NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Multiple Technology Appraisal

TNF-alpha inhibitors for ankylosing spondylitis and axial spondyloarthritis without radiographic evidence of ankylosing spondylitis (including a review of technology appraisal 143 and technology appraisal 233)

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of TNF-alpha inhibitors within their licensed indications for treating ankylosing spondylitis and axial spondyloarthritis without radiographic evidence of ankylosing spondylitis.

Background

Spondyloarthritis is a clinically heterogeneous group of inflammatory rheumatologic diseases which share common genetic, histological and clinical features. Diseases belonging to this group include ankylosing spondylitis, psoriatic arthritis, arthritis associated with inflammatory bowel disease, reactive arthritis and undifferentiated spondyloarthritis. Spondyloarthritis can be categorised as having predominantly axial (sacroiliac joints or spine) or peripheral involvement.

The term axial spondyloarthritis refers to a form of spondyloarthritis in which the predominant symptom is back pain, and where the sacroiliac joint at the base of the spine might or might not be inflamed on radiography (if the sacroiliac joint is inflamed the condition is termed sacroiliitis). If definite radiographic sacroiliitis on plain X-rays is present, the disease can be classified as ankylosing spondylitis. If definite sacroiliitis is absent on radiography, the disease is classified as axial undifferentiated spondyloarthritis.

In ankylosing spondylitis, sacroiliitis is present and this inflammation rises up the spine. The result is back pain and stiffness. Inflammation at entheses (the sites where ligaments and tendons attach to bone) can lead to new bone development and joint fixation (ankylosis). Other joints of the body may also be involved, and the eye, bowel and cardiovascular system can be affected. The course of the disease varies among patients. It is characterised by mild or moderate flares of active disease alongside persistent symptoms. Occasionally the disease is severe leading to spinal fusion and significant deformities that may require joint replacement surgery for some patients.

New criteria for the diagnosis of axial spondyloarthritis have been proposed recently by the Assessment of Spondyloarthritis International Society (ASAS).

As a result, limited epidemiology data are available for axial spondyloarthritis defined according to the new criteria. For ankylosing spondylitis, the prevalence is thought to range from 0.05% to 0.23%. Ankylosing spondylitis typically affects young people, with an average age of onset of 24 years. It is nearly 3 times more common in men than in women, and men are more likely to develop severe spinal disease.

Conventional therapy includes acute anti-inflammatory treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and local corticosteroids, disease-modifying drugs (DMARDs, such as sulfasalazine and methotrexate) and physiotherapy. Tumour necrosis factor-alpha (TNF-alpha) inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab and infliximab) are typically used when the disease has not responded adequately to conventional therapy. NICE technology appraisal 143 recommends adalimumab and etanercept as treatment options for adults with severe active ankylosing spondylitis only if certain criteria are fulfilled, but it does not recommend infliximab for ankylosing spondylitis. Golimumab is also recommended in NICE technology appraisal 233 as an option for the treatment of severe, active ankylosing spondylitis in adults only if it is used as described for adalimumab and etanercept in NICE technology appraisal 143.

The technology

Adalimumab (Humira, AbbVie), certolizumab pegol (Cimzia, UCB Pharma), etanercept (Enbrel, Pfizer), golimumab (Simponi, MSD), and infliximab (Remicade, MSD) inhibit the activity of tumour necrosis factor-alpha (TNF-alpha). TNF-alpha is an inflammatory cytokine or pro-inflammatory mediator which is involved in the inflammatory processes when present in excessive concentrations. Agents that inhibit the action of TNF-alpha might thus modify the inflammatory disease process. Adalimumab, certolizumab pegol, golimumab and infliximab are monoclonal antibodies, whereas etanercept is a recombinant human TNF receptor fusion protein.

Adalimumab, etanercept, golimumab and infliximab are licenced for the treatment of adults with severe active ankylosing spondylitis that has responded inadequately to conventional therapy. Certolizumab pegol is licensed for the treatment adults with severe active ankylosing spondylitis whose disease has responded inadequately to, or who are intolerant to, NSAIDs.

Adalimumab and certolizumab pegol are also licensed for the treatment of adults with severe axial spondyloarthritis without radiographic evidence of ankylosing spondylitis but with objective signs of inflammation, whose disease has responded inadequately to, or who are intolerant to, NSAIDs.

Etanercept, golimumab and infliximab do not currently have a UK marketing authorisation for axial spondyloarthritis. Etanercept and golimumab have been studied in clinical trials, compared with placebo, in people with axial spondyloarthritis without radiographic evidence of ankylosing spondylitis

whose disease has responded inadequately to NSAIDs. There are currently no clinical trials evaluating infliximab for axial spondyloarthritis.

Intervention(s)	• Adalimumab • Certolizumab pegol • Etanercept • Golimumab • Infliximab
Population(s)	• People with severe active ankylosing spondylitis that has responded inadequately to conventional therapy. • People with severe axial spondyloarthritis without radiographic evidence of ankylosing spondylitis but with objective signs of inflammation, whose disease has responded inadequately to, or who are intolerant to, NSAIDs.
Comparators	• The interventions listed above compared with each other • Established clinical management without TNF-alpha inhibitors
Outcomes	The outcome measures to be considered include: • disease activity • functional capacity • disease progression • pain • 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. The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.
Other considerations	If evidence allows, the appraisal should consider the sequential use of TNF-alpha inhibitors. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 233, August 2011, 'Golimumab for the treatment of ankylosing spondylitis'. Will be reviewed with TA143. Technology Appraisal No. 143, May 2008, 'Adalimumab, etanercept and infliximab for ankylosing spondylitis'.
Related National Policy	None.

Questions for consultation

Have all relevant comparators for adalimumab, certolizumab pegol, etanercept, golimumab and infliximab been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for ankylosing spondylitis and axial spondyloarthritis without radiographic evidence of ankylosing spondylitis?

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

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which adalimumab, certolizumab pegol, etanercept, golimumab and infliximab are licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

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

Do you consider that the use of the technologies 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.