Expert Views on second NICE Appraisal Consultation Document (ACD) on

Crohn's disease- Infliximab (review) and adalimumab

Monday 5 October 2009

From: NHS Quality Improvement Scotland

Section 1. Comments on the NICE ACD

In this section, we are particularly interested in receiving your comments on the ACD under the following general headings:

1. Whether you consider that all the relevant evidence has been taken into account.

   The relevant studies have all been taken into account.

2. Whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence..

Adalimumab is the stated preferred therapy for severe Crohn's disease on cost grounds. However, the licensed starting dose for Adalimumab in the UK is 80 then 40mg but in the USA it is 160 then 80mg. How the discrepancies came about is not clear. The CLASSIC 2 Study has shown that with maintenance therapy 30-50% of patients required the increased dose of 40mg once weekly rather than every two weeks to keep the patient in remission. The costs of Adalimumab in the NICE evaluation only considered the low doses of 80 and 40mg initiation therapy and 40mg every two weeks for maintenance. Therefore, in clinical practice, these doses may be exceeded, hence any cost difference narrowed.

3. Whether 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.

I am concerned that the presentation of the Appraisal Committee's recommendations (page 3 of 36) may be mistakenly interpreted as recommendations to use Adalimumab or Infliximab in patients with severe active Crohn's disease without having initial treatment with steroids and/or immunosuppressive therapy. The licences for both these drugs clearly state that patients should have had a trial of full and adequate treatment with an immunosuppressant and/or corticosteroid, or who are intolerant to, or have contraindications to such therapy. I think this point should be inserted in the Summary document to avoid any confusion. I think the document would benefit from having, and highlighting, a section on indications for commencing biological therapy. It seems to focus much more on the choice between the two available biologicals.

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Section 2. NICE ACD – The Scottish Dimension.

In this section, we are particularly interested in receiving your comments on the Scottish dimension of the ACD under the following headings.

1. Do you wish to highlight any areas of unmet need in relation to the relevant condition(s)?

2. How would the Health Technology fit into current patient pathways/treatment options? In particular what is the predominant patient pathway/treatment option in Scotland?

Current practice in Scotland is to use Infliximab first rather than Adalimumab and this NICE Guideline would therefore indicate a change in practice. However, I think the reasons given for preferring Adalimumab are reasonable. However, the cost implications may be exaggerated as the CLASSIC 2 Study showed that higher doses of Adalimumab maintenance therapy are often required and similar to the higher dose given routinely in the USA. The cost calculations for Adalimumab have been based on the low dose treatment.

3. Disease incidence and prevalence. Please estimate for Scotland (a) how many new patients with the indication might be eligible for the health technology and (b) how many existing patients there are with the indication that are eligible for the health technology?

I do not think this should markedly change the overall use of these biologicals in Scotland, though it may alter the particular one prescribed. Clinical practice in this area has been ahead of the latest Guidelines and therefore most people clinically requiring the biological treatment are receiving it.

I am concerned that the summary of the current NICE document could be misinterpreted as implying that Adalimumab or Infliximab should be given as primary therapy for patients with severe active Crohn's disease. I do not believe that it means this as the drugs are only licensed for treatment in patients who have already failed treatment with immunosuppressive therapy and/or corticosteroids. However, the document does need to make it clear in its summary that these drugs are only recommended for patients who have had initial therapy with corticosteroids and/or immunosuppressive treatment and have persisting severe active Crohn's disease. I think the document would benefit from having, and highlighting, a section on indications for commencing biological therapy. It seems to focus much more on the choice between the two available biologicals.

4. If you have knowledge of this particular new health technology for this indication, please describe how it might fit into your treatment plan.

As mentioned above, I do not think this document should substantially increase the number of patients receiving the biological therapy. However, the lack of clarity regarding the indications for commencing the treatment might inadvertently result in a patient receiving it at an inappropriately early stage in their management.