**Sequential use of Adalimumab, Etanercept and Infliximab for the treatment of Rheumatoid Arthritis**

**Royal College of Nursing**

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The RCN welcomes the opportunity to review the Appraisal Consultation Document (ACD) on the sequential use of Anti-TNFs for the treatment of Rheumatoid Arthritis.

## RCN Response to the ACD on the Sequential Use of Anti-TNFs

We thank NICE for giving us the opportunity to comment on this document and will respond under the following general headings:

*i). Do you consider that all of the relevant evidence has been taken into account?*

We feel that the Committee has failed to take all of the evidence into account for the following reasons:

Since the introduction of biologic therapies the patients who have had access to these drugs earliest, in routine practice, are those with longer disease duration and worse disease. They have already had numerous, if not all, the DMARD's prior to commencing anti-TNF.

We agree there is a sparsity of evidence, due to the fact that we have not had the experience using these drugs and having to go back to conventional therapy. To expect these patients to return to traditional DMARD's following failure of one anti-

TNF agent, having already failed this group makes no sense, especially when there is a potential for success with another untried agent.

Whilst the Appraisal Committee considered Rituximab, as the alternative treatment where patients had failed on one anti-TNF therapy, we have concerns that the DANCER trail (1) showed no efficacy in seronegative disease compared with placebo. In addition the REFLEX study (2) showed reduced efficacy in seronegative disease in comparison to seropositive disease. For this group of patients there is a reluctance to use Rituximab, indeed the EULAR guidelines for Rituximab (3) advise the avoidance in seronegative disease. In addition to this we have concerns that there is no data on the use of Rituximab long term in RA and the cumulative effect of B cell depletion on the immune system in these patients.

We are not familiar with the US National Databank for Rheumatic Diseases and would question whether the data collected (given the completely different healthcare system and the propensity to private practice) is accurate or transferable to the UK system. We would also query the use of including unpublished data in the ACD as we were under the impression that the Committee preferred to use published data as evidence?

*ii). Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate?*

We have commented in previous appraisals on our concerns of the BRAM and its continued use in appraisals.

We continue to contest that fall in HAQ is not a sensitive enough measure of outcome in this group of patients. We would also wish to comment that for patients on anti-TNF therapies, having had to fail at least 2 DMARDs before being allowed therapy, there is almost certainly considerable joint damage which will not lead to a significant reduction in HAQ as a result of anti-TNF and continues to falsely affect the economic models.

We also believe that it is unreasonable to assess health economics and not attempt to look at wider health and social care costs. Whilst it may be argued that these are

not available, is emerging evidence as seen in the article by Weiss et al (4) worth considering?

As representatives of rheumatology nurses who deal with these patients on a day to day basis, it is us who will be discussing options for treatment with them and strongly feel that to accept the ACD as it stands, without looking at some sort of wider health and social care cost is condemning a group of patients with the worst disease to nothing less than palliative care.

*iii). Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?*

There may be an additional factor that has not been considered in this judgement. Patient's perceptions and anxieties about being taken off treatment may result in extreme vigilance in relation to possible adverse event and thus focus on this issue. This has the potential to distort evidence in relation to the long term safety and efficacy data on these therapies.

For all the reasons stated above we consider that these provisional recommendations are not sound, and do not constitute a suitable basis for the preparation of guidance to the NHS. We request that this issue is explored further for the benefit of our patients.

## References


1. Emery P, Fleischmann R, Filipowicz-Sonowska A, et al. The efficacy and safety of rituximab in patients with active rheumatoid arthritis despite methotrexate treatment: results of a phase IIb double-blind, placebo-controlled, dose-ranging trial (DANCER). Arthritis Rheum 2006;54:1390-400.
2. Cohen S, Emery P, Greenwald M, et al. Rituximab for rheumatoid arthritis refractory to anti-tumour necrosis factor therapy. Arthritis Rheum 2006;54:2793-806
3. Smolen S, Keystone EC, Emery P, et al. Consensus statement on the use of rituximab in patients with rheumatoid arthritis. Ann Rheum Dis 2007;66:143-150.
4. Weiss RJ, Ehlin A, Montgomery SM, Wick MC, Stark A, Wrentenberg P. Decrease in RA related orthopaedic surgery of the upper limbs between 1998 and 2004: data from 54579 Swedish RA inpatients.