Etanercept, Infliximab, and Adalimumab for the treatment of psoriatic arthritis (review)

York Assessment Group response to Appraisal Consultation Document

The Assessment Group (AG) welcomes the opportunity to comment on the ACD. Our comments fall into two main categories:

1) Inaccurate numerical estimates in the ACD.
2) Consideration of skin response to therapy.

These are detailed below.

1) Inaccurate numerical estimates in the ACD.

Firstly, the AG noticed that several QALY and ICER values reported in the ACD were taken from a version of the AG report (4th December 2009) that has been superseded: following comments from consultees, the analyses in this report were revised and made available to NICE in advance of the Appraisal Committee meeting. Although the values in the revised analyses may not change the guidance, the AG feels these should be updated for the sake of accuracy. We have marked relevant changes in an accompanying document.

Secondly, the 12-week PASI outcomes for the ADEPT trial mentioned in Section 4.1.12 are incorrect (the values reported in the ACD are 24-week data from this trial). We have corrected these values in the accompanying document.

2) Consideration of skin response to therapy

Psoriatic arthritis is a disease of the skin as well as the joints and in patients with significant skin disease its response to therapy should, if possible, be taken into consideration. Although Section 4.3.2 of the ACD correctly states that most RCTs were designed to detect an effect on joint disease (as measured by PsARC), the observed improvements in skin disease (as measured by PASI) are likely to be attributable to biologic therapy, as evidenced by the almost total lack of PASI 75 response among patients receiving placebo (e.g. Table 5.17 of the AG report).

The ACD guidance requires patients to withdraw from the initial biologic therapy if they do not achieve a PsARC response at 12 weeks. The evidence synthesis of the trial data suggests that a small proportion of patients (0% for etanercept but about 8-9% for infliximab and adalimumab) might achieve a response to PASI 75 but not achieve a PsARC response (Table 6.4 of AG report), and this is reflected in the decision model. The decision rule built into the base case of the decision model is that patients withdraw if they do not achieve a PsARC response, and this is reflected in the ACD guidance. However, a sensitivity analysis (number 35 in the revised cost-effectiveness analysis) finds that if patients are permitted to continue after 12 weeks if they achieve either a PASI 75 or a PsARC response then lifetime costs would be similar to the PsARC-only rule, but outcomes would be slightly superior. Therefore the model suggests that allowing patients to continue if they achieve *either* PsARC or PASI 75 is (slightly) more cost-effective than discontinuing for lack of PsARC response at 12 weeks.

The AG recognises that this conclusion is based on the assumptions that (a) patients who withdraw go to palliative care (ie no biologic) and (b) patients who do not achieve PsARC at 12 weeks would nevertheless receive some HAQ benefit and stop the progression of arthritis while on a biologic. These assumptions mean that, in the model, even a partial response on biologic is more effective and cost-effective than palliative care, as this is the only alternative. In reality, patients who do achieve PASI 75 but not PsARC may be better off withdrawing and trying another biologic, a scenario that the AG did not

consider in the main analysis. Furthermore, the AG recognises that extending the continuation rule to include PASI 75 is only expected to affect a small proportion of patients. The majority of patients (80% or more from Table 6.4 of the AG) who have a PASI 75 response on biologic therapy would be expected also to have a PsARC response. The AG does not suggest that the guidance necessarily ought to be amended, but rather submit this response in order to check that psoriasis has been taken into account when drafting the ACD.