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Ms Natalie Bemrose
Technology Appraisal Project Manager
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MidCity Place
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London

Date 21st February 2008
Division/Dept. Health and Clinical Excellence
Care of
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Your letter
Your ref.

Dear Ms Bemrose,

Response to the Appraisal Consultation Document for Adalimumab 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 adalimumab 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. Clarification of cost-effectiveness and assumptions used in the decision-making
3. Re-review dates for adalimumab vs re-review of TA 103

Our comments fall under points 2 and 3 of the general headings requested:

ii) whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence, and that the preliminary views on the resource impact and implications for NICE are appropriate;

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 4.7 that etanercept is given continuously in routine clinical practice, despite this being contrary to that specified in the marketing authorisation[i]. This follows a similar statement made by the appraisal committee during the recent assessment of infliximab. In Technology Appraisal (TA) 134 of infliximab for the

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treatment of adults with psoriasis, continuous etanercept was regarded as a suitable comparator only as infliximab was recommended for very severe psoriasis patients with a total Psoriasis Area Severity Index (PASI) of 20 or more and a Dermatology Life Quality Index (DLQI) of more than 18.

In this Appraisal Consultation Document for adalimumab, however, the focus is on severe patients with a PASI of 10 or more and DLQI of more than 10. When etanercept and efaluzimab were assessed in TA 103 for this treatment group, intermittent etanercept therapy (74% of the continuous dose) was accepted as the appropriate comparator.

To add transparency to decision-making, can the Institute please clarify the appropriate comparator considered? Is it intermittent or continuous etanercept? If it is intermittent therapy, is it 74% or 88% of the continuous dose or an alternative?

2. Clarification of cost-effectiveness and assumptions used in the decision-making

The Appraisal Committee was concerned that in the manufacturer's analysis the dose of intermittent therapy of etanercept used to calculate costs was inconsistent with that used to calculate utility gain. The incremental cost per QALY for adalimumab compared to etanercept using the assumptions in TA103 was therefore £36,700. Despite this the committee felt that the true cost per QALY should take into account comparisons both with intermittent and continuous therapy. Based upon the lack of certainty around cost-effectiveness results the appraisal committee stated that 'clinicians would need to exercise their clinical judgement in choosing between the two treatments.' This decision does not seem to follow the criteria on which recommendations were made for etanercept and efalizumab in TA 103. We therefore believe there needs to be consistency in the assumptions used for calculation of cost-effectiveness, particularly given the uncertainty over the comparator and the high cost per QALY ratio of adalimumab when using the appropriate TA 103 intermittent etanercept comparator (i.e. 74% of continuous dose).

3. Re-review dates for Adalimumab vs re-review of TA 103

In the past year NICE will have issued guidance with regard to Single Technology Appraisals of both infliximab and adalimumab. We do not believe that a review date for adalimumab of June 2011 is appropriate 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.

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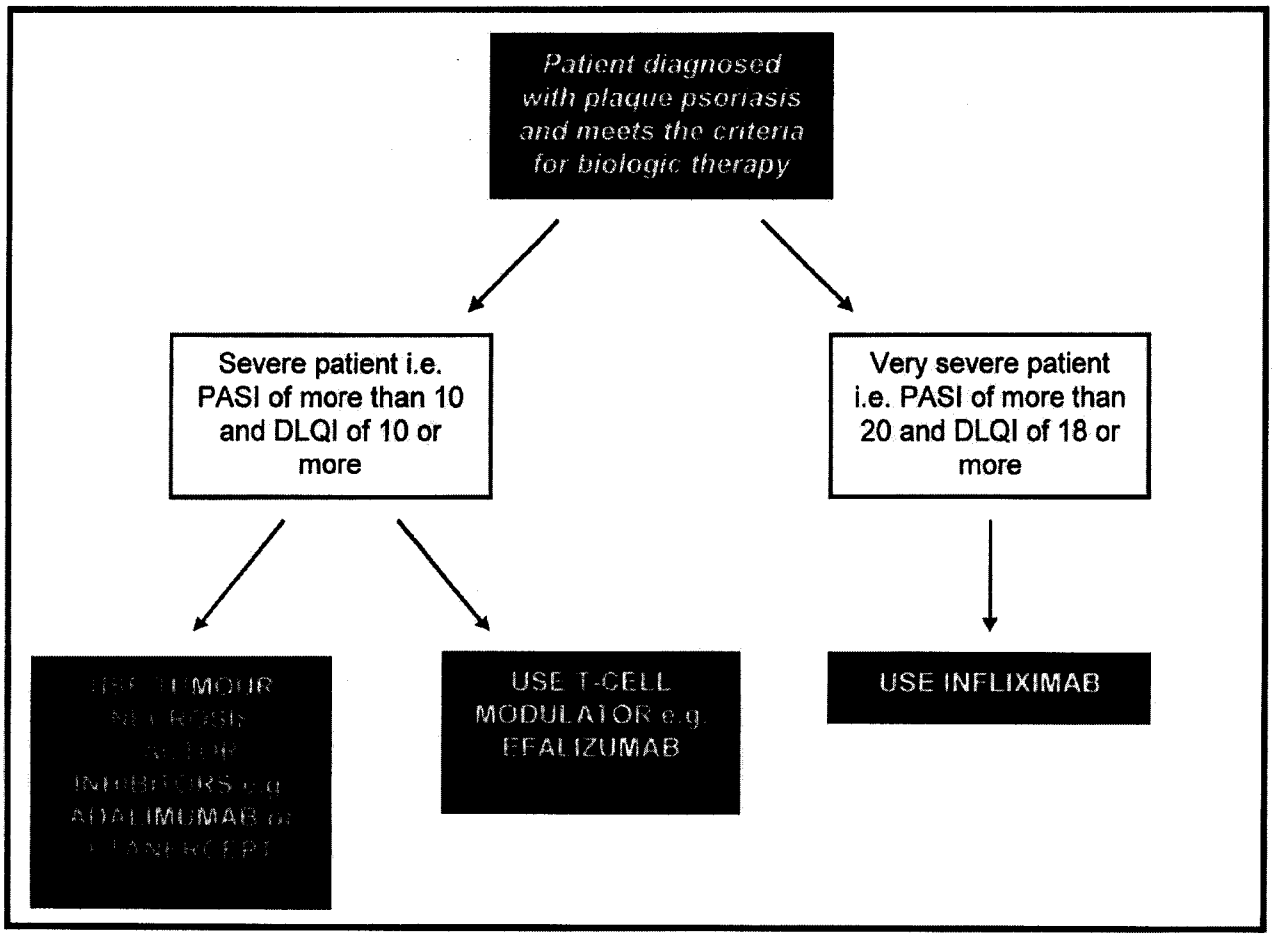
Further criteria that needs consideration in this review, particularly given the chronic nature of plaque psoriasis, is both the long-term efficacy and the effect a specific mode of action has upon this. This should encapsulate assumptions around tumour necrosis factor inhibitors alluded to in technology appraisals for other indications (for example Rheumatoid Arthritis).

Given NICE's decision that infliximab be used in very severe patients, we could envisage a treatment cascade as in figure 1 below. If a re-review of TA 103 were to proceed, such guidance will provide greater clarity on the place of all four biological therapies, evaluated on an equivalent basis, in the treatment pathway.

Figure 1: Possible pathway for treatment of psoriasis with biologic therapy



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Conclusion

Merck Serono believe that NICE should recommend adalimumab as an option for patients with severe psoriasis on the condition that it meets cost-effectiveness criteria based upon the assumptions used in TA 103. If this is not the case, then we feel that adalimumab should not be recommended for the treatment of psoriasis patients with PASI of 10 or more and DLQI of more than 10 until the review of TA 103 (which needs to be initiated as a matter of urgency), where the original assumptions can be assessed and all four biologic therapies can be evaluated on the same basis.

If adalimumab is recommended based upon etanercept usage being between intermittent (74% of continuous dosage) and continuous, then efaluzimab would be deemed cost-effective on this basis to give patients an added choice of treatment, particularly if the Appraisal Committee now feels that intermittent therapy as defined in the etanercept SPC[1] (i.e. up to 24 weeks for each treatment cycle) is more appropriate than that defined in TA 103.

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

[redacted]

[1] Etanercept SPC
http://emc.medicines.org.uk/ Accessed 19th February 2008

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