NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Tocilizumab for the treatment of rheumatoid arthritis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of tocilizumab within its licensed indication for the treatment of rheumatoid arthritis.

Background

Rheumatoid arthritis (RA) is a chronic, multi system, disabling condition characterised by inflammation of the, joints, causing pain, swelling, stiffness and progressive joint destruction as well as premature mortality. It affects between 0.5% and 1% of the population, or approximately 400,000 people in England and Wales. Of these, approximately 30 to 40% have moderate to severe disease despite treatment with conventional disease modifying anti-rheumatic drugs (DMARDs).

Treatment aims to control pain and inflammation, and reduce joint damage, disability and loss of function, thereby improving quality of life. It involves a combination of pharmacological and non-pharmacological interventions. Pharmacological interventions include non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, analgesics and disease-modifying anti-rheumatic drugs (DMARDs) of which methotrexate or sulfasalazine are most commonly used as initial therapy. Non-pharmacological therapies include surgery, physiotherapy and occupational therapy.

For people with RA who have had an inadequate response to at least two DMARDs, including methotrexate, current NICE guidance states that the TNF inhibitors adalimumab, etanercept or infliximab (in combination with methotrexate) are recommended. There is an ongoing appraisal of the use of a second TNF inhibitor after the first has failed. The current NICE Guidance states that abatacept is not recommended for the treatment of people with rheumatoid arthritis, and that rituximab in combination with methotrexate is recommended for people with severe RA in whom TNF-inhibitor therapy has failed.

The technology

Tocilizumab (Roche) is a humanised monoclonal antibody that inhibits the activity of the cytokine interleukin-6 (IL-6). IL-6 is a pro-inflammatory mediator and reducing the activity of IL-6 may reduce inflammation in the joints, prevent long-term damage, improve QoL and function and relieve certain systemic effects of RA.

Tocilizumab has no marketing authorisation for the use in RA in the UK. It has been studied in clinical trials as monotherapy and in combination with

methotrexate in adults with moderate to severe RA in whom previous DMARD therapy has failed. The anticipated marketing authorisation for tocilizumab will be for adults with moderate to severe RA in whom DMARDs or a TNF inhibitor has failed. Tocilizumab is administered as an intravenous injection.

Intervention(s)	Tocilizumab alone or in combination with methotrexate
Population(s)	Adults with moderate to severe rheumatoid arthritis
Comparators	Management strategies involving DMARDs without tocilizumab, including treatment with: • conventional DMARDs • biologic agents including adalimumab, etanercept, infliximab and rituximab
Outcomes	The outcome measures to be considered include: • disease activity • physical function • joint damage/radiographic progression • joint replacement • pain • mortality • fatigue • health-related quality of life • adverse effects of treatment
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. Where evidence allows, subgroup analysis may be carried out in sero-positive and sero-negative patients or any other bio-markers that may define subgroups

Related NICE recommendations	Related NICE technology appraisals: • Technology Appraisal No 126, August 2007, Rituximab for the treatment of rheumatoid arthritis (expected review date July 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 141, April 2008, Abatacept for the treatment of rheumatoid arthritis (expected review date July 2010) • Technology Appraisal No 72, November, 2003, Anakinra for the treatment of rheumatoid arthritis, the review of this guidance will be incorporated within in the ongoing clinical guideline (see below). Ongoing NICE technology appraisals: • Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis (anticipated date of publication TBC) Ongoing NICE clinical guidelines: • Rheumatoid arthritis in adults, earliest anticipated date of publication February 2009. Related Interventional Procedures: None Related Public Health Guidance/Guidelines: None