

Comments on the NICE Technology Assessment Report (TAR) “- Etanercept, infliximab, and adalimumab for the treatment of Psoriatic arthritis (Review)”

This large document is based on a number of assumptions relating to:

- treatment groups
- inclusion & exclusion
- stopping therapies

Internal Validity

As with emerging work of this type, the assessment adopts a number of assumptions, which require to be assessed in order to evaluate the internal validity of the document.

In general the work appears to be very robustly undertaken, with the assumptions being reasonable in the circumstances.

External Validity / Generalisability

The authors admit that the group who are examined within the trials are not representative of the type of people who are likely to present in a typical PCT.

Section 2.5 lists a large number of uncertainties about the comparisons used, all of which raise fundamental questions about how the trials relate to everyday practice. (*“The patients in most trials are not precisely representative of the population recommended for biologics in current guidelines. It is unclear whether the beneficial effects are similar in those treated in routine clinical practice.” p24*)

Were the study groups comparable with general practice populations or even the groups currently prescribed these drugs? (commented on later in the document). Indeed, section 5.2.2.1 states *“the populations in these trials of etanercept are not representative of the patients for whom etanercept is licenced for use.....”(p48)* and section 5.2.2.2 states *“Relative to the patients for whom infliximab treatment is recommended in practice, these trial populations may be less severely affected, with only around half in IMPACT and possibly even fewer in IMPACT 2 having failed to respond to two or more DMARDs..”(p54)*

It is not clear how this flaw may influence the usefulness of the treatment or the cost-effectiveness for use by a PCT. Further clarification of this point would be useful.

Tables 5.3, 5.7 and 5.11 containing RCT data on efficacy outcomes: although p-values for the 95% CIs are quoted for the majority of outcome data, there are several instances where p-values are absent and would have been helpful to produce a better overall picture of efficacy in terms of statistical significance.

The Technology Assessment Report uses different scoring systems for psoriasis severity (PsARC and ACR for arthritis component and PASI for the skin component) and 4 different economic analyses were used (3 pharmaceutical industry and 1 developed by York); are these reflective of everyday practice for initiation, monitoring progress and discontinuation of therapy? (p112-118)

The PASI scoring system has a number of deficiencies (described on p33-4) such as the criteria that 3% of the of the body surface area has to be affected for the PASI score to be used. The clinical impression from GP representatives in Hull is that patients with less than 3% could have psoriasis and joint involvement as well – it would have been helpful

to have had more discussion on this and the effect on the generalisability of the study findings in the light of this, in the main discussion on p147-151.

Health Economics Modelling

The authors have taken a lot of trouble to try to ensure that the model parameters are appropriate, with a robust evidence synthesis and a structured elicitation of expert opinion.

The York model adopts a NHS perspective. We would like to see a supplementary societal perspective discussion or at least an explanation of why this was not undertaken.

The Markov structure is appropriate. The re-entry pathway following a failed treatment is good. The Incremental Cost Effectiveness Ratios explanation is intuitive and helpful and the use of sensitivity analysis good. The discussion on p126 of the expected QALYs is easy to understand to a health economist, but the general reader might not understand. The diversity of the four models is of concern but the explanation of flaws in the industry models is useful in allaying concerns around this. (p 146 – 151.)

We feel confident in the principal findings on page 153. Page 157 gives a useful list of uncertainties.

The authors rightly point out (p160) that larger datasets would enhance knowledge of the beneficial treatments effects. The recommendation on safety monitoring is sound practice. The importance of examining patients who might not quite reach current criteria is, in our view important.

Summary

We believe that the health economics component of this report is a very thorough and balanced piece of work and we feel confident in its conclusions, within the author's comments on uncertainties and future research needs.

However, in practical terms and in the light of comments above regarding generalisability of findings, will the guidance reflect the hierarchy of recommendations, if indeed that is what the study discussion allows? We will be most interested to see how the NICE Appraisal Committee interprets this report and sets out the final TAG recommendations.

We would like to thank NICE for the opportunity to take part in this consultation and to observe at first hand the thoroughness of the process of guidance development.

Combined Comments from NHS Hull representatives:

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19th January 2010