HEALTH TECHNOLOGY APPRAISAL: NICE Health Technology Appraisal - Appraisal Consultation Document Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis	
TO: NICE	[redacted] **8 April 2010**

1. Do you consider that all the relevant evidence has been taken into account? All relevant information has been included in this document.

2. Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence? Yes

3. Are the provisional recommendations of the Appraisal Committee sound and do they constitute a suitable basis for the preparation of guidance to the NHS? *If not, why do you consider that the recommendations are not sound? Yes*

4. Are the patient pathways and treatment options described in the assessment applicable to NHSScotland? Yes

5. Would the provisional recommendations change the patient pathways and/or patient numbers in NHSScotland? The lack of recommendation regarding sequential treatment with anti TNF may change the practice of using a second agent when the first is stopped due to loss of effect.

6. Do you think there is any reason why this provisional guidance would not be as valid in Scotland as it is in England and Wales? *No*

[redacted]

1. Do you consider that all the relevant evidence has been taken into account? *If not, what evidence do you consider has been omitted, and what are the implications of this omission on the results?*

I note that this Appraisal Consultation Document on Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis. As such it does not focus on conventional disease modifying therapy and omits golimumab. The inclusion of PASI scores in the economic analysis further complicates interpretation as the 2 processes are disconjugate in individual patients.

The methodology differs from SIGN guidance where much of the data was obtained from meta-analysis and systematic reviews. The validity of the assessment group meta-analysis for NICE cannot be commented upon without further information.

For etanercept the two studies referenced are Mease 2000 and Mease 2004. Recently Sterry et al BMJ 2010 have published on the PRESTA study comparing two different strategies for etanercept dosing. This is unlikely to have an impact on the conclusions of this document as the benefits were on speed of skin improvement rather than improvement in articular outcomes. Economic analysis is unlikely to prove favourable. Zachariae (Acta Derma Venereol 2008) also showed enhanced benefits of combination of methotrextae and etanercept on skin outcomes. In other studies this combination has not been shown to have enhanced effect on articular outcomes however may affect the assessment groups model of cost effectiveness.

Although erosion scores were included in the clinical outcome for Mease etanercept and adalimumab studies, it is only in subsequent publications for infliximab (Van Der Heijde Ann Rheum Disease 2005;64 Suppl3:109) that the inhibition of erosions has been shown to be statistically significant. It could be interpreted that all three biologics inhibit erosions and therefore the omission of erosive scores in the economic analysis is unlikely to effect outcome.

2. Are the provisional recommendations of the Appraisal Committee sound and do they constitute a suitable basis for the preparation of guidance to the NHS? *If not, why do you consider that the recommendations are not sound?*

The summaries of clinical and cost effectiveness seem reasonable given the above points.

3. Are the patient pathways and treatment options described in the assessment applicable to NHSScotland? *If not, how do they differ in Scotland?*

Many of the studies of anti-TNF agents enrolled patients who had disease activity less than that suggested by NICE and often they had not failed 2 standard disease modifying anti-rheumatic drugs (DMARDs) . This has been commented upon in the preliminary recommendation.

It was commented that the adverse event profile of anti TNF agents was comparable to that of conventional DMARDs yet no references were given for this statement. Withdrawal rates in studies using conventional DMARDs are often much higher than withdrawals from anti TNF agent studies. As such they may be said to have a worse toxicity to efficacy ratio.

It is interesting that it is suggested that a trial of two conventional DMARDs are used prior to anti TNF agents. Again this statement doesn't have a particularly strong evidence base. Sulfasalazine and methotrexate were mentioned as DMARDs of choice. Up until recently there was very little evidence base for methotrexate and the data on sulfasalazine is very weak. Leflunomide is not mentioned despite it being mentioned in SIGN guidance. The evidence is lacking on the effectiveness of a second DMARD when the first has failed. This seems to be a pragmatic stance to limit economic impact and maintain a similarity with the guidance on rheumatoid arthritis.

The pathways and treatment options do seem to be applicable to NHS Scotland perhaps with some debate over how many DMARDs should be tried before anti-TNF

4. Would the provisional recommendations change the patient pathways and/or patient numbers in NHSScotland? *If so, please describe what these changes would be.* No

5. Do you think there is any reason why this provisional guidance would not be as valid in Scotland as it is in England and Wales? *If yes, please explain why this is the case.* No

[redacted]

8 April 2010