

Appraisal of anti-TNF treatments for Crohn's Disease

NACC Comments on the Report to NICE from the Decision Support Unit dated 10th June 2009.

Overview and Summary

1. The DSU had four elements to their analysis:
 1. Review of the relapse rates in IBD
 2. Reconciliation of the existing models
 3. Exploring, if appropriate, different durations of maintenance treatment
 4. Conducting some sensitivity analyses
 - We were pleased to see the thorough review of relapse rates which we feel is very helpful and addresses one of our major criticisms of the Assessment Group Model.
 - The reconciliation of the different models was also very clear, but raises some issues about whether the resulting adapted Assessment Group Model is an adequate basis for the Committee to make a proper assessment of the cost-effectiveness.
 - We were disappointed that a detailed discussion of the work of Dr Bodger and colleagues, which was informally submitted to the Committee in 2008 and referred to in the interim DSU report in January 2009, was not included in the final DSU Report although it has been published in the interim. This is a significant missed opportunity to provide the Committee with all the available evidence to take into account in making their decision.
 - The sensitivity analyses are helpful, but we question whether they provide sufficient information for the Committee to be able to reach a properly informed decision using the adapted Assessment group model.
2. We welcome the conclusion of the DSU that maintenance treatment with adalimumab is cost-effective, which effectively removes the issue of the episodic use of this therapy. The latter was a proposal that we would not have been able to support as it did not conform to current clinical practice in the UK, (and to our knowledge anywhere in the world) and was one for which there was no clinical trial evidence.
3. We question whether the range of ICERs for treatment with infliximab are a sufficiently robust basis for the Appraisal Committee to reach a decision on the cost-effectiveness of this therapy, either for episodic or maintenance use. We welcome the fact that maintenance is presented as more cost-effective than episodic treatment, because we feel that this approach is generally in the best interests of patients well-being and the efficiency of IBD Service. However, we are surprised by the ICERs produced for episodic treatment and they contribute to our continuing concerns about the validity of the AG Model.

4. Maintenance treatment with infliximab is presented as cost-effective only in one of the twelve scenarios the DSU consider. Although they do not draw this conclusion, the step-wise consideration might encourage a view that when all scenarios are considered the balance of probability is in favour of infliximab maintenance not being cost-effective.
5. Our concern is that the Appraisal Committee might incline towards a view on the following lines:

'There has been considerable expense and delay involved in this appraisal. The DSU Report indicates that the only alternative approach at this stage would be to construct an entirely new model, which is undesirable in terms of delay and resource cost.

The DSU Report concludes that one of the two treatments is cost-effective and that the other is more likely than not to be outside the threshold for maintenance use.

On balance, decide to accept the conclusions, reassured that one anti-TNF maintenance treatment will be available to patients.'

6. There are very strong arguments against such an approach, which can be summarised as follows:
 - The two anti-TNFs are not interchangeable; individual patients will respond or not respond differently to the two drugs.
 - In clinical practice world-wide clinicians will consider moving the patient from one therapy to the other if the patient does not respond or if the effectiveness of a particular therapy tails off.
 - The two therapies are administered differently – adalimumab as costed is based on self-administration at home – whereas some patients may not prove to be suitable for home administration. The choice as to which suits individual patients is very important.
7. Our view is that the adapted AG model does not form a satisfactory basis for the Committee to make a proper judgement of cost-effectiveness and that the Committee should commission the construction of a model de novo with the benefit of full collaborative input from the professional societies and patient organisation representatives. It is our belief that much of the difficulty and delay in this Appraisal could have been avoided with a fully collaborative approach in the construction of the first model.
8. Our continuing concerns about the adapted AG Model are summarised on the following page.

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NACC (15th July 2009)

Summary of concerns re the adapted AG Model and DSU discussion

1. The adapted AG Model only considers as a benefit the state of full-remission, yet we know that one third of patients respond but do not achieve full remission. This response is still of real clinical benefit in managing the disease and offers a quality of life improvement to patients. This benefit is not captured in the AG Model and therefore undervalues the benefit of treatment. We consider this to be an error in the preparation of the Schering-Plough Model also.

It is interesting to note that this partial benefit is taken into account both in the Abbott model and in the model created by Dr Bodger and colleagues. The latter paper found both adalimumab and infliximab to be cost-effective in NHS terms. The fact that partial benefit is taken into account in both these models is, we believe, contributing to the ICERs for infliximab being above the threshold.

2. The Silverstein cohort models the course of disease and standard care for a whole IBD population. Their rate of surgery is likely to be significantly lower than the population of patients who are considered for treatment with biologics. We find it very difficult to know whether this has been fully taken into account and whether the assumptions on surgery reflect clinical reality.
3. The assumed weight of the average patient is obviously one determinant of the cost of therapy. We believe that the DSU adapted model retains the assumption that the average patient is 80kgs. If so, this has been disputed previously in responses from consultees.
4. No weighting has been given to the different changes and ICERs in the Report, yet change 12 – Post-surgery remission rates are clearly critical.
5. The DSU discussion does not reconcile or compare the AG Model with the model developed by Dr Bodger and colleagues and now published. This is the only non-commercial economic modelling of biologics and Crohn's disease other than the NICE Assessment Group Model undertaken in the UK and we find it inconceivable that the Committee should not have access to a proper review and comparison of that work with the other three models. This is particularly important as the ICERs for infliximab produced by Dr Bodger's modelling are significantly different and show the therapy as cost-effective for maintenance.

NACC (15th July 2009)