less impact within the linear HAQ progression model as the change in HAQ was set to occur at regular intervals, for example every 2.778 years (0.125/0.045) whilst on cDMARDs, which had an annual HAQ increase of 0.045

2) Calculation Error within the life tables sheet.

Pfizer identified an error within the model, which is described below and has been amended. Pfizer stated that the impact of the error was minimal.

Within the 'Lifetables' worksheet for cell M25 the formula was:

=IF(basesex = 0, VLOOKUP(L25,$A$9:$I$110,3),VLOOKUP(L25,$A$9:$I$110,5))

whereas it should have been:

=IF(basesex = 0, VLOOKUP(L25,$A$9:$I$110,5),VLOOKUP(L25,$A$9:$I$110,9))

This formula should then be dragged down to cell M108

Impact of these errors:

These amendments lowered the results within the Assessment Group base case ICERs and in the exploratory analyses where it is assumed that only those patients with the greatest HAQ progression are treated. For definition of these latter groups refer to the DSU report.[3] In addition, scenarios assuming the discount rates used by NICE prior to 2008 and a mapping from HAQ to utility provided in Malottki at al.[6] have been re-analysed, although these are not the Assessment Group preferred options.

In all cases the ICER produced by the HAQ progression estimation estimated from the ERAS data is reduced as i) there are more costs associated with cDMARDs, due to the assumed relationship between HAQ score and costs incurred, and ii) the utility associated with cDMARDs is lower, due to the assumed relationship between utility and HAQ and pain. Results assuming a linear HAQ progression are provided for completeness although the Assessment Group does not believe these to be appropriate. These have not changed from those already reported.[1]

The results for populations 2 and 3 are provided in Table 1 and supersede all previous results. The fully incremental results for the eight scenarios in Table 1 are provided in Table 4 through to Table 13.

Updated results are also provided for those who cannot take methotrexate. These are summarised in Table 2 with fully incremental results provided in Table 14 and Table 15.

The same change in methodology was also made for the methotrexate naïve group (population 1). However, the sequences evaluated were changed to provide an estimation of methotrexate, intensive cDMARDs and non-biologic therapy sequence compared with an etanercept + methotrexate, rituximab + methotrexate, tocilizumab + methotrexate, methotrexate, intensive cDMARDs and non-biologic therapy sequence. The change was made to remove a second methotrexate trial between intensive cDMARDs and non-biologic therapy which was not deemed appropriate.

Within the linear model for population 1 it was now assumed that the linear progression would begin from the first cDMARD, rather than after intensive cDMARDs which had the impact of significantly reducing the ICER. Summarised results are presented in Table 3 with fully incremental results presented in Table 16 through to Table 19.

Table 1: Summary of median ICERs from the Assessment Group base case results and exploratory scenario analysis in people who can receive methotrexate

	Assumed HAQ progression	Base Case	Assuming patients with the greatest HAQ progression can be identified	Using discount rates of 6% for costs and 1.5% for benefits	Assuming utility mapping from Malottki et al.	Relationship between HAQ and pain taken from ERAS.
Population 2 (severe MTX –experienced)	ERAS	£41,600	£25,300	£27,700	£34,700	£51,000
	Linear	£37,900	-	£22,300	£32,400	£46,300
Population 3 (moderate MTX-experienced)	ERAS	£51,100	£28,500	£32,700	£36,300	£58,100
	Linear	£37,500	-	£21,800	£31,300	£48,300

All numbers rounded to the nearest £100

Table 2: Summary of median ICERs Assessment Group base case results for people who cannot receive methotrexate

	Assumed HAQ progression	Base Case			Assumed HAQ progression	Base Case
Population 2 (severe MTX –experienced)	ERAS	£48,300		Population 3 (moderate MTX-experienced)	ERAS	£58,800
	Linear	£39,600			Linear	£38,500

All numbers rounded to the nearest £100

Table 3: Summary of Assessment Group base case results for population 1 (severe RA methotrexate naïve)

	Assumed HAQ progression	Base Case			Assumed HAQ progression	Base Case
Those who can take methotrexate	ERAS	82,900		Those who cannot take methotrexate	ERAS	£81,600
	Linear	65,500			Linear	£75,100

All numbers rounded to the nearest £100

Table 4: Base case results – severe, MTX-experienced, RA population

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 41,647	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 39,142	£ 39,142
IFX + MTX	[redacted]	[redacted]	£ 39,884	Dominated
CTZ + MTX	[redacted]	[redacted]	£ 41,015	Ext Dominated
ADA + MTX	[redacted]	[redacted]	£ 42,194	Dominated
GOL + MTX	[redacted]	[redacted]	£ 42,087	Ext Dominated
ETN + MTX	[redacted]	[redacted]	£ 42,014	£ 74,290

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 5: Base case results – moderate, MTX-experienced, RA population

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 51,559	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 47,533	£ 47,533
IFX + MTX	[redacted]	[redacted]	£ 48,424	Dominated
ADA + MTX	[redacted]	[redacted]	£ 51,472	Dominated
CTZ + MTX	[redacted]	[redacted]	£ 50,467	Ext Dominated
GOL + MTX	[redacted]	[redacted]	£ 51,111	Ext Dominated
ETN + MTX	[redacted]	[redacted]	£ 51,436	£ 95,714

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 6: Results assuming only those with greatest HAQ progression are treated - severe MTX-experienced, RA population

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 25,638	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 23,361	£ 23,361
IFX + MTX	[redacted]	[redacted]	£ 23,783	Dominated
CTZ + MTX	[redacted]	[redacted]	£ 24,747	Ext Dominated
ADA + MTX	[redacted]	[redacted]	£ 25,267	Dominated
GOL + MTX	[redacted]	[redacted]	£ 25,344	Ext Dominated
ETN + MTX	[redacted]	[redacted]	£ 25,703	£ 59,496

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 7: Results assuming only those with greatest HAQ progression are treated - moderate MTX-experienced, RA population

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 29,206	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 26,136	£ 26,136
IFX + MTX	[redacted]	[redacted]	£ 26,641	Dominated
CTZ + MTX	[redacted]	[redacted]	£ 27,943	Ext Dominated
ADA + MTX	[redacted]	[redacted]	£ 28,524	Dominated
GOL + MTX	[redacted]	[redacted]	£ 28,688	Ext Dominated
ETN + MTX	[redacted]	[redacted]	£ 29,265	£ 77,020

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 8: Severe, MTX-experienced, RA population assuming discount rates of 6% for costs and 1.5% for health

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 28,495	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 25,618	£ 25,618
IFX + MTX	[redacted]	[redacted]	£ 26,007	Dominated
CTZ + MTX	[redacted]	[redacted]	£ 26,875	Ext Dominated
ADA + MTX	[redacted]	[redacted]	£ 27,750	Dominated
GOL + MTX	[redacted]	[redacted]	£ 27,682	Ext Dominated
ETN + MTX	[redacted]	[redacted]	£ 27,670	£ 50,770

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 9: Moderate, MTX-experienced, RA population assuming discount rates of 6% for costs and 1.5% for health

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 33,821	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 30,491	£ 30,491
IFX + MTX	[redacted]	[redacted]	£ 30,880	Dominated
ADA + MTX	[redacted]	[redacted]	£ 32,723	Ext Dominated
CTZ + MTX	[redacted]	[redacted]	£ 32,079	Ext Dominated
GOL + MTX	[redacted]	[redacted]	£ 32,788	Ext Dominated
ETN + MTX	[redacted]	[redacted]	£ 32,801	£ 57,940

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 10: Severe, MTX-experienced, RA population assuming the utility mapping from Malottki et al

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 34,734	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 32,613	£ 32,613
IFX + MTX	[redacted]	[redacted]	£ 33,193	Dominated
CTZ + MTX	[redacted]	[redacted]	£ 34,158	Ext Dominated
ADA + MTX	[redacted]	[redacted]	£ 35,234	Dominated
GOL + MTX	[redacted]	[redacted]	£ 34,912	Ext Dominated
ETN + MTX	[redacted]	[redacted]	£ 34,984	£ 61,719

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 11: Moderate, MTX-experienced, RA population assuming the utility mapping from Malottki et al

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 36,290	Ext Dominated
IFX + MTX	[redacted]	[redacted]	£ 34,666	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 34,147	£ 34,147
ADA + MTX	[redacted]	[redacted]	£ 36,848	Dominated
CTZ + MTX	[redacted]	[redacted]	£ 36,272	Ext Dominated
GOL + MTX	[redacted]	[redacted]	£ 36,573	Dominated
ETN + MTX	[redacted]	[redacted]	£ 36,834	£ 69,318

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 12: Severe, MTX-experienced, RA population assuming the relationship between HAQ and pain from ERAS.

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 50,985	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 47,972	£ 47,972
IFX + MTX	[redacted]	[redacted]	£ 48,393	Dominated
ADA + MTX	[redacted]	[redacted]	£ 51,133	Ext Dominated
CTZ + MTX	[redacted]	[redacted]	£ 49,945	Ext Dominated
GOL + MTX	[redacted]	[redacted]	£ 51,058	Ext Dominated
ETN + MTX	[redacted]	[redacted]	£ 51,019	£ 83,942

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 13: Severe, MTX-experienced, RA population assuming the relationship between HAQ and pain from ERAS.

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
TCZ + MTX	[redacted]	[redacted]	£ 57,687	Ext Dominated
IFX + MTX	[redacted]	[redacted]	£ 56,810	Ext Dominated
ABT i.v. + MTX	[redacted]	[redacted]	£ 55,790	£ 55,790
ADA + MTX	[redacted]	[redacted]	£ 58,483	Dominated
CTZ + MTX	[redacted]	[redacted]	£ 58,078	Ext Dominated
GOL + MTX	[redacted]	[redacted]	£ 59,136	Ext Dominated
ETN + MTX	[redacted]	[redacted]	£ 59,475	£ 88,312

ABT i.v. – abatacept intravenous; ADA – adalimumab; CTZ – certolizumab pegol; ETN – etanercept; GOL – golimumab; IFX – infliximab; MTX – methotrexate; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 14: Severe, MTX-experienced, RA population who cannot receive MTX.

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
SSZ	[redacted]	[redacted]	-	-
ADA	[redacted]	[redacted]	£ 48,306	Ext Dominated
ETN	[redacted]	[redacted]	£ 48,528	Ext Dominated
TCZ	[redacted]	[redacted]	£ 46,327	£ 46,327

ADA – adalimumab; ETN – etanercept; SSZ – sulfasalazine; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 15: Moderate, MTX-experienced, RA population who cannot receive MTX.

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
SSZ	[redacted]	[redacted]	-	-
ADA	[redacted]	[redacted]	£ 58,798	Ext Dominated
ETN	[redacted]	[redacted]	£ 59,036	Ext Dominated
TCZ	[redacted]	[redacted]	£ 58,673	£ 58,673

ADA – adalimumab; ETN – etanercept; SSZ – sulfasalazine; TCZ – tocilizumab
CPQ – cost per QALY gained. Ext - extendedly

Table 16: Severe, MTX-naive, RA population who can receive MTX.

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
ETN + MTX	[redacted]	[redacted]	£ 82,885	£ 82,885

ETN – etanercept; MTX – methotrexate
CPQ – cost per QALY gained. Ext - extendedly

Table 17: Severe, MTX-naive, RA population who can receive MTX – Linear model.

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
ETN + MTX	[redacted]	[redacted]	£ 65,453	£ 65,453

ETN – etanercept; MTX – methotrexate
CPQ – cost per QALY gained. Ext - extendedly

Table 18: Severe, MTX-naive, RA population who cannot receive MTX.

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
ETN + MTX	[redacted]	[redacted]	£ 83,034	£ 83,034

ETN – etanercept; MTX – methotrexate
CPQ – cost per QALY gained. Ext - extendedly

Table 19: Severe, MTX-naive, RA population who cannot receive MTX – Linear model.

First Intervention in the strategy	Discounted Costs	Discounted QALYs	CPQ compared with MTX strategy	Incremental CPQ
MTX	[redacted]	[redacted]	-	-
ETN + MTX	[redacted]	[redacted]	£ 64,567	£ 64,567

ETN – etanercept; MTX – methotrexate
CPQ – cost per QALY gained. Ext - extendedly

Conclusion

The updated base case Assessment Group ICERs for bDMARD strategies compared with a non-biologic therapy strategy within this report are markedly lower than the ICERs previously presented by the Assessment Group.[4] This change is due to a more appropriate method of simulating HAQ progression in cDMARDs. However, the base case ICERs remain greater than £40,000 per QALY gained for both the severe RA and moderate RA populations.

In the scenario where it is assumed possible that only those patients with the greatest HAQ progression whilst on cDMARDs would receive a bDMARD the ICER is approximately £25,000 for those with severe RA and approximately £28,000 for those with moderate RA. However, it is not known currently how to predict such patients a priori.

Using the discount rates recommended by NICE until 2008 reduces the ICER in the entire population to £27,700 for those with severe RA and to £32,700 for those with moderate RA.

Using a mapping between HAQ and utility taken from Malottki et al, the ICERs reduce but still remain above £30,000 for both groups. Using the relationship between HAQ and pain exhibited in ERAS the ICERs increase to greater than £50,000 for both populations.

The ICER increases for patients who cannot receive methotrexate and is over £45,000 for those with severe RA and over £55,000 for those with moderate RA.

The ICERs are greater for those patients who are methotrexate-naïve with severe RA and are in excess of £80,000 per QALY gained in this group.

Further exploratory analyses on the assumed duration of HAQ progression, removal of rituximab and tocilizumab from the sequence and the impacts of incorporating biosimilars for infliximab are contained in a separate document.

[1] Stevenson M, Archer R, Tosh J, Simpson E, Everson-Hock E, Stevens J et al. 2015 Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for the treatment of rheumatoid arthritis not previously treated with disease-modifying anti-rheumatic drugs and after the failure of conventional disease-modifying anti-rheumatic drugs only: systematic review and economic evaluation https://www.nice.org.uk/guidance/gid-tag313/documents/rheumatoid-arthritis-adalimumab-etanercept-infliximab-certolizumab-pegol-golimumab-abatacept-and-tocilizumab-review-appendix-1-updated-assessment-report2

[2] Stevenson M, Archer R, Tosh J, Simpson E, Everson-Hock E, Stevens J et al. 2015 Addendum to: Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for the treatment of rheumatoid arthritis not previously treated with disease-modifying anti-rheumatic drugs and after the failure of conventional disease-modifying anti-rheumatic drugs only: systematic review and economic evaluation. Amendments to the model inputs since the first NICE appraisal committee and how these changes impact on the estimated cost per QALY gained ratios. https://www.nice.org.uk/guidance/gid-tag313/documents/rheumatoid-arthritis-adalimumab-etanercept-infliximab-certolizumab-pegol-golimumab-abatacept-and-tocilizumab-review-assessment-report-addendum2

[3] Gibson L. Hernandez Alava M, Wailoo A. 2015 Progression of disease on people with rheumatoid arthritis treated with non biologic therapies. https://www.nice.org.uk/guidance/gid-tag313/documents/rheumatoid-arthritis-adalimumab-etanercept-infliximab-certolizumab-pegol-golimumab-abatacept-and-tocilizumab-review-decision-support-unit-report

[4] Stevenson M, Wailoo A. 2015 Assessing how the results from the DSU report on HAQ progression affect the cost per QALY gained ratios https://www.nice.org.uk/guidance/gid-tag313/documents/rheumatoid-arthritis-adalimumab-etanercept-infliximab-certolizumab-pegol-golimumab-abatacept-and-tocilizumab-review-appendix-1-updated-assessment-report2

[5] Stevenson M, Wailoo A. 2015 Exploratory analyses following comments received in April 2015 and further clarification on Assessment Group model parameter values.

[6] Malottki K., Barton P., Tsourapas A., Uthman A.O., Liu Z., Routh K. et al. Adalimumab, etanercept, infiximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a tumour necrosis factor inhibitor: A systematic review and economic evaluation. *Health Technology Assessment* 2011; 15(14)