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2nd September 2008

Dear Eloise

Re: Infliximab for acute exacerbations of ulcerative colitis - ACD

The Royal College of Physicians and British Society of Gastroenterology are grateful for the opportunity to respond to the above consultation. We would like to make the following joint comments:

i) Do you consider that all of the relevant evidence has been taken into account?

Yes

ii) Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence, and that the preliminary views on the resource impact and implications for the NHS are appropriate?

Probably. However the calculations of cost appear to have been done on the basis of 3 infusions of infliximab being given, when the evidence that exists for efficacy of infliximab in this setting relates to a single infusion (5mg/kg) (Jarnerot 2005). This should be redressed.

iii) Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

Yes but the contra-indications to ciclosporin listed in 4.10 should also include a history of epilepsy, other neuropsychiatric disturbance, malignancy, and the patient being in a hospital where there is not immediate access to plasma ciclosporin as well as electrolyte levels including magnesium.

iv) Are there any equality related issues that need special consideration that are not covered in the ACD?

Only in so far as patients in hospitals unable to assay ciclosporin levels promptly should not be denied infliximab as an alternative to surgery.

Other comments on the ACD:

Para 3.3: As we pointed out at the meeting in July, the placebo failure rate in the Lichtiger 1994 paper on ciclosporin in refractory acute severe UC has been presented inaccurately. In fact, 9/9 patients (100%) given placebo failed to respond, 5 then being rescued with open-label ciclosporin. It is inappropriate therefore to use in this context a 44% surgery rate for the placebo patients, since all would have had surgery had some not been rescued with ciclosporin.

Para 3.4: For the same reason, we think the figure of 0.67 for the probability of a patient having colectomy in the first 3 months is too low: almost all patients failing to respond to iv steroids given placebo need surgery (eg 100% in Lichtiger paper (see above), 66% in Jarnerot paper).

Para 4.6: Adjust line 2 to make clear that that this statement applies to 'intravenous steroid-refractory' acute severe UC.

Para 4.8: We believe that the existing evidence supports use of only 1 infusion (not 3) of infliximab in refractory acute severe UC (Jarnerot 2005).

Appendix B, para C: The name of one of the clinical specialists attending the meeting has been omitted (Prof DS Rampton, Barts and the London NHS Trust).

I trust these comments will be of use.

Yours sincerely

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