NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Canakinumab for the treatment of systemic juvenile idiopathic arthritis

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of canakinumab within its licensed indication for the treatment of systemic juvenile idiopathic arthritis.

Background

Juvenile idiopathic arthritis (JIA) is a term that covers a heterogeneous group of syndromes in which the onset of inflammatory arthritis occurs before the age of 16 years and lasts for more than 6 weeks. It is characterised by persistent joint swelling, pain and limitation of movement. The cause of JIA is poorly understood, but may relate to genetic and environmental factors.

A classification system for JIA has been developed by the International League of Associations for Rheumatology. There are seven categories of JIA: systemic, oligo arthritis (formerly pauciarticular), polyarthritis rheumatoid factor positive, polyarthritis rheumatoid factor negative, enthesitis related arthritis, psoriatic arthritis and unclassified (types that do not correspond to any, or to more than one, category). The clinical manifestations and severity of the different sub-types varies considerably. Systemic JIA is a multi-organ disease characterised by arthritic symptoms, fever, transient rash, liver and spleen enlargement.

JIA can lead to growth retardation, joint contractures, eye problems, destructive joint disease requiring joint replacements, and permanent disability. JIA can impair children's personal and social functioning and development. Children often miss out on schooling and normal childhood activities, and as adults they may be limited in, or unable to work. It may also have a considerable impact upon the family of the child.

JIA is a relatively rare disease, with an estimated incidence in the UK of 0.1 per 1000 children, equivalent to 1000 children diagnosed per year. The prevalence is in the order of 1 per 1000 children, and about 10,000 children in the UK are affected. Approximately 10% of children diagnosed with JIA have systemic disease.

Treatment aims to control pain, fever and inflammation, and reduce joint damage, disability and loss of function, thereby improving quality of life. The standard treatment for systemic JIA includes combinations of non-steroidal anti-inflammatory drugs (NSAIDs), analgesics, corticosteroids and disease modifying anti-rheumatic drugs (DMARDs). Methotrexate is used as initial therapy when DMARDs are considered necessary, although no DMARD is

licensed for use in children in the UK. There are currently no biologics specifically licensed in the UK for the treatment of systemic JIA in children and young people. Etanercept, infliximab and anakinra are also used to treat children and young people whose disease has inadequately responded to methotrexate. Further treatment options that may be considered include non-drug therapies such as surgery and physical therapy.

NICE has issued guidance (technology appraisal 35) on the use of etanercept for the treatment of polyarticular JIA. This guidance recommends etanercept for children aged 4 to 17 years with active polyarticular-course juvenile idiopathic arthritis (characterised by arthritis in at least five joints) whose condition has not responded adequately to, or who have proved intolerant of, methotrexate.

The technology

Canakinumab (Ilaris, Novartis Pharmaceuticals UK) is a monoclonal antibody that inhibits the activity of cytokine interleukin-1 beta (IL-1 beta), which may reduce inflammation and tissue destruction. Canakinumab is administered by subcutaneous injection.

Canakinumab does not currently have a UK marketing authorisation for the treatment of systemic JIA. It has been studied in clinical trials compared with placebo in children and young people aged 2 to 19 years with active systemic JIA.

Intervention(s)	Canakinumab
Population(s)	Children and young people (aged 2 to 17 years) with systemic juvenile idiopathic arthritis
Comparators	Management strategies without canakinumab, including: • conventional DMARDs • biologic DMARDs: including etanercept and infliximab • anakinra • tocilizumab (subject to ongoing NICE appraisal)

Outcomes	The outcome measures to be considered include: • disease activity • physical function • joint damage • pain • steroid sparing • 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No.35, March 2002, 'The use of etanercept for the treatment of juvenile idiopathic arthritis'. Static guidance. Ongoing Technology Appraisals: Technology Appraisal in Preparation, 'Tocilizumab for the treatment of systemic juvenile idiopathic arthritis'. Earliest anticipated publication date: December 2011. Suspended technology appraisal, 'Abatacept for the treatment of juvenile idiopathic arthritis'.

Questions for consultation

What is the age cut off for somebody to be diagnosed with JIA, and treated for JIA?

- How are people aged 18 years and older with systemic JIA treated in UK clinical practice?

- Should the population also include people aged over 18 years, in line with the population included in the key clinical trials?

Have the most appropriate comparators for canakinumab for the treatment of systemic juvenile idiopathic arthritis been included in the scope?

- Are the comparators listed routinely used in clinical practice?

- Are adalimumab and abatacept used to treat systemic juvenile idiopathic arthritis in UK clinical practice?

Are there any 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?

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)