National Institute for Health and Care Excellence
Centre for Health Technology Evaluation

Pro-forma Response

Executable Model

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) [ID695]

The economic model enclosed and its contents are confidential and are protected by intellectual property rights, which are owned by **School of Health & Related Research University, University of Sheffield (ScHARR)**. It has been sent to you for information only. It cannot be used for any other purpose than to inform your understanding of the appraisal. Accordingly, neither the model nor its contents should be divulged to anyone other than those individuals within your organisation who need to see to them to enable you to prepare your response. Those to whom you do show the documents must be advised they are bound by the terms of the Confidentiality Acknowledgement and Undertaking Form that has already been signed and returned to the Institute by your organisation.

You may not make copies of the file and you must delete the file from your records when the appraisal process, and any possible appeal, are complete. If asked, you must confirm to us in writing that you have done so. You may not publish it in whole or part, or use it to inform the development of other economic models.

The model must not be re-run for purposes other that the testing of its reliability.

Please set out your comments on reliability in writing providing separate justification, with supporting information, for each specific comment made. Where you have made an alteration to the model details of how this alteration was implemented in the model (e.g. in terms of programme code) must be given in sufficient detail to enable your changes to be replicated from the information provided. Please use the attached pro-forma to present your response.

Please prepare your response carefully. Responses which contain errors or are internally inconsistent (for example where we are unable to replicate the results claimed by implementing the changes said to have been made to the model) will be rejected without further consideration.

Results from amended versions of the model will only be accepted if their purpose is to test robustness and reliability of the economic model. Results calculated purely for the purpose of using alternative inputs will not be accepted.

No electronic versions of the economic model will be accepted with your response.

Responses should be provided in tabular format as suggested below (please add further tables if necessary).

July, 2014

Issue 1 Premodel sheet, range E120:E123 (baseline health state utilities)

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
The formula to calculate standard error from standard deviation is given as $SE/\sqrt{n}$. It seems that /5 should be put inside of the radical symbol.	/5 should be put inside of the radical symbol.	This will reduce the standard error, therefore the uncertainty around utility values.

Issue 2 Premodel sheet, cells C177 and D177 (rate of post-surgery complication)

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
In the Arai publication[1] there were 140 patients without complications and 156 with complications. For cells C177 and D177, it seems that alpha should be 156 instead of 140, and beta should be 140 instead of 156 (cf. Table 1 in the Arai publication). Furthermore, the reference year in the model was incorrect (2006 instead of 2005).	The calculation should be further reviewed and updated.	The post-surgery complication rate increases from 0.47 to 0.53 after the change.

[1] Arai K, Koganei K, Kimura H, Akatani M, Kitoh F *et al*. Incidence and outcome of complications following restorative proctocolectomy. Am J Surg. 2005; 190(1): 39-42.

Issue 3 Premodel sheet, row 188 (probability of peri-operative death)

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
It is understood that data were obtained from the UK IBD Audit report[Error! Bookmark not defined.]; however the AG report refers to an oral presentation which did not provide the same information. In section 1.3.1ii UC section in the Audit report, causes of death included heart disease, respiratory disease, post-operative complications, and gastrointestinal bleeding. It is unclear whether the first two causes can be considered as excess mortality associated with surgery. This approach risks double-counting the background mortality. Furthermore, a beta distribution was assumed and the beta term should be the number of non-events. However, in the model, the sample size was used.	Further justification on the calculation of excess mortality should be made available. The calculation process should be reviewed and updated.	The mean probability will slightly increase after implementing the changes.

Issue 4 Premodel sheet, cost of aminosalicylates

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
Costs are calculated using the lowest recommended dose, no justification is provided.	Justification should be made available.	Not applicable.

Issue 5 Trial data sheet, rows 53, 93-95 and 138-140, the choice of parametric distribution

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
The model assumes a gamma distribution if the number of patients in one health state is less than 340, otherwise a normal distribution. There is no explanation on the choice of such threshold or the assumption on the normal distribution. In the version of the model we received, there is no health state that has more than 340 patients (in the model that the evidence review groups disseminated), which means that a gamma distribution is always used.	Justification should be made available.	Not applicable.

Issue 6 Miscellaneous

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
Premodel sheet, cell C196: the number of mg in an adalimumab vial should be 40mg. Table 72 of AG report: adalimumab dosing is 160mg, 80 mg, and then two 40mg doses during the induction phase. The latter doses are missing from the table in the report but are considered in the model.	Update.	Not applicable. These issues do not affect the execution of the model however they should be addressed for the sake of consistency.