National Institute for Health and Care Excellence

Multiple Technology Appraisal

TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis (including a review of TA143 and TA233)

AbbVie's Response to the Appraisal Consultation Document

Dear Meindert

AbbVie welcomes the opportunity to comment on the Appraisal Consultation Document (ACD).

We are pleased with the preliminary decision to recommend adalimumab, certolizumab pegol, etanercept and golimumab as treatment options for active ankylosing spondylitis (AS) and adalimumab, certolizumab pegol and etanercept, as treatment options for non-radiographic axial spondyloarthritis (nr-ax SpA).

We have some comments which we present under the questions asked by NICE and we propose that our feedback is taken into consideration at the next appraisal meeting.

Section 1. Has all of the relevant evidence been taken into account?

1.1 Sequential treatment

1.1.1 Removal of the restriction on switching to an alternative anti-tumour necrosis factor in the event of a patient not responding or losing initial response

AbbVie welcomes the acknowledgement in the ACD that there are data showing the benefits of switching to another anti-tumour necrosis factor (anti-TNF) in case of treatment failure.

Whilst AbbVie understands that the Committee was unable to recommend switching due to the lack of cost-effectiveness data, AbbVie notes the Committee considered the evidence for sequential treatment is based on registry data alone (underlined text):

4.59. The Committee considered the clinical evidence for treatment with a second or third TNF-alpha inhibitor for a person whose disease does not respond to treatment, or for someone who experiences a loss of response (sequential treatment)… However, the Committee was concerned that <u>this evidence was based on registry data alone</u> and was uncertain about the true magnitude of the benefit of sequential treatment in ankylosing spondylitis

AbbVie wishes to point out that in the Assessment Report reference is made to the RHAPSODY study, described in more detail in the AbbVie submission. Briefly, in this large, European, open-label study 326 participants were treated with adalimumab after infliximab or etanercept, or after both these drugs. Response rates at 12 weeks in the anti-TNF experienced participants who discontinued a prior anti-TNF due to loss of response, although lower than in the anti-TNF naïve participants, were still high: BASDAI 50 – 42% and ASAS40 – 43%. Additionally, AbbVie notes that the RAPID-axSPA study with certolizumab pegol, mentioned in the ACD, and discussed in the Assessment Report and the manufacturer's submission, was a randomised, double-blind, placebo controlled trial which included both anti-TNF naïve and experienced patients. It appears from the ACD that this information may not have been considered by the Committee.

AbbVie considers that given the typical age of patients starting anti-TNF therapy and the need for lifelong control of their disease it is very important for NICE to permit switching of anti-TNF therapy in case of treatment failure due to loss of efficacy. We believe this view is supported by patients, as reflected in the near unanimous response of the members of the National Ankylosing Spondylitis Society (NASS) to the question on whether patients should try a second anti-TNF if a first one's effectiveness wears off over time. This is also supported by the ASAS/EULAR recommendations for the management of ankylosing spondylitis[1].

AbbVie is also aware that there are instances where patients are able to access a second anti-TNF, but that this depends on the clinical commissioning group to which the patient belongs i.e. postcode prescribing, which is not in the spirit of ensuring that all patients have access to the same drug.

Lastly, whilst the ACD acknowledges that extra-articular manifestations (EAMs) should be considered when choosing an anti-TNF, EAMs may only become apparent during the course of the disease, i.e.

after the start of treatment. In such instances a patient would benefit from switching to another anti-TNF if such treatment has greater efficacy for the particular EAM than the first anti-TNF.

Based on the points outlined above, AbbVie would request reconsideration on the recommendation not to switch anti-TNF therapy (Section 1.6).

Removal of this restriction would bring the guidance for AS and non-radiographic axial SpA in line with NICE recommendations for psoriatic arthritis, psoriasis, Crohn's Disease and ulcerative colitis, none of which contain a recommendation against switching to a different anti-TNF in case of treatment failure.

2 Are the summaries of clinical and cost-effectiveness reasonable interpretations of the evidence?

2.1 Wording on choice of treatment

2.1.1 Amendment to section 1.4 to clarify choice of treatment

The preliminary recommendations state that:

1.4 The choice of treatment should be made on an individual basis after discussion between the responsible clinician and the patient about the advantages and disadvantages of the treatments available, and may include consideration of associated conditions. If more than 1 treatment is suitable, the least expensive should be chosen

AbbVie considers the wording "associated conditions" in the above section may be ambiguous in its current format. If it is meant to refer to extra-articular manifestations as per the discussions in sections 4.50, 4.58 and 4.71 then we request that the wording in section 1.4 be amended to the underlined text below:

1.4 The choice of treatment should be made on an individual basis after discussion between the responsible clinician and the patient about the advantages and disadvantages of the treatments available, and may include consideration of associated conditions <u>such as extra-articular manifestations</u>. If more than 1 treatment is suitable, the least expensive should be chosen

This amendment would enable the reader to understand what is meant with the term "associated conditions" without the need to review the whole document.

2.2 Yearly cost for infliximab

2.2.1 Amendment to cost of infliximab

The ACD states that

3.18 …For a patient with a body weight of 73 kg, the annual cost for first year of treatment with infliximab therapy (including 3 induction doses) is estimated at between £16,785 and £13,428 (depending on whether the maintenance infusions are repeated every 6 or 8 weeks).

As stated in our response to the Assessment Group report, AbbVie considers it is important to consider the distribution of patient weight rather than summary statistics for weight alone when the treatment cost for a population is being calculated. Measures other than the mean cost calculated based on patient weight distribution do not provide information about the cost of treating all patients.

As such, AbbVie requests that the mean cost for infliximab should be amended in ACD to take account of the full distribution in patient weight of AS patients. This will result in a more accurate and reasonable estimation of the annual treatment cost of infliximab.

3. Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

AbbVie has no comments on this point.

4. Are there any aspects of the recommendations that need particular consideration to ensure NICE avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

AbbVie has no comments on this point.

REFERENCES

[1] Braun J, van den Berg R, Baraliakos X et al. 2010 update of the ASA/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis 2011; 70; 896-904