NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Tocilizumab for the treatment of systemic juvenile idiopathic arthritis

Final Scope

Remit / appraisal objective

To appraise the clinical and cost-effectiveness of tocilizumab within its licensed indication for 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. JIA 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 (ILAR). 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 multiorgan 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 (characterized by arthritis in at least five joints) whose condition has not responded adequately to, or who have proved intolerant of, methotrexate.

The technology

Tocilizumab (RoActemra, Roche Products) is a humanised monoclonal antibody that inhibits the activity of the cytokine interleukin-6 (IL-6). IL-6 is a pro-inflammatory mediator. It has been hypothesised that the over-expression of IL-6 in systemic onset JIA is one of the factors responsible for the damaging processes which affect articular cartilage and bone. Tocilizumab is administered intravenously.

There is currently no UK marketing authorisation for the use of tocilizumab for the treatment of systemic JIA. It has been studied in children and young people 2 years and older with systemic JIA which has responded inadequately to previous therapy with one or more NSAIDs and systemic corticosteroids. It has been studied as a monotherapy or in combination with methotrexate compared with placebo.

Interventions	Tocilizumab with or without methotrexate
Population	1. Children and young people 2 years and older with systemic JIA which has not responded adequately to prior NSAID(s) and systemic corticosteroids. 2. Children and young people 2 years and older with systemic JIA which has not responded adequately to prior NSAID(s), systemic corticosteroids and methotrexate.

Comparators	1. For children and young people 2 years and older with systemic JIA which has not responded adequately to prior NSAID(s) and systemic corticosteroids: • methotrexate 2. For children and young people 2 years and older with systemic JIA which has not responded adequately to prior NSAID(s), systemic corticosteroids and methotrexate. • TNF inhibitors (for example, etanercept and infliximab) • anakinra
Outcomes	Outcomes 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 time horizon for the economic evaluation should reflect the chronic nature of the condition. 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 'Adalimumab for the treatment of juvenile idiopathic arthritis'. Earlier publication date: January 2012.