

8 October 2015

Dear

**RE: Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed [ID537]**

We are grateful for the opportunity to respond to your letter and that you have agreed to hold an appeal panel hearing, based on our ground 2 point. However, we would be grateful if you would reconsider your decision in relation to our ground 1 points and set out our reasoning below.

This appraisal has been ongoing for 2 years. However, until approximately 2 weeks before the meeting on 21 May this year all the ICERs produced by the DSU for all patients – independent of disease severity - were considerably outside the range accepted by NICE. Our written response made to the committee was made with this information. However, after all responses had been submitted, the DSU produced new ICERs that were below the £30,000 threshold for patients with both severe and moderate disease who had a poor prognosis. We argued at the meeting on the 21<sup>st</sup> May that rheumatologists could identify these patients on clinical grounds but there was not an opportunity to refer the committee to the evidence base in support of this information. The first opportunity to refer the committee to published scientific data was in response to the ACD. The fact that the new ICERs for moderate disease were dependent on identifying patients with the worst prognosis meant that the committee needed to be aware of the evidence base relating to this aspect. How rheumatologists can predict prognosis in patients with moderate disease was not a consideration prior to the publication of the new ICERs.

As you know, the purpose of an ACD is to allow consultees to respond to the committee on their consideration and interpretation of the evidence base. We refer to the *Guide to the methods of technology appraisal 2013*:

*6.1.5 Usually, the Appraisal Committee's provisional recommendations are released in an appraisal consultation document for widespread consultation with consultees, commentators and the public. In reviewing responses to consultation, the Committee is principally interested in comments on its preliminary recommendations within the context of the evidence base reviewed at its first meeting and its consideration of that evidence. The comments received on the key issues identified at the first meeting are carefully reviewed.*

However, because the relevant ICERs were published so late, and the published data relating to predicting prognosis could only be submitted following the ACD, the relevant evidence base in identifying the worst prognosis in patients with moderate disease could not be brought to the attention of the committee until the final meeting in July. The first recommendations based on consideration of this evidence were published in the FAD, not in an ACD. The recommendations of the committee on this key issue have not been put forward for consultation.

Following the 22 July meeting and the publication of the FAD, it was apparent that the committee had misunderstood some of this evidence, as there were several factual inaccuracies in the FAD. Had we been given the opportunity to make these proposals based on the revised ICERs before the ACD was written, the BSR would have had the opportunity to address the committee's misunderstanding of the data in an ACD. If a second ACD was published instead of the FAD, the BSR would then have had the opportunity to address the

misconceptions regarding the proposed definition of the indicators for poor prognosis. As such, the BSR has been denied an opportunity to respond to the committee's inaccurate comments. It is therefore unfair to patients with moderate disease not to have had a second ACD following the committee's consideration of new evidence. We would therefore kindly request that you reconsider this point and accept this as a ground for the appeal.

In addition, we would be grateful if you would also reconsider your decision on our second ground 1 point. We accept your point that *'A committee which judges even on brief inspection that relevant evidence is in fact unlikely to assist it and need not be reviewed in detail is unlikely to have acted unfairly.'* However, the new evidence we submitted to the committee was entirely relevant to informing the committee how to identify moderate patients with an ICER below the £30,000 threshold. We consider that the conclusions of the committee reflect the fact that the committee did not review the evidence in detail. For example, we refer to information made in our ground 2 point:

*"The Committee also noted that, although individually validated, the measures were not necessarily independent of each other"*

This is factually incorrect. We referenced the fact that they are independent factors. One of the major conclusions of a large long term study by Syverson et al (a 10 yr follow up study), ref 13, was: *Conclusions: Anti-CCP, IgM RF, ESR and female gender were independent predictors of radiographic progression and could be combined into an algorithm for better prediction.* This is stated in the abstract of the paper. We are not aware of any data that contradicts this statement. It is difficult to understand how the committee could draw their conclusion if this study had been reviewed.

We listed several factual inaccuracies in the FAD in relation to our Ground 2 point. We consider that these inaccuracies support our view that the members of the committee could not have considered the scientific studies that were referenced. This is not a matter of judgement but of factual evidence supplied to the committee. We accept that the committee may judge the strength of evidence, but it is clear from comments in the FAD that all of this evidence was not considered. In view of your comment that *"A committee which is unaware of relevant evidence will usually have acted unfairly"*, and that this evidence is critical in determining whether the patients with moderate disease and an ICER below £30,000 could be defined, we kindly request you reconsider whether this point could be included at the appeal hearing.

Yours sincerely,

BSR President

BSR nominated expert

BSR nominated expert

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