NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Etanercept, abatacept, adalimumab and tocilizumab for treating juvenile idiopathic arthritis (including review of TA35)

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of etanercept, adalimumab, tocilizumab and abatacept within their licensed indications for treating juvenile idiopathic arthritis[1].

Background

Juvenile idiopathic arthritis (JIA) describes a group of conditions that involve joint inflammation which lasts for more than 6 weeks in people under 16 years of age. JIA causes pain, swelling and limitation of movement, and in more severe cases growth retardation, joint contractures, eye problems, joint disease requiring joint replacements, and permanent disability. JIA can impair personal and social functioning and development. Children often miss out on schooling and other childhood activities, and as adults they may be limited in their ability to work. JIA may also have a considerable impact on the family of the child. About 50% of children with JIA will not achieve remission from the condition, despite treatment, and will need further rheumatological care as adults.

- Oligoarthritis is the most common type of JIA, accounting for 50% of new diagnoses in Europe each year. It is diagnosed when 4 or fewer joints are affected in the first 6 months of disease.

- Polyarthritis accounts for 25% of new diagnoses and is diagnosed when 5 or more joints are affected in the first 6 months of disease. Polyarthritis can be further divided into rheumatoid factor positive arthritis, rheumatoid factor negative arthritis, and extended oligoarthritis (where more than 4 joints are affected after 6 months).

- Systemic JIA accounts for 5 to 10% of new diagnoses and is diagnosed when arthritis is part of a general illness involving fever, tiredness, rash, loss of appetite and weight loss.

[1] Golimumab is not included in the remit of this appraisal as the manufacturer is no longer pursuing a licence for this indication.

- Enthesitis-related arthritis accounts for 2 to 10% of new diagnoses and is diagnosed when areas where tendons attach to the bones (entheses) are affected.

- Psoriatic arthritis accounts for 2 to 15% of new diagnoses and is diagnosed when there is joint pain associated with psoriasis (a skin condition).

JIA has an annual incidence of 0.1 per 1,000 children in the UK (equivalent to 1000 children diagnosed per year). The prevalence of JIA is approximately 1 per 1,000 children. This equates to about 10,000 children affected in the UK, however the condition may continue into adulthood, so there are also adults who have JIA.

Treatment aims to control joint pain and inflammation; reduce joint damage, disability and loss of function; and maintain or improve quality of life. Standard treatment for JIA includes the use of the disease modifying anti rheumatic drugs (DMARDs), usually methotrexate, alongside intra-articular and systemic corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDS). Other treatments such as abatacept (a T-cell activation inhibitor), adalimumab (a TNF inhibitor), etanercept (a TNF inhibitor) and tocilizumab (an interleukin inhibitor) may also be used. NICE has recommended etanercept (technology appraisal guidance 35) for the treatment of active polyarticular JIA in children aged 4 to 17 years whose condition has not responded adequately to methotrexate or who have been unable to tolerate treatment with methotrexate. NICE has also recommended tocilizumab (technology appraisal guidance 238) for the treatment of children and young people with systemic JIA if their disease has not responded to NSAIDs, systemic corticosteroids and methotrexate.

The decision to review NICE technology appraisal guidance 35 was based on the following information:

- Although there have been no major developments in the evidence base for TA35, this guidance is now out of date. This is because the licensed therapeutic indication for etanercept has changed and is now broader than that covered by 1.1 of the guidance. In addition to active polyarticular juvenile idiopathic arthritis, etanercept is now licensed for extended oligoarthritis (from the age of 2 years), psoriatic arthritis (from the age of 12 years) and enthesitis-related arthritis (from the age of 12 years). The lower age range for treating polyarticular disease has been reduced from 4 years to 2 years and the marketing authorisation no longer specifies an upper age limit of 17 in the therapeutic indications section of the summary of product characteristics.

- Other biological agents (abatacept, adalimumab and tocilizumab) have been licensed for the treatment of polyarticular juvenile idiopathic arthritis since TA35 was published.

The technology

Etanercept (Enbrel, Pfizer) is a recombinant TNF inhibitor. It is administered by subcutaneous injection. Etanercept has a UK marketing authorisation for

- polyarthritis (rheumatoid factor positive or negative and extended oligoarthritis) in children and adolescents from the age of 2 years who have an inadequate response to, or who have proved intolerant of, methotrexate.

- psoriatic arthritis in adolescents from the age of 12 who have had an inadequate response to, or who have proved intolerant of, methotrexate.

- enthesitis-related arthritis in adolescents from the age of 12 who have an inadequate response to, or who have proved intolerant of, conventional therapy.

Abatacept (Orencia, Bristol-Myers Squibb) is a selective co-stimulation modulator which prevents T-cell activation. It is administered by intravenous infusion. Abatacept in combination with methotrexate has a UK marketing authorisation for moderate to severe active polyarthritis (rheumatoid factor positive or negative) in children and adolescents from the age of 6 years who have had an insufficient response to other disease-modifying anti-rheumatic drugs (DMARDs), including at least 1 tumour necrosis factor (TNF) inhibitor.

Adalimumab (Humira, AbbVie) is a recombinant TNF inhibitor. It is administered by subcutaneous injection. Adalimumab has a UK marketing authorisation for active polyarthritis in children and adolescents from the age of 2 years who have had an inadequate response to 1 or more DMARDs. Adalimumab should be given with methotrexate except where methotrexate is not tolerated or is considered inappropriate.

Tocilizumab (RoActemra, Roche) is a humanised monoclonal antibody that inhibits the cytokine interleukin-6. It is administered by intravenous infusion. Tocilizumab has a UK marketing authorisation for active systemic onset arthritis and polyarthritis (rheumatoid factor positive or negative and extended oligoarthritis) in children and adolescents from the age of 2 years who have not responded to other NSAIDs and corticosteroids. Tocilizumab should be used in combination with methotrexate except in patients for whom methotrexate is inappropriate.

Interventions	Etanercept, abatacept, adalimumab and tocilizumab
Population	People with juvenile idiopathic arthritis (excluding systemic juvenile idiopathic arthritis[2])
Comparators	• Disease modifying anti-rheumatic drugs (DMARDs) (such as methotrexate) • Etanercept, abatacept, adalimumab and tocilizumab should be compared with each other where appropriate Biosimilars are not expected to be in established NHS practice at the time of appraisal and are not included as comparators.
Outcomes	The outcome measures to be considered include: • disease activity • physical function • joint damage • pain • corticosteroid reducing regimens • mortality • 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.

[2] An appraisal of treatments for systemic juvenile idiopathic arthritis will be considered separately when a review proposal for TA238 is developed.

Other considerations	Where the evidence allows, subgroups by type of JIA will be considered: oligoarthritis, polyarthritis (rheumatoid factor positive, rheumatoid factor negative, and extended oligoarthritis), enthesitis-related arthritis and psoriatic arthritis. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 35, Mar 2002, 'Etanercept for the treatment of juvenile idiopathic arthritis'. Currently being updated. Related NICE Pathways: NICE Pathway: Musculoskeletal conditions, Pathway created Dec 2013. http://pathways.nice.org.uk/pathways/musculoskeletal-conditions
Related National Policy	NHS (2012) Manual for prescribed specialised services. Page 318. http://www.england.nhs.uk/wp-content/uploads/2012/12/pss-manual.pdf

Questions for consultation

Have all relevant comparators for etanercept, abatacept, adalimumab and tocilizumab been included in the scope? Are infliximab, golimumab, rituximab and certolizumab pegol used for treating JIA in clinical practice?

Which treatments are considered to be established clinical practice in the NHS for the treatment of juvenile idiopathic arthritis? Are non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular and systemic corticosteroids, and disease modifying anti-rheumatic drugs (DMARDs) (such as methotrexate) used for the patient group for which biologics would be considered a treatment option?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom etanercept, abatacept, adalimumab and tocilizumab are expected to be more clinically effective and cost effective or other groups that should be examined separately?

Should adults who had JIA be included in the assessment of this appraisal? What evidence is there for the efficacy of these drugs in adults (aged over 17 years)? Should this appraisal be restricted to children and adolescents?

Where do you consider etanercept, abatacept, adalimumab and tocilizumab will fit into the existing NICE pathway, Musculoskeletal conditions?

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 abatacept, adalimumab, etanercept and tocilizumab are or will be 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 etanercept, abatacept, adalimumab or tocilizumab 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 etanercept, abatacept, adalimumab or tocilizumab 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 Multiple Technology Appraisal (MTA) 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)