NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Rituximab for the treatment of methotrexate-naive rheumatoid arthritis and of rheumatoid arthritis after the failure of disease-modifying anti-rheumatic drugs

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of rituximab within its licensed indications for the treatment of methotrexate-naive rheumatoid arthritis or 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 heterogeneous, it is usually a chronic relapsing condition which has a pattern of flare-ups followed by periods of lower disease activity, but for a minority of 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 1% of the population, or approximately 400,000 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 Guidelines (CG 79) recommend 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) recommends the use of TNF inhibitors etanercept, infliximab, and adalimumab after the failure of two conventional DMARDs, including methotrexate. NICE guidance (TA126) also recommends the use of rituximab in combination with methotrexate after the failure of a TNF-α inhibitor.

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 has been studied in clinical trials in comparison with placebo in adults with active methotrexate-naive rheumatoid arthritis and in those who have had an inadequate response to conventional DMARDs. It is administered by intravenous infusion.

Intervention(s)	Rituximab
Population(s)	People with rheumatoid arthritis who have not been previously treated with methotrexate. People with rheumatoid arthritis who have had an inadequate response to conventional DMARDs.
Comparators	For people with rheumatoid arthritis who have not been previously treated with methotrexate: • Combination therapy with conventional DMARDs (including methotrexate and at least one other DMARD, such as sulfasalazine and leflunomide), or DMARD monotherapy (excluding methotrexate) with dose escalation For people with rheumatoid arthritis who have had an inadequate response to conventional DMARDs: • Treatment with biological agents (including adalimumab, etanercept, infliximab, tocilizumab, certolizumab pegol, golimumab)

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	If evidence allows, the appraisal will consider subgroups of people identified as sero-negative or sero-positive. If the evidence allows, the appraisal will consider the costs of joint replacement therapy and hospital admissions. Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 141, April 2008, Abatacept for the treatment of rheumatoid arthritis. Currently subject to review. Earliest anticipated date of publication June 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. Technology Appraisal No. 126, August 2007, Rituximab for the treatment of rheumatoid arthritis. Currently subject to review. Earliest anticipated date of publication June 2010. Ongoing Technology Appraisals: Technology Appraisal in Preparation, Certolizumab pegol for the treatment of rheumatoid arthritis. Earliest anticipated date of publication February 2010. Technology Appraisal in Preparation, Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of the first TNF inhibitor. Earliest anticipated date of publication June 2010. Technology Appraisal in Preparation, Tocilizumab for the treatment of rheumatoid arthritis. Earliest anticipated date of publication February 2010. Technology Appraisal in Preparation (Suspended), Golimumab for the treatment of rheumatoid arthritis after failure of previous disease-modifying antirheumatic drugs. Earliest anticipated date of publication TBC. 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.

Questions for consultation

Have the most appropriate comparators for the treatment of methotrexate-naive rheumatoid arthritis and of rheumatoid arthritis failing to respond to conventional DMARDs been included in the scope?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)