National Institute for Health and Clinical Excellence

Etanercept, Infliximab and Adalimumab for the Treatment of Psoriatic Arthritis

Comments on the Assessment Report - Wyeth Pharmaceuticals

Points to Highlight	Section / Page Number	Consultee comment
Extent of redacted information	Throughout	Many of the references to the inputs, assumptions, model structure and results from the economic evaluation submitted by Wyeth have been unnecessarily redacted in the published Assessment Report. Appendix 2 of the Wyeth submission was marked as AIC to prevent the disclosure of the report in its entirety ahead of publication in a peer reviewed journal. It was not intended to restrict the abstraction and reporting of the requisite data to enable a comparison between the evaluation undertaken by the manufacturers and the Assessment Group. Apologies for any ambiguity.
Mode of action of biologics	Section 2.1 Page 20	The report refers to biologics targeting pathologic T-cell activity, whereas it is customary to refer to the three biologics licensed for psoriatic arthritis as targeting tumour necrosis factor (TNF).
Suggestion of higher incidence of TB reactivation with etanercept than adalimumab	Section 2.4 Page 22	Data from the BSRBR registry suggests that the risk of TB reactivation is higher with the monoclonal antibodies (adalimumab and infliximab) than with etanercept, which is not acknowledged within the Assessment Report. There are data from a number of European registries that suggest rates of TB reactivation are lower with etanercept than with the monoclonal antibodies : Dixon et al, (2009), examining data from rheumatology patients in the BSRBR, come to the conclusion that the rate of TB in patients with RA treated with anti-TNF therapy was 3-4 fold higher in patients receiving infliximab and adalimumab compared to etanercept. Data from the French RATIO database suggests that exposure to infliximab or adalimumab versus etanercept was an independent risk factor for TB (Tubach 2009) in their cohort of patients on anti-TNF treatment. BIOBADASER data (Gomez-Reino, 2007) suggests that, although the number of cases was very small for all three anti-TNFs, the incidence ratio was higher for both infliximab and adalimumab compared to etanercept. The Swedish ARTIS data also shows the same trends, with the risk of TB being higher with infliximab and adalimumab than etanercept. In addition, the recent Cochrane Review (Singh 2009) of biologics for rheumatoid arthritis, refers to a report from the FDA (2008) that states : “Data from clinical trials and preclinical studies suggest that the risk of reactivation of latent tuberculosis infection is lower with Enbrel than with

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		TNF-blocking monoclonal antibodies."
Anticipated costs of biological interventions	Section 3.3 Page 36	The differences in cost between etanercept and adalimumab are due to rounding errors in (hypothetical) cost of a single 25mg vial of etanercept (see Table 10.13.2). It is unclear how the 'annual costs thereafter' have been derived.
Exclusion of the PRESTA data	Section 5.2.2.1 Page 47	Given the need to consider a comprehensive evidence base reference should have been made to the randomised, multi-centre outpatient study conducted in 752 subjects with PsA (PRESTA), which supports and extends the information of the efficacy and safety of etanercept available from controlled trials.
Safety of biologics	Section 5.2.3.1 Page 78	The focus in this section are data observed from RCTs and some observational studies, which are within the boundaries of the inclusion criteria for the systematic review, however, there are data published from European registries that we believe should also be included in the review of adverse events with biologics: There is some reference to data from the Spanish BIOBADASER and German RABBIT registries already in this section, however, there is also pertinent data published from the BSRBR on serious infections and latent tuberculosis reactivation, and also data from the Swedish ARTIS registry and the French RATIO database. There has also recently been data presented on skin cancer from the BSRBR, at the ACR conference 2009. In addition, there is no reference to the recent Cochrane review (Singh et al, 2009) of biologics in rheumatoid arthritis, in which the authors conclude that there is less withdrawal due to adverse events with etanercept, compared with anakinra, infliximab and adalimumab.

Doses of etanercept	Section 10.13 Page 327	There is no evidence to suggest that the posology of etanercept in practice exceeds the licensed recommendation of 50mg per week in PsA patients. Thus it is unclear why it is assumed that 26 rather than 24 vials are used in subsequent 3 month (12 week) cycles.
Cost of infliximab infusion	Section 10.13 Page 329 Table 10.13.2	This report sources the cost of infusion as an elective inpatient excess bed day @ £144 whilst a recent NICE costing template (TA 126) utilised HRG H26 @ £793 per day. It would seem appropriate to use a common infusion cost across all appraisals.