From:

Sent: 09 September 2008 16:10

To:

Cc:

Subject: Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis after failure of a previous TNFa inhibitor

Importance: High

9 September 2008

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Dear

Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis after failure of a previous TNFa inhibitor

Thank you for your letter of 3 September 2008. This letter represents my final decision on the initial scrutiny of your appeal points.

Point one has already been accepted as valid.

Point two: insufficient consideration to the alternatives after failing a first anti-TNF therapy

The appeal panel directed the committee as follows:

The Appeal Panel suggests that the Appraisal Committee reassess the evidence for the cost-effectiveness of a second antiTNF treatment with an extended sensitivity analysis that considers a wider possible range of effectiveness for standard disease-modifying agents when used after antiTNF therapy, a wider possible range of doses for infliximab, and a more complete examination of the minimum effectiveness that would be required of a second antiTNF treatment for it be marginally cost-effective.

The scope of the appraisal was not modified, so that only the original treatments were to be considered. If I have understood your letters correctly you are arguing:

- That it was perverse not to analyse patients who had a partial response to a first anti TNF as a subgroup distinct from the patient population as a whole
- That patients who are seronegative should have been treated separately in analyses (I think by not using rituximab as a comparator for those patients?)
- Generally that the analysis of rituximab was not satisfactory.

On the second and third points, I note that Rituximab was not assessed in this appraisal, and it does not appear from the FAD that it was used as the primary comparator. It seems to me that the committee may have been mindful of the need for broad comparability between rituximab, which had been assessed in TA126 and recommended for use after failure of a TNFa inhibitor, and these technologies. I can also see that the committee may have felt the need to address the question of which of rituximab and a second TNFa inhibitor should have been preferred, if the result of the appraisal had been that both were in principle to be recommended. However as I have read the FAD, the recommendation for sequential use only in a research context is based on the comparison with DMARDs, and the discussion of rituximab does not seem to have been the main, or possibly any, reason for the recommendation. A full discussion of rituximab appears in TA 126 and I can understand why it is not repeated here. I do not think, therefore, that the FAD can be said to be arguably perverse in this regard.

On the first bullet point, this seems to be a repeat of your remaining point below.

Point 3 The committee perversely rejected sequential anti-TNF therapy due to lack of data

With some hesitation, I am going to allow this point to go forward. I am not sure that your argument goes any further than that more analysis into the position of secondary failures could reasonable have been considered, which would not approach the threshold of perversity. However I do also note that this could be said to have been within the issues which the appeal panel directed the committee to reconsider as a result of the last appeal, and so I think it would be wrong not to allow a second appeal panel to scrutinise what has been done.

For clarity and to assist in preparation for the appeal, my understanding of your point is that either the ReACT study was itself sufficiently large and suitable designed to allow subgroup analysis of secondary failures, or that data from the BSRBR could be combined with data from the ReACT study and that that combined data would have permitted such analysis, and that in either case such analysis would be sufficiently robust that it was perverse not to carry it out.

Therefore, the first and the third points of your original letter will now go forward to an appeal.

Yours sincerely

Mark Taylor
Appeals Committee Chair
National Institute for Health and Clinical Excellence