Healthcare Improvement Scotland

NICE Health Technology Appraisal - Assessment Report On (insert topic)	
TO: NICE 01 February 2015	FROM: Healthcare Improvement Scotland

Thank you very much for inviting me to make technical comments on NICE MTA assessment report on TNF-alpha inhibitors for ankylosing spondylitis and nr-SpA. Given the complexity and holiday period I wish there was bit more time to review it but within in the available time I made following observations. I am very conscious that comments will be coming from a number of people therefore I made brief comments about the points that I felt have major significance. I note Golimumab and Infliximab do not currently have UK marketing authorization for nr-SpA.

Given the high placebo response for BASDAI 20/ASAS 20 using BASDAI 50 as a response measure is appropriate (page 183).

The cost of individual anti TNF in different models is quite different varying between 3K-5K for AS and is almost two-fold for nr-SpA, I agree ICER estimates reported by manufacturer must be considered both speculative and highly uncertain. Hence I think alternative YORK model is quite useful but I am somewhat concerned about some assumptions. Despite BASDAI remaining same, BASFI scores deteriorate over time leading to assumption of a link between BASFI and biological process (page 150) which I feel is not justified as a number of other factors may influence one's function and I am unsure to what extent early evidence of reduction in structural change after 4 years of treatment is included in the analysis. Graphs show that intervention with anti TNF seems to result in worse long term outcome in both BASDAI and BASFI(page 154) which is somewhat against the logic.

Improvement in BASDAI and BASFI is higher for Adalumimab than Certolizumab in AS when compared with conventional care however applied QUALYs are same for all biologic agents(page 154). There is no denying of class effect but by using class effect model in the meta-analysis any differences in the efficacy and side effects between different agents are not being considered especially given the task of this exercise is to find cost-effectiveness of individual drug on the basis of efficacy and safety which mean extraneous factors are determining it (page 54).

Although I understand the logic of responders and non-responders imparting higher baseline scores (page 184) for non-responders is not supported by ASAS consensus statement – Ann rhe dise 2006. Rebound equal to gain in BASDAI/BASFI is although

a possibility it is somewhat inconceivable that there won't be any residual benefit bearing in mind there may be effect on structure after 4 years of treatment.

In the studies that were included nr-SpA population is heterogenous and perhaps overall number of patients with and without objective inflammation are equal and prevalence of HLA B27 is much lower when compared to AS patients raising question on applicability of data in some one who has evidence of inflammation. However application of more stringent criteria to define nr-SpA such as positive MRI or raised CRP might improve accuracy of diagnosis and therefore assess its impact more accurately (page 42).

It was not clear if baseline BASFI scores employed for nr-SpA are same as AS or lower – later may be more appropriate given GESPIC cohort information (page 95) However by assuming similar process as AS long term BASFI scores may have been overestimated as there is some evidence showing that all nr-SpA do not progress although evidence is just beginning to accumulate (page 182).

As acknowledged by the report (page 30) impact of disease in nr-SpA is same or even more when compared to AS and hence I presume extent of conventional management is similar in both patient groups but yet baseline QUALYs in nr-SpA is significantly higher (page 209), is it justified?

Benefit in nr-SpA is similar to what is noted in AS but due to clinical heterogeneity in nr-SpA it was suggested that it may not be relevant to clinical practice which in my opinion is not correct(page 219) as patients in research studies are thought to be more homogenous than clinical practice.

York model suggests cost effectiveness is dependent on several factors. Of the five factors that are identified on page 213 barring Infliximab anti TNFs appears to be cost effective across most scenarios and acquisition cost is the only factor that is determining the cost-effectiveness in both AS and nr-SpA which is simply stating the obvious (213).

Inclusion costs in relations to AE were said to be included in the economic model but it was not obvious i.e. if these are different for each drug or same (page 204).

Comment provided to Healthcare Improvement Scotland by:
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This is a very comprehensive review and document.

I did not detect any important data/paper omissions and all the assumptions used for the modelling appeared robust and justified. The identified areas of uncertainty reflect gaps in the evidence base rather than missing data or false assumptions.

There is more long-term data emerging suggesting beneficial effects of TNFi on preventing radiographic progression as well as prognostic factors identifying patients at higher risk of radiographic progression, but these are still largely in abstract form and likely to have fallen outside the predefined search period.

The only statement I disagreed with is on page 33:
"Biologic drugs are the only therapies shown to be efficacious in the treatment of the signs and symptoms of disease activity in axSpA and AS"

- There is clear evidence to indicate that NSAIDs and physiotherapy are efficacious for these signs and symptoms, so this statement is misleading and should be amended. This is particularly true in patients with milder disease, but also applies in patients who also require TNFi.

Comment provided to Healthcare Improvement Scotland by:

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