NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Rituximab for the treatment of rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of rituximab within its licensed indication for the treatment of rheumatoid arthritis after the failure of disease modifying anti-rheumatic drugs.

Background

Rheumatoid arthritis is a chronic, disabling autoimmune disease characterised by inflammation of the synovial tissue of the peripheral joints, which causes swelling, stiffness, pain and progressive joint destruction. For a small proportion of people, inflammatory disease outside the joints (for example, eye and lung disease, vasculitis) can also pose a significant problem. Rheumatoid arthritis is often a chronic relapsing condition which has a pattern of flare-ups followed by periods of lower disease activity; however, for some people, the disease is constantly progressive. Most people develop damage to affected joints due to inflammation with the amount of damage ranging from mild to severe. Rheumatoid arthritis has a severe impact on quality of life and it is estimated that 40% of people with RA will stop working within 5 years of diagnosis.

Rheumatoid arthritis is three times more prevalent in women than in men. It can develop at any age, but usually starts between 40 and 60 years of age. Rheumatoid arthritis affects 0.7% of the population, or approximately 350,000 people in England and Wales. Of these, approximately 15% have severe disease.

People with rheumatoid arthritis are usually treated in an out-patient setting and then in primary care. There is no cure for rheumatoid arthritis and treatment aims to improve quality of life and to prevent or reduce joint damage. Treatment for rheumatoid arthritis usually includes: non-steroidal anti-inflammatory agents (NSAIDs), which reduce pain, fever and joint swelling / inflammation; disease modifying anti-rheumatic drugs (DMARDs), which slow the disease process and reduce joint damage; and corticosteroids, which also control inflammation. DMARDs may be broadly classed as either conventional or biologic, the latter group including, but not limited to, tumour necrosis factor (TNF) inhibitors.

NICE Clinical Guideline (CG 79) recommends the use of a combination of DMARDS (including methotrexate and at least one other DMARD) as first-line

treatment, ideally beginning within 3 months of the onset of persistent symptoms. Where combination therapies are not indicated (such as in cases of methotrexate intolerance), CG79 recommends monotherapy with fast escalation to a clinically effective dose. NICE guidance (TA130, TA186) recommends the use of TNF inhibitors etanercept, infliximab, adalimumab, and certolizumab pegol as treatment options for people with active disease who have tried two conventional DMARDs, including methotrexate, and have a disease activity severity score greater than 5.1.

The technology

Rituximab (MabThera, Roche Products) is a genetically engineered chimeric monoclonal antibody that depletes the B-cell population by targeting cells bearing the CD20 surface marker. It is administered by intravenous infusion.

Rituximab does not have a UK marketing authorisation for the treatment of rheumatoid arthritis after the failure of only conventional DMARDs. Rituximab has been studied in clinical trials in comparison with placebo in adults who have had an inadequate response to conventional DMARDs.

Intervention(s)	Rituximab
Population(s)	People with rheumatoid arthritis who have had an inadequate response to or have intolerance to conventional DMARDs.
Comparators	• Treatment strategies with biological agents (including adalimumab, etanercept, infliximab, certolizumab pegol, golimumab) • Conventional DMARDs such as sulfasalazine and leflunomide

Outcomes	The outcome measures to be considered include: • disease activity • physical function • joint damage • pain • mortality • fatigue • radiological progression • extra-articular manifestations of disease • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	This appraisal will only consider the use of rituximab after the failure of conventional disease-modifying anti-rheumatic drugs alone. It will not include a review of the guidance in technology appraisal 195 relating to the use of rituximab after the failure of a TNF inhibitor. If evidence allows, the appraisal will consider subgroups of people defined by their auto-antibody status (for example, rheumatoid factor status and CCP antibody status). If the evidence allows, the appraisal will consider the costs of joint replacement therapy and hospital admissions. If evidence allows, the appraisal will allow for variability in the time to re-treatment with rituximab. If evidence allows, the appraisal will consider the effects of treatment continuation and/or stopping rules. Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 198, August 2010, Tocilizumab for the treatment of rheumatoid arthritis. Expected review date June 2013. Technology Appraisal No. 195, August 2010, Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of the first TNF inhibitor. Expected review date June 2013. Technology Appraisal No. 186, February 2010, Certolizumab pegol for the treatment of rheumatoid arthritis. Expected review date September 2010. Technology Appraisal No.130, October 2007, Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis. Superseded technology appraisal No. 36. Expected review date September 2010. Ongoing Technology Appraisals: Technology Appraisal in Preparation, Golimumab for the treatment of rheumatoid arthritis after failure of previous disease-modifying antirheumatic drugs. Earliest anticipated date of publication March 2011. Technology Appraisal in Preparation (Suspended), Golimumab for the treatment of methotrexate-naïve rheumatoid arthritis. Earliest anticipated date of publication TBC. Related Guidelines: Clinical Guideline No. 79, February 2009, Rheumatoid arthritis: the management of rheumatoid arthritis in adults.