NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Tofacitinib for the treatment of moderate to severe active rheumatoid arthritis

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of tofacitinib within its licensed indication for the treatment of rheumatoid arthritis 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 can have a severe impact on quality of life and it is estimated that approximately one third of people with rheumatoid arthritis stop working within 2 years of diagnosis.

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 between 40 to 70 years.

There is no cure for rheumatoid arthritis. 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, TA186 and TA 225) recommends the use of the TNF inhibitors etanercept, infliximab, adalimumab, certolizumab pegol and golimumab in people with severe active rheumatoid arthritis after the failure of two conventional DMARDs, including methotrexate, who have a disease activity severity score greater than 5.1. NICE has also issued guidance (TA195, TA198 and TA225) on the treatment of rheumatoid arthritis after the failure of TNF inhibitors but this will not be addressed in this appraisal. There is currently a NICE rapid review of NICE guidance TA 198.

The technology

Tofacitinib (Brand name unknown, Pfizer) is a selective inhibitor which blocks intracellular signalling through the gamma chain-containing cytokines and can prevent full activation of lymphocytes and interrupt the inflammatory process. Tofacitinib is administered orally.

Tofacitinib does not currently have a UK marketing authorisation for the treatment of moderate to severe active rheumatoid arthritis. It has been studied in combination with methotrexate in adults whose rheumatoid arthritis is resistant to treatment with methotrexate or whose rheumatoid arthritis has had an inadequate response to, or who are intolerant to one or more conventional non-biological DMARDs including methotrexate, compared with placebo or adalimumab plus methotrexate.

Intervention(s)	Tofacitinib
Population(s)	Adults with moderate to severe rheumatoid arthritis whose disease is resistant to treatment with methotrexate, or whose disease has had an inadequate response to, or who are intolerant to, one or more conventional non-biological DMARDs including methotrexate
Comparators	Management strategies involving DMARDs without tofacitinib including: • biologics (adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab (subject to an ongoing NICE appraisal)) • 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: • Baseline severity of disease activity

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No 234, August 2011, Abatacept for the treatment of rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs. Expected review date July 2014. Technology Appraisal No 225, June 2011, Golimumab for the treatment of rheumatoid arthritis after failure of previous disease-modifying anti-rheumatic drugs. Expected review date June 2014. Technology Appraisal No 198, August 2010, Tocilizumab for the treatment of rheumatoid arthritis. Under NICE rapid review. 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. 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 TBC Technology Appraisal No.130, October 2007, Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis. Superseded technology appraisal No. 36. Expected review date TBC Technology Appraisal No.224, June 2011, Golimumab for the treatment of methotrexate-naïve rheumatoid arthritis (Terminated). Ongoing Technology Appraisals: Technology Appraisal in Preparation (Suspended), Rituximab for the treatment of rheumatoid arthritis after failure of disease-modifying anti-rheumatic drugs. Earliest anticipated date of publication TBC. Technology Appraisal in Preparation, Tocilizumab for the treatment of rheumatoid arthritis (Rapid review of TA198). Earliest anticipated date of publication TBC Related Guidelines: Clinical Guideline No. 79, February 2009, Rheumatoid arthritis: the management of rheumatoid arthritis in adults. Expected review date February 2012.

Questions for consultation

Have the most appropriate comparators for tofacitinib for the treatment of moderate to severe active rheumatoid arthritis been included in the scope? Are the comparators listed routinely used in clinical practice?

Are the subgroups suggested in 'other considerations appropriate?

- Are there any other subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

- Should there be a subgroup based on antibody status including rheumatoid factor status and anti-CPP status?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

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)