



8th April 2010

██████████
Technology Appraisal Project Manager
National Institute for Health and Clinical Excellence
MidCity Place, 71 High Holborn
London WC1V 6NA

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RE: Etanercept, Infliximab and Adalimumab for the Treatment of Psoriatic Arthritis: Comments on the Appraisal Consultation Document (ACD)

Schering-Plough welcomes the opportunity to comment on ACD for the appraisal of TNF- α inhibitors in psoriatic arthritis. Following a thorough review of the ACD and the accompanying amendments to The CRD/CHE Technology Assessment Group (TAG) analysis, this letter sets out Schering-Plough's comments – a summary of what we perceive to be the shortcomings of the TAG analysis and the resultant significant findings for infliximab which we believe the Appraisal Committee (the Committee) should consider.

1 Inappropriate consideration of evidence

1.1 Incomplete presentation of evidence on infliximab

The calculations of the treatment costs of TNF- α inhibitors presented by the TAG in their original technology assessment report (TAR) (Table 10.13.3; Page 329) and the amendment following the Committee meeting (Table 10.13.3) seem to suggest that the TAG conducted two separate analysis with a mean of 3 or 4 vials of infliximab for up to 60kg and 70-80kg patient body weight with no vial sharing. However, TAG has only presented the results for the 70-80kg patients with no vial sharing in the base case and restricted the 60kg patient scenario as a sensitivity analysis in TAR. No such analysis was presented in the amendment dated 23rd February 2010, after the costs for adalimumab and etanercept were corrected.

The Committee's request for further sensitivity analyses seems to suggest the Committee's acknowledgment of comparable efficacy between adalimumab and etanercept, and superior efficacy of infliximab (ACD section 4.3.9). Schering-Plough therefore believes that for the PsA

patients requiring infliximab dosing of 3 vials per infusion, infliximab is a cost effective treatment option over and above adalimumab and etanercept (ICER = £8,377/QALY compared to subcutaneous TNF- α inhibitors) and should therefore be recommended.

Schering-Plough therefore urges the Committee to reconsider their guidance and recommend the TNF- α inhibitor with cheapest acquisition cost depending on local arrangements to be used in practice. This is in accordance with the precedent set in the most recent appraisal of TNF- α inhibitors in Crohn's disease wherein the Committee allowed equal access to all the available TNF- α inhibitors and recommended the use of TNF- α inhibitor with the cheapest treatment cost including cost of administration.

1.2 No consideration of vial optimisation for infliximab

Vial optimisation with infliximab has significant implications on the resulting ICERs. The TAG did not consider vial optimization in their analysis, even as part of sensitivity analysis. A recent survey of rheumatology centres across England and Wales suggested that 63% of all rheumatology patients undertake vial optimisation and a minimum of 50% of drug wastage is avoided in centres that undertake vial optimisation.

Vial optimisation has also been considered in other appraisals. In a previous appraisal for an asthma medication, omalizumab, the Committee has considered vial optimisation while issuing their guidance (Technology Appraisal 133)¹. Paragraph 4.12 of TA 133 states:

“The Committee considered the basis for estimating omalizumab drug costs in the manufacturer's model. It noted that this had been done on a per-mg basis (assuming no wastage and reuse of unused vial portions) and that in scenarios in which omalizumab drug costs were estimated on a per-vial basis, the ICERs for omalizumab were higher. It was mindful that vial sharing might not be feasible in primary care settings. However, the Committee heard from patient experts and clinical specialists that vial wastage could be avoided reasonably easily in regional specialist centres where larger numbers of patients are treated. The Committee therefore concluded that the ICERs for omalizumab in comparison with standard therapy may be lower when omalizumab is administered in a dedicated session in a specialist day care setting where vial wastage can be minimised.”

As infliximab is administered within specialist centres, it may be reasonably assumed that vial optimisation may be applicable. Indeed, the ongoing NICE appraisal of infliximab for the treatment of Crohn's disease recently released an Appraisal Consultation Document which stated that local vial sharing arrangements should be taken into account in the consideration of which treatment should be administered².



Schering-Plough therefore strongly urges that the TAG considers vial optimisation in their analysis prior to presenting this evidence to the Committee. Schering-Plough believes that both the changes suggested above will further improve the ICER for infliximab in comparison with other TNF- α inhibitors.

2 Significant findings for infliximab

The indirect comparison results from the TAG analysis suggested that infliximab is consistently superior to etanercept and adalimumab on all of the treatment outcomes. This was most evident on psoriasis outcomes and among patients with significant psoriasis. Although the results did not reach statistical significance this could be attributed to underpowering of the clinical trials on psoriatic outcomes. The feedback from the clinical experts during the Committee meeting also suggested a wider clinical view that infliximab is a superior TNF- α inhibitor in psoriasis. The superiority of infliximab in psoriasis has already been acknowledged in a previous appraisal (TAG 134; Pages 12-13) and has been recommended based on its superior clinical outcomes. Schering-Plough therefore urges the Committee to view following cost effectiveness results in this context and allow unrestricted use of infliximab at least for patients with significant psoriasis.

2.1 Treatment of choice for patients with significant psoriasis

The TAG concludes that among PsA patients with moderate to severe psoriasis, if the response is defined as PsARC or PASI 75 then infliximab has the highest probability of being cost effective at a threshold of £30,000 per QALY. If a higher threshold of PsARC and PASI response is used then infliximab has the highest probability of being cost effective at both £20,000 per QALY and £30,000 per QALY thresholds.

2.2 Treatment of choice for patients requiring inpatient treatment

The TAG also concludes that for uncontrolled moderate to severe psoriasis patients requiring inpatient treatment infliximab is likely to be the most cost effective strategy at a threshold of £20,000 per QALY.

In summary, Schering-Plough urges the Committee to consider infliximab's superior efficacy on all outcomes and its significant benefit to 'difficult to treat' PsA patients with moderate to severe psoriasis whilst recommending the TNF- α treatment. Once again, we are grateful for the opportunity to comment on the TAR and look forward to continued dialogue with NICE regarding the issues raised in this response.

Sincerely,

Schering-Plough



¹ NICE Final Appraisal Determination (TA 133), Omalizumab for severe persistent allergic asthma, August 2007, available at <http://www.nice.org.uk/nicemedia/pdf/FADOmalizumabAsthma.pdf>.

² NICE. Crohn's Disease: Infliximab and adalimumab. Appraisal Committee Document. Section 4.3.11. Available from: <http://www.nice.org.uk/guidance/index.jsp?action=folder&o=46233>