

Public Summary Document

Product: Adalimumab, pre-filled syringe, 40 mg per 0.8 mL, Humira[®]
Sponsor: Abbott Australasia Pty Ltd
Date of PBAC Consideration: March 2006

1. Purpose of Application

This submission sought an extension of the current Pharmaceutical Benefits Scheme (PBS) Section 85 listing to include the treatment of severe, active psoriatic arthritis.

2. Background

The Pharmaceutical Benefits Advisory Committee (PBAC) had not previously considered a submission from the sponsor for listing the product for severe, active psoriatic arthritis.

3. Registration Status

The TGA approved indication includes the treatment of signs and symptoms of moderate to severely active psoriatic arthritis in patients where the response to previous DMARDs has been inadequate. Adalimumab is not indicated for the treatment of psoriasis that is not associated with manifestations of arthritic disease.

4. Listing Requested and PBAC's View

The submission requested an authority required listing which was consistent with the PBAC recommended restriction for etanercept in severe psoriatic arthritis.

See Recommendations and Reasons for PBAC's View.

5. Clinical Place for the Proposed Therapy

Patients with severe, active psoriatic arthritis have a reduced quality of life compared to the healthy population and the impact appears to be similar to that occurring in severe, active rheumatoid arthritis, for which adalimumab is already listed on the PBS.

Adalimumab, as a tumour necrosis factor (TNF) antagonist drug, represents an alternative treatment option for psoriatic arthritis to the currently available DMARDs.

6. Comparator

The submission nominated etanercept as the main comparator. The PBAC agreed this was appropriate.

7. Clinical Trials

The submission was based on an indirect comparison of adalimumab and etanercept using placebo as the common reference. Two randomised trials (M02-518 & M02-570) comparing adalimumab and placebo and two randomised trials (Mease et al, 2000 & 2004) comparing etanercept and placebo were presented. The submission also included a supplementary trial, M0-537 (open label single arm extension of trials M02-518 and M02-570).

None of the adalimumab trials were published at the time of submission. Both etanercept trials were published as follows:

Trial/First author	Protocol/Publication title	Publication citation
Mease P et al.	Etanercept in the treatment of psoriatic arthritis and psoriasis: A randomised trial.	Lancet 2000, 356(9227): 385-390.
Mease P et al.	Etanercept treatment of psoriatic arthritis: Safety, efficacy, and effect on disease progression.	Arthritis and Rheumatism 2004, 50(7): 2264-2272.

8. Results of Trials

With respect to the individual trials, both adalimumab and etanercept statistically significantly increased the proportion of patients achieving an ACR 20 (at 12 weeks) compared to the placebo. The same conclusion was also true with respect to other clinical outcome- ACR 20 (at 24 weeks), ACR 50, PsARC and PASI75. (ACR = American College of Rheumatology; PsARC = Psoriatic Arthritis Response Criteria; PASI = psoriasis area and severity index).

With respect to the indirect comparison of the pooled outcomes, there was no statistically significant difference across the differences in the proportions of patients achieving ACR 20 (at 12 weeks) responses between adalimumab versus placebo and etanercept versus placebo. The indirect comparison of differences in clinical effect of adalimumab versus placebo and etanercept versus placebo with respect to other endpoints (ACR 20 at 24 weeks, ACR 50 at 12 weeks and PsARC) also demonstrated an absence of statistical significance.

The toxicity profile for adalimumab in psoriatic arthritis was similar to that of etanercept in terms of general adverse events. However, it appeared that, compared with etanercept, treatment with adalimumab was associated with a reduced likelihood of having an injection-site reaction. This was likely to be due to the fact that adalimumab was administered less frequently than etanercept.

9. Clinical Claim

The submission claimed that based on the results of the key trials and the pooled analysis, adalimumab was at least as effective as the comparator (etanercept) in treating the symptoms of psoriatic arthritis, and appears more effective than etanercept in treating the skin manifestation of psoriasis. Further, treatment with adalimumab resulted in less injection site reactions than treatment with etanercept.

The PBAC accepted that adalimumab is no worse than etanercept in terms of effectiveness and safety when used in the treatment of psoriatic arthritis.

10. Economic Analysis

The submission presented a preliminary economic evaluation, which was a cost-minimisation analysis of adalimumab against etanercept. The equi-effective doses in the context of cost-minimisation were adalimumab 40mg every other week and etanercept 25mg twice weekly (the same as in rheumatoid arthritis).

11. Estimated PBS Usage and Financial Implications

The submission estimated the total number of patients to be < 10,000 in Year 3 of listing. This was considered to be a likely underestimate.

The submission estimated the financial impact on the PBS of adalimumab for severe, active psoriatic arthritis, assuming it shared the market evenly with etanercept, to be < \$10 million per year. These figures were based on the assumption that adalimumab would compete directly with etanercept. Therefore, no additional financial implications for the PBS budget were expected.

12. Recommendation and Reasons

The PBAC recommended listing on a cost-minimisation basis concluding that the indirect comparison showed that adalimumab is no worse than etanercept in terms of effectiveness and safety when used for the treatment of psoriatic arthritis. The equi-effective doses are adalimumab 40mg every second week compared with etanercept 25mg twice a week. The PBS restriction to apply to adalimumab should align as closely as possible to the recommended restriction for etanercept for the treatment of psoriatic arthritis, taking into account differences in the dosage regimens that apply.

The PBAC considered that it would be appropriate for interchangeability arrangements, similar to the current arrangements for the biological disease modifying antirheumatic drugs (DMARDs) in the treatment of rheumatoid arthritis and ankylosing spondylitis, to also apply to the bDMARDs for the treatment of psoriatic arthritis at the time more than one bDMARD is PBS listed for this condition. The PBAC considered that a 5 year exclusion period for each bDMARD included in the interchangeability arrangements, following failure to demonstrate a response as defined in the continuation restriction, would be appropriate.

The PBAC requested that the sponsor provide the PBAC with data, as it becomes available, relating to the cost-effectiveness of using adalimumab following failure to demonstrate a response to a previously administered bDMARD for the treatment of psoriatic arthritis.

The PBS restriction will be posted on the PBAC outcomes website when finalised.

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

The sponsor did include data on the comparative effectiveness of Humira[®] in treating the skin manifestation of psoriatic arthritis. This analysis used the Psoriasis Area Severity Index (PASI) as a measure of effectiveness. The PASI is a measure of the average redness, thickness and scaliness of psoriatic lesions. For patients with severe psoriasis a 75 percent improvement is seen as clinically meaningful. The PASI 75% was reported in the pivotal Humira[®] trial, M-02-518. The PASI 75% response in the trial was 49% - odds ratio of 21.37 (95%CI: 6.13, 74.56). The sponsor did however only seek a listing on the basis of cost-minimisation with etanercept and fully supports the decision of the PBAC.