Ms Natalie Bemrose
Technology Appraisal Project Manager
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14th September 2007

Dear Ms Bemrose,

Response to the Appraisal Consultation Document for Infliximab for the treatment of adults with psoriasis

Merck Serono appreciates the opportunity to comment on the evidence base used to inform NICE's preliminary decision regarding Infliximab for the treatment of adults with psoriasis in England and Wales.

Merck Serono would like to comment on the following areas of the ACD:

1. Information presented in relation to TA 103
2. Re-review dates for Infliximab vs re-review of TA 103 and STA for Adalimumab
3. Efalizumab as a comparator to Infliximab

Our comments fall under points 1 and 3 of the general headings requested:

i) whether you consider that all of the relevant evidence has been taken into account;

iii) whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS.

1. Information presented in relation to TA 103

Merck Serono agrees with the Appraisal Committee's description of the use of etanercept in paragraph 4.3 that etanercept is given continuously in routine clinical practice, despite this being contrary to that

specified in marketing authorisation[1]. This conclusion is of crucial importance in conclusions derived with regards the Technology Assessment (TA) 103 of etanercept and efalizumab. The continuous use of etanercept is counter to that stated in TA 103 and was of crucial importance for decisions made in leading to the final recommendation.

In TA 103 etanercept was assumed to be used intermittently. This resulted in a lower treatment acquisition cost for etanercept versus efalizumab, and etanercept was stated to be more cost effective principally because of the treatment-free periods that characterize intermittent therapy. As a result it was recommended for treatment ahead of efalizumab.

With this new understanding of the continuous use of etanercept; the treatment costs are as follows:

- Etanercept used continuously: £9295.52 annual drug acquisition cost (104, 25mg vials)
- Efalizumab: £8798.40 annual drug acquisition cost (52, 125mg vials)

Given this information, the proposed re-review of TA 103 should be brought forward, to allow a recalculation of relative cost effectiveness between the two treatments.

2. Re-review dates for Infliximab vs re-review of TA 103 and STA for Adalimumab

In the coming year NICE will be issuing guidance both with regard to Single Technology Assessments of Infliximab and potentially adalimumab, as well as re-reviewing TA 103 Multiple Technology Assessment. Given the contrasting assumptions utilised in this appraisal versus that in TA 103, we believe it would be optimal to organise one multiple technology appraisal (MTA) of all recently introduced biological products in the treatment of psoriasis to produce a better integrated piece of guidance that reviewed all four technologies in the same context, and thus ensured a level playing field between them.

3. Efaluzimab as a comparator to Infliximab

Whilst both infliximab and efalizumab are indicated for the treatment of patients with moderate to severe chronic plaque psoriasis, the Appraisal Committee does not utilize relevant advice from a previous decision, concerning use of biologics in Rheumatoid Arthritis. In that assessment, the appraisal committee have previously considered that using a second drug from the same class (in this case TNF-α blockers) would not be cost effective. Efalizumab, being a T Cell modulator, has a different mode of action to the TNF-α blockers and it should be considered first line in patients who are not suitable for anti TNF therapy to be consistent with conclusions made in other guidance regarding these technologies.

In addition, infliximab has good short term efficacy but, like the other anti-TNF drugs, suffers from a plateau of efficacy. Section 3.4 of the ACD assesses relative efficacy over a 12 week period using a meta analyses. The appraisal committee should give more weight to data supporting continuous long term

efficacy given the chronic nature of psoriasis, and high rates of relapse, a 24 week or longer treatment assessment may be more appropriate.

As well as a discussion of efficacy, if a comparison of infliximab with etanercept and efaluzimab is carried out, VAT costings should be an additional consideration for treatments administered in the hospital setting in comparison to those at home.

Infliximab would be most suited to a particular population of patients with psoriasis as follows:

- Disease rating (PGA) of severe or very severe
- Patients who require rapid response to treatment
- And are willing to tolerate the potential side effects and required hospital visits for treatment.

This is a group of patients for whom there are few other treatment options and infliximab is an ideal option given its rapid response. In addition, given such rapid response, infliximab may also be considered as an ideal treatment for controlling a patient's symptoms over a short period of time before transfer to a biologic intervention with a known longer duration of efficacy. Such a treatment practice would be optimal with regards patient outcomes and NHS resources and also address issues of diminishing efficacy over time which has been observed in the use of TNF inhibitor treatments.

Conclusion

Merck Serono would encourage NICE to recommend infliximab for patients with severe psoriasis who require a rapidly effective treatment. We believe infliximab is an efficacious treatment for that specific group of patients and we would urge NICE to make it available for patients who otherwise would have no other alternative treatment available to them

I do hope that you find our comments to be of value and do please contact me if you require clarification on any point.

Yours sincerely

Stephen J Ralston
Director Health Policy
Merck Serono
UK and Ireland

[1] Etanercept SPC
http://emc.medicines.org.uk/ Accessed 10th Sept 2007