Dear Jo Annah

Thank you for sending the Response to clarification questions raised by the ERG and the NICE technical team. Following the review of your responses, there are a few more questions, listed below, which we would like clarified:

1) Section 6.3.1, Page 129. The trial by Kay et al. (2008) was used in the meta-analyses (as stated in Tables 18 and 19, pages 60-61) and in the mixed treatment comparison analysis (as stated in Table 54, pages 77-78) for the DMARD population. However, Section 6.3.1 states that only the GO-FORWARD and GO-AFTER trials were used for the clinical efficacy parameters in the cost-effectiveness analysis. Please clarify whether the Kay et al. (2008) trial was used in the cost-effectiveness analysis. If this trial was not used in the cost-effectiveness analysis, please provide a justification for this exclusion.

2) Clarification responses Question A10, Page 17. Table 20 of the clarification responses lists a number of adverse events trials as being 'included.' However, it is unclear how these trials were included in the assessment. Please state clearly how these identified adverse events trials were used in the assessment. Please also provide details of the study drug(s) and study design of these trials.

3) Section 5.8., Page 86 onwards. For all adverse events meta-analyses please state at what timepoint the outcomes are reported (eg. at 24 weeks?)

4) Clarification responses Question A35, Page 42. Please clarify in full the handling of data from:
i) patients who received rescue/early escape therapy and crossover therapy in the GO-FORWARD and GO-AFTER studies
ii) patients who received infliximab crossover therapy in the Kay et al. trial.

5) Section 5.3.7, Page 57. The MS states in the clinical effectiveness section: 'For golimumab, subgroup analyses were conducted based on demographic features, geographic region, baseline disease characteristics, and baseline medications for RA in GO-FORWARD and GO-AFTER trials...Separate post-hoc analyses were conducted comparing individual golimumab doses with placebo on some of the baseline demographics and disease characteristics.' Please state the location (section and page number) of the description and results of each of these subgroup analyses in the MS.

6) Section 5.6 and Appendix 17. The report states that when estimating the relative risks (RRs) for ACR20 in the mixed treatment comparison, the numbers achieving ACR 20 were estimated by taking the ACR50 responders away to identify the group who were exclusively ACR20 responders. However the source code in Appendix 17 suggests that this has not been undertaken. Please can you clarify if the source code in Appendix 17 is correct and whether the RRs for ACR20 are for only those patients who were an ACR20 and not an ACR50 responder.

Please can you provide a response to these questions by **17:00, 27 August 2010**.
If you have any queries, please do not hesitate to contact me.

Kind regards
Sally

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