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)

Final scope

Remit/Appraisal objective

To appraise the clinical and cost effectiveness of TNF 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. People with spondyloarthritis often have the genetic marker human leukocyte antigen (HLA)-B27. The clinical presentation can include back pain, usually inflammatory in nature, oligoarthritis (predominantly of the lower limbs), enthesitis, dactylitis ('sausage-like' digits) and extra-articular manifestations such as uveitis, inflammatory bowel disease and psoriasis.

Spondyloarthritis can be categorised as having predominantly axial (sacroiliac joints or spine) or peripheral involvement. In people with axial spondyloarthritis, the predominant symptom is back pain – with inflammation of the sacroiliac joints, the spine or both – but they may also have peripheral joint involvement or extra-articular manifestations of spondyloarthritis. In the early stages of disease, radiographs of the sacroiliac joints and spine can be normal (so-called 'non-radiographic' disease) although sacroiliitis or inflammation of the spine may be visible on MRI before structural damage occurs. If definite radiographic sacroiliitis (abnormalities seen in plain x-rays of the sacroiliac joints, such as erosions, sclerosis, and partial or total ankylosis) is present, the disease can be classified as ankylosing spondylitis. Radiographic changes to the spine are not part of the classification criteria, but new bone formation (such as syndesmophytes and ankylosis of the vertebral column) is characteristic of ankylosing spondylitis.

New criteria for the classification of axial spondyloarthritis have been proposed by the Assessment of Spondyloarthritis International Society (ASAS). Limited epidemiological data are available for axial spondyloarthritis

defined according to these relatively new criteria. For ankylosing spondylitis, the prevalence is thought to range from 0.05% to 0.23%. Ankylosing spondylitis is about 3 times more common in men than in women. Non-radiographic axial spondyloarthritis affects approximately equal numbers of men and women, but men are more likely to develop radiographically evident disease. The onset of symptoms typically occurs in the third decade of life.

Conventional therapy for axial spondyloarthritis includes acute anti-inflammatory treatment with non-steroidal anti-inflammatory drugs (NSAIDs) 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 of 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 (including elevated C-reactive protein (CRP) and/or positive MRI), 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 are being 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 whose disease has responded inadequately to, or who are intolerant to, non-steroidal anti-inflammatory drugs (NSAIDs). • 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 • peripheral symptoms (including enthesitis, peripheral arthritis and dactylitis) • symptoms of extra-articular manifestations (including uveitis, inflammatory bowel disease and psoriasis) • 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.