**PUBLIC SUMMARY DOCUMENT**
**Product:** EFALIZUMAB, injection set containing 4 vials powder for injection 125 mg and 4 pre-filled syringes solvent 1.3 mL, Raptiva®
**Sponsor:** Serono Australia Pty Ltd
**Date of PBAC Consideration:** November 2005

## 1. Purpose of Application

This submission sought a Section 85 authority required listing for the treatment of severe chronic plaque psoriasis in a population who have been described as 'high needs' patients ie with refractory psoriasis.

## 2. Background

The Pharmaceutical Benefits Advisory Committee (PBAC) has rejected two previous applications to list efalizumab on the Pharmaceutical Benefits Scheme (PBS).

The first submission was rejected in November 2004 because, despite PBAC accepting that there was evidence of clinical effectiveness, the base case modelled incremental cost per extra discounted quality adjusted life year (QALY) gained was considered unacceptably high.

The second submission was considered at the July 2005 PBAC meeting. The PBAC again agreed that efalizumab is an effective drug in terms of a PASI 50% improvement. The PBAC also noted that by adjusting some of the parameters modelled in the submission there was a major improvement in the cost per QALY gained. Despite some concerns with the derivation of the utility values used in the economic model, the PBAC considered that the incremental cost per extra QALY gained was reasonably robust, although it would increase if a recommendation to list under section 85 of the PBS (i.e. as an authority required item) were made instead of section 100 prescribing. Although considering efalizumab effective and recognising a clinical need, the PBAC considered that the base case cost-effectiveness ratio was high and rejected the submission because of unacceptable cost-effectiveness.

## 3. Registration Status

Efalizumab is TGA registered for marketing in Australia for the 'Treatment of adult patients with moderate to severe chronic plaque psoriasis, who are candidates for phototherapy or systemic therapy. Safety and efficacy beyond 12 months have not been established.'

## 4. Listing Requested and PBAC's View

The submission requested an authority required listing under Section 85. Under the requested listing, initial treatment would be limited to adult patients with severe chronic plaque psoriasis who meet certain criteria including a failure to achieve an adequate response to specified psoriasis therapies and a PASI score > 15. Eligibility for continuing PBS-subsidised treatment would be contingent on the achievement and maintenance of a reduction of at least 75% in the PASI score

*For the PBAC's view see Recommendations and Reasons.*

## 5. Clinical Place for the Proposed Therapy

Psoriasis is a chronic, incurable inflammatory disorder that, although not life-threatening, can severely impact on a patient's quality of life. Current psoriasis therapies reduce the symptoms

for this chronic disease. Efalizumab is proposed as a treatment for patients with severe refractory psoriasis who have little or no alternative therapies.

## 6. Comparator

The submission nominated placebo as the comparator, which was considered appropriate by the PBAC.

## 7. Clinical Trials

The key clinical trial evidence reflects the specific population of severe psoriasis sufferers that would be eligible for subsidised treatment. The key clinical trial evidence came from a single double blind placebo controlled study (24011) of efalizumab 1mg/kg/week in "high needs" patients who were unresponsive, intolerant or contraindicated to ≥2 systemic therapies and had a baseline PASI >15. Longer term, 24 month, supportive evidence came from study 2390 and its open label extension 2391. The clinical trial evidence in the submission was the same as that submitted to the July 2005 PBAC meeting, and included data on PASI 75% improvement over baseline in the "high needs" population.

At the time of submission, two studies had been published as follows:

| Trial/first author | Protocol title | Publication citation |
|---|---|---|
| 2390/<br>1. Gordon<br>2. Papp<br>Ricardo | Efalizumab for patients with moderate to severe plaque psoriasis. | 1. JAMA 2003; 29: 3073 – 3080<br>2. Drugs of Today 40 (?) 00- 00<br>3. Cutis 2004; 74 (Sept): 193 – 200 |
| 2391/<br>Menter | Efficacy and safety observed during 24 weeks of efalizumab therapy in patients with moderate to severe psoriasis. | Arch Dermatol 2005; 141: 31-38 |

Results from Study 24011 were presented at the European Association of Dermatology and Venereology (EADV) Conference in Budapest in April 2004.

## 8. Results of Trials

In trial 24011 there was a statistically significant difference in the proportion of patients achieving at least a 50% reduction in their PASI score in the efalizumab group (approximately 50%) compared to the placebo group (approximately 13%).

There was also a statistically significant difference in the proportion of patients achieving at least a 75% reduction in their PASI score in the efalizumab group (approximately 29%) compared to the placebo group (approximately 3%).

## 9. Clinical Claim

The submission, as in the July 2005 submission, claimed that efalizumab was significantly more effective than placebo, but is more toxic, which reflects one of the categories for claims within the PBAC guidelines.

This claim has been previously accepted by PBAC.

## 10. Economic Analysis

An updated modelled economic evaluation was presented. The model differed from that presented in the July 2005 submission by adjusting a number of key parameters including

using a criterion for response of PASI $\geq$ 75% rather than PASI $\geq$ 50% after 12 weeks of initial treatment.

The base case cost modelled incremental cost per discounted quality adjusted life year (QALY) was lower than in the previous submission and within the range of $45,000 - $75,000.

*For PBAC's view see recommendation and reasons.*

## 11. Estimated PBS Usage and Financial Implications

The submission estimated that the likely number of patients to be eligible for treatment with efalizumab per year to be <10,000 at Year 4 with a financial cost per year to the PBS of between up to $30 - $60 million per year by Year 4 of listing.

## 12. Recommendation and Reasons

The PBAC recommended listing on the basis of acceptable cost-effectiveness compared to no systemic treatment in the defined population.

The PBAC considered that the incremental cost per extra QALY gained was still high but acceptable, and that treatment would now be targeted to a more severely affected patient group. Furthermore, with the exception of the impact of allowing subsequent re-treatment following failure to respond to efalizumab, the economic model had also adequately dealt with other known and important uncertainties by adopting assumptions which were accepted to be plausible or not biased in favour of efalizumab.

The PBAC recommended that, to achieve the dual objective of identifying severe refractory psoriasis, the restriction include the requirement for a baseline PASI score of greater than 15 and that this must be assessed following treatment with each of the three nominated therapies (methotrexate, cyclosporin and phototherapy) with dosage regimens and minimum durations as included in the requested restriction. It was agreed that failure to demonstrate a response to each of these three therapies would be demonstrated by the patient, at the time of application, still having a PASI score of greater than 15 despite previous treatment at the stated doses and duration of treatment. Consistent with the bDMARD rheumatoid arthritis restrictions, a patient can be exempted from demonstrating failure to any one of the three therapies in circumstances where that therapy is contraindicated or intolerance develops as specified in the requested restriction. In such circumstances, the patient must still have a PASI score of greater than 15, either to demonstrate failure to the remaining therapies, or in the particular circumstance of a patient who is contraindicated or intolerant of all three therapies as specified in the restriction, in the absence of these therapies. Special consideration may be given to the circumstance of a patient who has demonstrated failure to both methotrexate and phototherapy and, despite responding to cyclosporin, is reaching cumulative levels of renal toxicity sufficient to require permanent treatment withdrawal (this is likely to need a more objective definition). In this circumstance, evidence of a pre-cyclosporin PASI score of greater than 15 should be acceptable rather than requiring that the patient deteriorate past this threshold simply to become eligible for efalizumab.

With respect to the criteria to be met in order to qualify for continuing therapy with efalizumab, the PBAC recommended at least a 75% improvement in the patient's baseline PASI score following at least 12 weeks of therapy would be required. The restriction should

also include the requirement for patients to complete the informed consent process similar to that included in the PBS restriction for the biological DMARDs for the treatment of rheumatoid arthritis, so they are aware of the criteria to be met to qualify for ongoing therapy, prior to commencing treatment.

The PBAC also accepted in principle the additional set of restrictions to identify patients with severe refractory psoriasis of the face, hands and/or feet as being eligible and noted that modifications might be appropriate to bring these in line with the above general objectives of the main initial and continuing restrictions.

The PBAC noted that there were still some outstanding issues with respect to the restrictions, and that the Department should finalise these, taking into account the Committee's recommendations, in consultation with the sponsor, Medicare Australia and the Australian College of Dermatologists.

***Insert Link to Restriction …***

## 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 recommendation by the PBAC to list of Raptiva on the PBS will offer significant benefits to patients suffering severe psoriasis who are uncontrolled by current systemic therapy. Following the announcement by the Health Minister, Hon. Tony Abbott that Raptiva will be made available on the PBS on April 1st 2006, we would like to acknowledge the contribution of all the people who have worked so constructively to ensure that Raptiva will soon be available under reimbursement.