

From: [REDACTED] [REDACTED]
Sent: 27 February 2008 16:44
To: Natalie Bemrose
Subject: Use of second TNF in RA comments

Attachments: Consultation comments on CE of sequential use of TNF_February 2008 - Wyeth.doc; Consultation comments on DMARD use_February 2008 - Wyeth.doc;

Dear Natalie,

Thank you very much for the opportunity to comment on documents produced for the technology appraisal for adalimumab, etanercept, and infliximab for the treatment of rheumatoid arthritis.

We have reviewed the documents you sent, and feel they contain a comprehensive review of the available data. The documents seem credible and balanced.

Please find attached our comments.

If you've any questions, please don't hesitate to contact me.

Best wishes

[REDACTED]

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National Institute for Health and Clinical Excellence

Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis
Further cost-effectiveness analysis of sequential TNF inhibitors for rheumatoid arthritis patients

Consultee	Section / page number	Consultee comment	Developer comment
Wyeth	Part 1 What is the cost effectiveness of using a second TNF inhibitor as compared to returning to conventional DMARDs?	<p>“New” values were taken by applying the placebo change in the key abatacept trial (DSU, 2007 citing Genovese, personal communication).’</p> <p>Whilst we agree with the DSU that it is not exactly equivalent to the data required in the analysis, we support its use.</p>	
Wyeth	Part 3 What is the impact on cost effectiveness of using alternative dosing assumptions for infliximab including more frequent dosing, dose escalation and vial optimisation?	<p>The institute should base its decision finding with regards to the use of infliximab as a second TNF on the findings for dose-escalation.</p> <p>According to the results of a retrospective evaluation of rheumatoid arthritis patients, development of anti-infliximab antibodies may in some cases reduce the clinical efficacy of infliximab, necessitating dose-escalation¹.</p>	

¹ Haraoui B, et al. Anti-infliximab antibodies in patients with rheumatoid arthritis who require higher doses of infliximab to achieve or maintain a clinical response. The Journal of Rheumatology 2006; 33:31-36.

National Institute for Health and Clinical Excellence

Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis
The effectiveness of non-biologic DMARDS after anti TNF- α inhibitor failure

Consultee	Section / page number	Consultee comment	Developer comment
Wyeth	3.3.1. Abatacept and rituximab studies	<p>'Therefore, whilst neither study provides direct evidence of initial response to conventional DMARDS in those that have withdrawn from a TNF-α inhibitor, there is some indication given as to the long term effect and may provide an indication of the lower bound of initial effect.'</p> <p>Whilst we agree with the DSU that it is not exactly equivalent to the data required in the analysis, we support its use.</p>	
Wyeth	4. Summary of findings	<p>'We have not identified any evidence that directly considers the effectiveness of non biologic DMARDS in the population of interest – patients that have failed treatment with a TNF-α inhibitor.'</p> <p>Even if Genovese¹, et al. do not provide direct evidence of initial response to conventional DMARDS, this study should be used to inform decision making.</p>	
Wyeth	5. References	The references for the Genovese studies are missing.	

¹ Genovese MC, et al. Abatacept for Rheumatoid Arthritis Refractory to Tumor Necrosis Factor α Inhibition. N Engl J Med 2005;353:1114-23.