Introduction

With a membership of over 395,000 registered nurses, midwives, health visitors, nursing students, health care assistants and nurse cadets, the Royal College of Nursing (RCN) is the voice of nursing across the UK and the largest professional union of nursing staff in the world. RCN members work in a variety of hospital and community settings in the NHS and the independent sector. The RCN promotes patient and nursing interests on a wide range of issues by working closely with the Government, the UK parliaments and other national and European political institutions, trade unions, professional bodies and voluntary organisations.

Response to the Appraisal Consultation Document on the use of Rituximab for the treatment of Rheumatoid Arthritis (RA)

Having read all the evidence submitted to we make the following response as requested:

Relevance Evidence taken into account:

Rheumatoid Arthritis is a complex chronic condition and as such truly evaluating the global ramifications of the condition and potential benefits to
treatment is challenging. This can be seen in the recent appeal related to the Final Appraisal Determination in relation to Anti-TNFα therapies.

The Roche model has attempted to include additional components of management and used two possible scenarios.

Scenario One: return to DMARDs (palliative care)

Scenario Two: TNF inhibitor used sequentially (DMARDs (Leflunomide, Gold, Ciclosporin) (palliative care).

We concur that greater level of analysis is required on issues outlined: (1.2.1 – 1.2.3)

**Our response in relation to the model of the two scenarios:**

We believe these two models are appropriate models to apply in the management pathway of patients with RA.

The second scenario would currently reflect a significant number of patients in clinical practice who have severe long standing disease.

DAS 28 is a more suitable clinical practice tool for assessing disease activity although it has to be accepted that there are limitations in identifying patients who may have extra-articular features not documented on the DAS 28 that require optimisation of treatment (for example cardiac, respiratory involvement).

**Reasonableness of the summaries of clinical effectiveness and cost effectiveness**

For those who are eligible for anti-TNFα, they will on average have disease duration of 14 years (as currently documented with the British Society for Rheumatology Biologics Register (BSRBR)). These patients currently have multiple co-morbidities and refractory disease.
We would suggest that the Health Assessment Question (HAQ) deterioration being considered as equal for all treatment arms is flawed. DMARDs may be ineffective (particularly if received as a re-treatment having previously failed such a therapy prior to anti-TNFα). Disease progression and ultimately HAQ deterioration is likely to escalate when receiving sub-optimal treatment. HAQ changes relates to the individual’s disease severity and equally disease duration. The average HAQ score on the British Society for Rheumatology Biologics Register (BSRBR)) for patients at baseline was 2.1. HAQ is an important measure that has strengths and weaknesses. It should be used in the context of other patient reported outcomes to triangulate evidence and costing assumptions.

**Direct Costs:** Costs related to hospital care and direct costs appear to be significantly under-estimated. This is not only related to the limitations in this model but in larger assumptions about the management and treatment needs of patients with RA particularly in those who have had sub optimal treatment. This is reflected in the minimal hospital data collected in relation to cardiovascular, respiratory or other co-morbidities that should be more clearly attributed to the RA.

The NOAR data has been criticised as model to use in economic assumptions particularly as they are based on a community based group of patients with inflammatory arthritis (not necessarily diagnosed as RA) and treated promptly and aggressively at presentation. They may not reflect the RA community in general. Despite this point, hospital admission related to cardiovascular disease which was published demonstrated hospitalisation for cardiovascular disease is common for patients with Inflammatory arthritis.

The cost effectiveness calculations related to joint replacement surgery for patients we would suggest is an underestimation. Studies have shows that radiological damage progresses at a constant rate. In a UK study 11% of patients (with an age range of 17 – 84 years median age of onset 55 yrs) had joint replacement surgery at 5 years. These operations are often considered technically more complex than routine joint replacement surgery and also
include a greater range of joints requiring surgery including small joint surgery. Early studies show superior reduction in joint damage attributed to anti-TNFα therapies and reductions in joint replacement surgery.⁴ ⁵

Hospitalisation rates have changed significantly in the last ten years with an increasing level of day case activity and reduced rheumatology inpatient admissions. We note hospital admissions in this model include xx

We understand NICE are also referring to the on-going appeal in regard to anti-TNFα inhibitors (adalimumab, etanercept and infliximab) related to cost effectiveness and clinical effectiveness.

2.1.1. Cost effectiveness direct comparisons:

Sub group analysis regarding greater length of time to re-treatment for patients who have failed one TNFα inhibitors may reflect patients who have had their disease treated promptly and proactively and therefore have an optimal response to treatment. Patients with long standing refractory disease may be harder to achieve optimum disease control due to high inflammatory markers that are perpetuated (they may reflect the patients with the most aggressive disease in the sense of disease control and progression).

Whether evidence and preliminary views of the resource impact and implications are appropriate

The direct costs related to managing patients with Rituximab are related to day cases x 2 for infusions plus assessment and review. However, follow up appointments are reduced significantly and patient’s work related activities should benefit from treatment.

We suggest that having Rituximab in the treatment pathway will have additional important reductions in long term costs for patients with RA. This is partly due to the optimising of treatment along the patient pathway of care – and potentially reducing palliative care issues seen prior to the introduction of effective disease controlling therapies. These issues include tissue viability
issues, hospital inpatient stays, community and social care (including occupational therapy and adaptations for the home).

However, currently the economic modelling requires further work to be able to clearly identify the key issues in patient outcomes and ultimately where Rituximab can effectively sit in the treatment options (scenario 1 or 2).

**Whether we consider that the provisional recommendations of the Appraisal Committee are sound and a suitable basis for the preparation to the NHS.**

Clinical practice currently suggests for instance that patients eligible for TNF inhibitors have already failed between 4 to 6 DMARDs, this is reflected in the British Society for Rheumatology Biologics Register.

There are important additional considerations in the sense of providing a treatment option for those who are contra-indicated TNFα inhibitors who may well be eligible for treatment with Rituximab (for example the patient with malignancy within the last ten years).

Leflunomide is an important DMARD and should be considered as part of the treatment pathway for patients with active disease and frequently will have already been considered prior to starting TNFα inhibitors. However, it should not be considered as an alternative to B cell depletion therapy. Equally many DMARDs fail to maintain disease control in the long term and this is also the case with Leflunomide.

Rituximab must be considered as an alternative for those who fail TNFα inhibitors. Evidence is evolving that demonstrates the unique and variable aspects of the disease in the sense of treatment response rates. Patients may fail to respond well to TNFα inhibitors, however, there are also some patients who fail to gain significant benefit and the disease continues to progress. My experience with Rituximab is that for some patients this has been the only treatment to control the disease and ultimately reduce functional limitations.
We feel that the appraisal committee should re-consider their decision in the light of Rituximab’s unique treatment potential for those who fail TNFα inhibitors. We will be failing the patients if we return them to palliative care.

It is hoped that Rituximab will become a therapy that will be observed in the same way as TNFα inhibitors as part of the BSRBR data collection. If this were the case we could review important considerations such as time to re-treatment and review response measurements as part of a large observational study with a control cohort.
Reference List


