[redacted], **Ph.D**
Healthcare Management Director

Wednesday 24th March 2010

Jeremy Powell
MidCity Place
71 High Holborn
London
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BY E-MAIL

Dear Jeremy,

Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor

Thank you for the opportunity to respond to the Appraisal Committee Document.

The response to the ACD is provided under the four standard headings below.

Please do not hesitate to contact us should you require any further information or clarifications.

Yours Sincerely,

[redacted]

1. Has all of the relevant evidence been taken into account?

Roche is not aware of any other data that would assist the Committee in addressing the decision problem for this appraisal. Roche believe that high quality RCT data should be used to appropriately guide clinical practice.

2. Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

Roche believe that the summaries of clinical and cost effectiveness data pertaining to rituximab are accurate in this patient population.

3. Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

Roche consider that one area of clarification is needed. This relates to section 1.4:

"*1.4 The TNF inhibitors adalimumab, etanercept, and infliximab are recommended for the treatment of rheumatoid arthritis after the failure of a previous TNF inhibitor only in the context of research. Such research (including but not limited to clinical trials) should be designed to evaluate the clinical effectiveness of adalimumab, etanercept and infliximab when used sequentially after the failure of a previous TNF inhibitor, in comparison with management strategies that do not include the use of TNF inhibitors.*"

Roche agree with the need for randomised, controlled clinical trials demonstrating efficacy of a second anti-TNF, as systematic reviews have consistently identified gaps in the hierarchy of evidence. This has been a clear area of concern in that establishing the magnitude of treatment effect of the 2nd aTNF was not possible and therefore a recommendation could not be given. According to the NICE guide to methods hierarchy of evidence it is clear that only robustly designed RCTs, or prospective, comparative high quality studies, with efficacy as a primary end point should be used for cross trial comparisons and mixed treatment comparisons. Otherwise there would be little or no improvement on the existing evidence base and the fundamental question would remain unanswered.

In addition, clarification on the extent of the mandatory funding directive in the context of future research would be helpful, given the current wording of this recommendation.

4. Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?

None