NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Abatacept 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 abatacept within its licensed indication for the treatment of rheumatoid arthritis only after the failure of conventional 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 which has a pattern of flare-ups followed by periods of lower disease activity; however, for some people, the disease is constantly progressive. 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 580,000 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 onset in the UK is about 40-70 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 and TA186) recommends the use of the TNF inhibitors etanercept, infliximab, adalimumab and certolizumab pegol in people with severe active rheumatoid arthritis after the failure of two conventional DMARDs, including methotrexate, and have a disease activity severity score greater than 5.1. NICE has also issued guidance (TA195 and TA198) on the treatment of rheumatoid arthritis after the failure of TNF inhibitors but this will not be addressed in this appraisal.

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 in combination with methotrexate received a UK marketing authorisation in May 2005 for the treatment of moderate to severe active rheumatoid arthritis in adult patients who responded inadequately to previous therapy with one or more DMARDs including at least one TNF inhibitor. In May 2010, abatacept received a licence extension which allows it to be used for the treatment of moderate to severe active rheumatoid arthritis in adult patients who responded inadequately to previous therapy with one or more DMARDs including methotrexate or a TNF-alpha inhibitor.

Intervention(s)	Abatacept in combination with methotrexate
Population(s)	Adults with rheumatoid arthritis who have had an inadequate response to one or more conventional DMARDs including methotrexate
Comparators	Management strategies involving DMARDs without abatacept including: • biologics (adalimumab, etanercept, infliximab, certolizumab pegol, golimumab) • conventional DMARDs (for example sulfasalazine, leflunomide)
Outcomes	The outcome measures to be considered include: • disease activity • physical function • joint damage • pain

	• mortality • fatigue • 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. If the evidence allows, the appraisal will consider subgroups based on: • Severity of disease activity: moderate to severe disease and severe disease • Auto antibody status including rheumatoid factor and anti CCP Consultees at the scoping workshop highlighted that abatacept had a unique mechanism of action to the other available biologic therapies. This appraisal will consider the use of abatacept only after the failure of conventional DMARDs alone. It will not include a review of the guidance in technology appraisal 195 relating to the use of abatacept after the failure of a TNF inhibitor.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No 198, Tocilizumab for the treatment of rheumatoid arthritis. Expected review date June 2013. Technology Appraisal No 195, Adalimumab, etanercept, infliximab, rituximab and abatacept for the

	treatment of rheumatoid arthritis after the failure of the first TNF inhibitor. Superseded technology appraisal Nos. 126, 141 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. Technology Appraisal in Preparation, Rituximab for the treatment of rheumatoid arthritis after failure of disease-modifying anti-rheumatic drugs. Earliest anticipated date of publication July 2011 Related Guidelines: Clinical Guideline No. 79, February 2009, Rheumatoid arthritis: the management of rheumatoid arthritis in adults. Expected review date February 2012.