

NICE
MidCity Place
71 High Holborn
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15 June 2011

Dear Sir/ Madam

Re: BSR comments on Abatacept for the treatment of rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs appraisal consultation document

This commentary is focussed on the use of Abatacept in patients with rheumatoid arthritis (RA) who:

- have a DAS>5.1 despite treatment with two conventional DMARDs (including Methotrexate)
- have a contraindication to the use of TNF antagonists.

This group of patients will not progress well if they continue with DMARDs alone, and are likely to accumulate irreversible joint damage due to inadequate suppression of inflammatory disease activity. This not only impacts on their joints, but there is increasing evidence for the effects of inadequate disease control on mortality, with increased cardiovascular disease in patients with ongoing raised inflammatory markers.

Current NICE TAs do not allow the use of any of the alternative biologic therapies unless TNF antagonists have been used. Thus patients with a contraindication to TNF antagonists may not be given the chance of responding to Abatacept despite this agent being licensed in the DMARD inadequate responder population.

Sections 4.9 – 4.19 discuss the use of Abatacept in this scenario.

The base case ICER of £29,700 after the ERG had corrected for arithmetical errors in the manufacturers submission is noted. This figure could represent an effective use of NHS resources, being in the region of ICERs that have previously been accepted as representing value to the NHS.

4.12 – The HAQ scores used in the model are derived from patients in clinical trials with a much longer disease duration (Phase IIb 9 yrs, AIM 8 YRS, ATTEST 8 yrs) at study entry than that in clinical practice today where the time to first biologic in patients poorly responsive to conventional DMARDs (i.e. persistent DAS>5.1) can be as little as 1 year. A disease duration of ~ 8 years will be associated with the accrual of irreversible damage which will constrict the responsiveness of the HAQ score to therapies. Therefore HAQ changes derived from these trials will be an underestimate of the changes seen in patients with earlier disease in routine care today, and thus the ICER for routine care today is likely to be lower.

4.13 – The implication of the text is that the committee viewed with scepticism the extremely poor quality of life associated with rheumatoid arthritis when HAQ is mapped to EQ-5D. As such it seems that the committee favour an alternative (non linear) approach to mapping which diminishes this effect and increases the ICER. There is no rationale given to accept or reject this alternative, beyond the (lack of) willingness to accept that a person with RA may have a quality of life worse than being dead. This is a speculative interpretation of the data, of insufficient merit to change the ICER from the base case of £29,700.

4.15 – Abatacept is unique amongst biologics in consistently showing incremental benefit beyond 1 year in most of the clinical trials. The disease may therefore be expected to get better with time, yet the model takes no account of this. This omission will not favour the benefits of Abatacept, and as such the ICER is likely to be lower.

4.16 – Adverse events are lower for Abatacept than other biologics, and remain similar to DMARDs in long term extension studies (up to 7 years). An assumption that they are likely to rise in line with other biologics is not founded on evidence, and provides no justification to assume a rise in the base case ICER above £29,700

4.17 –Comments regarding the plausibility of having to increase the dose of Abatacept with time based on the necessity to do this with other biologic agents (e.g. Infliximab) are unsupported by clinical evidence. They also contradict the clinical trial observations of an incremental benefit beyond 1 year of Abatacept treatment, which in turn might permit a dose reduction with time. Thus, speculation of dose changes over time are more likely to result in an improvement in the ICER following a dose reduction, than a worsening of the ICER following a dose increase.

In light of these points the committee’s assertion that the alternative scenarios proposed are ‘more realistic’ or contain ‘plausible assumptions’, which will always lead to an increase in the base case ICER, are not a reasonable interpretation of the evidence. Instead no alteration or an improvement in the ICER is more likely in several of these scenarios.

In conclusion, the base case ICER does support the use of Abatacept for the relatively small number of patients who are eligible for anti-TNF therapies but are contraindicated. These patients will not do well with continued conventional DMARDs, yet marketing authorisation and guidelines from BSR, EULAR and ACR permit the use of Abatacept as a first line biologic at this stage. The ACD relies upon many assumptions to reach its conclusions, some of which misrepresent the clinical trial evidence, as outlined. There is a significant body of evidence to support the use of Abatacept in this important group of patients, with respect to efficacy, safety, retention and incremental benefit, and insufficient evidence to justify the assumptions that the base case ICER is likely to be higher than the quoted figure of £29,700.

Yours sincerely



Consultant Physician and Rheumatologist

On behalf of the British Society for Rheumatology