NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Abatacept for the treatment 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 abatacept within its licensed indication for the treatment of rheumatoid arthritis after the failure of disease-modifying anti-rheumatic drugs.

Background

Rheumatoid arthritis is an inflammatory autoimmune disease that typically affects the synovial tissue of the small joints of the hands and feet but can affect any synovial joint, causing swelling, stiffness, pain and progressive joint destruction. It is a systemic disease and can affect the whole body, including the lungs, heart and eyes. Rheumatoid arthritis is usually a chronic relapsing condition with flare-ups followed by periods of lower disease activity, but may be constantly progressive in some people. Rheumatoid arthritis has a severe impact on quality of life and it is estimated that approximately one third of people stop work within 2 years because of the disease, and this prevalence increases thereafter.

Rheumatoid arthritis affects approximately 0.8% of the population, or approximately 400,000 people in the UK. Of these, approximately 15% have severe disease. It is about two to four times more prevalent in women than in men. It can develop at any age, but the peak age of incidence in the UK is about 70 years

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 and disease modifying anti-rheumatic drugs (DMARDS) which slow the disease process and reduce joint damage. Corticosteroids may also be used to control inflammation. The main aim of management in early disease is to suppress disease activity, prevent loss of function, control joint damage, maintain pain control and enhance self-management. In established disease, management should address complications and associated comorbidity; and the impact of the condition on the patient's quality of life.

For people with newly diagnosed rheumatoid arthritis, NICE Clinical Guideline (CG 79) recommends a combination of DMARDS (including methotrexate and at least one other DMARD plus short term glucocorticoids) as first-line treatment, ideally beginning within 3 months of the onset of persistent symptoms. Where combination therapies are not appropriate (such as in

cases of methotrexate intolerance) DMARD monotherapy is recommended. NICE guidance (TA 130) recommends the use of the TNF inhibitors etanercept, infliximab, and adalimumab in people with severe active rheumatoid arthritis after the failure of two conventional DMARDs, including methotrexate. NICE guidance (TA 126) recommends the use of rituximab in combination with methotrexate when there has been an inadequate response to other DMARDs, including at least one TNF-α inhibitor. Current NICE Guidance (TA 141) states that abatacept is not recommended for the treatment of people with rheumatoid arthritis after the failure of a TNF inhibitor.

The technology

Abatacept (Orencia, Bristol-Myers Squibb) is a selective modulator of the T lymphocyte activation pathway. It acts by binding to molecules on the surface of antigen presenting cells which prevents full activation of the T lymphocytes and interrupts the inflammatory process. It is administered by intravenous infusion.

Abatacept does not have a UK marketing authorisation for the treatment of rheumatoid arthritis after the failure of DMARDs. It currently has marketing authorisation for the treatment of moderate to severe active rheumatoid arthritis after the failure of DMARDs including at least one TNF inhibitor. Clinical trials have compared combination treatment of abatacept plus methotrexate compared with infliximab and adalimumab in combination with methotrexate in patients who have had an inadequate response to methotrexate. It has also been studied in comparison with placebo in patients who have had an inadequate response to methotrexate.

Intervention(s)	Abatacept in combination with methotrexate
Population(s)	Adults with rheumatoid arthritis who have had an inadequate response to one or more disease modifying antirheumatic drugs (DMARDs) including methotrexate
Comparators	Management strategies involving DMARDs without abatacept including: • conventional DMARDs (for example sulfasalazine, leflunomide) • adalimumab, etanercept, infliximab • tocilizumab, certolizumab pegol, rituximab (subject to ongoing appraisals) • golimumab (subject to marketing authorisation)
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	Guidance will only be issued in accordance with the marketing authorisation If the evidence allows, the appraisal will consider the costs of joint replacement therapy and hospital admissions.
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 May 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. Technology Appraisal in Process, Rituximab for the treatment of methotrexate-naive rheumatoid arthritis and of rheumatoid arthritis after failure of disease-modifying anti-rheumatic drugs. 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 rheumatoid arthritis been included in the scope? Are the comparators listed routinely used in clinical practice? Should methotrexate and other conventional DMARDs be included as comparators?

Are there any 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?

How does the appraisal of abatacept for the treatment of rheumatoid arthritis relate to potential reviews, ongoing and proposed technology appraisals for other rheumatoid arthritis technologies?

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