

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

**Canakinumab for treating systemic juvenile idiopathic arthritis**

**Final Scope**

**Remit**

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. The cause of JIA is poorly understood, but may relate to genetic and environmental factors. Systemic JIA is a multi-organ disease characterised by arthritis symptoms (persistent joint swelling, pain and limitation of movement), intermittent fever, transient rash, liver and spleen enlargement.

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

JIA is a relatively rare disease, with an estimated incidence in the UK of 0.1 per 1000 children per year, 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 JIA.

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. Oral corticosteroids such as prednisone are used initially before progressing to non-biological disease modifying anti-rheumatic drugs (DMARDs) such as methotrexate. If symptoms are not adequately controlled with methotrexate, anakinra or tocilizumab are used when considered necessary. Tocilizumab is currently the only biologic DMARD licensed in the UK for the treatment of active systemic JIA in children and young people. NICE has recommended tocilizumab for the treatment of systemic JIA in children and young people whose disease has responded inadequately to NSAIDs, systemic corticosteroids and methotrexate (NICE technology appraisal No. 238).

Further treatment options that may be considered include non-drug therapies such as surgery and physical therapy.

### The technology

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

Canakinumab has a UK marketing authorisation for “the treatment of active systemic juvenile idiopathic arthritis in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs and systemic corticosteroids”. It can be administered as monotherapy or in combination with methotrexate.

<b>Intervention(s)</b>	Canakinumab (with or without methotrexate)
<b>Population(s)</b>	<ul style="list-style-type: none"> <li>• People aged 2 years and older with active systemic juvenile idiopathic arthritis whose disease has responded inadequately to previous therapy with NSAIDs and systemic corticosteroids.</li> <li>• People aged 2 years and older with active systemic juvenile idiopathic arthritis whose disease has responded inadequately to previous therapy with NSAIDs, systemic corticosteroids and methotrexate.</li> </ul>
<b>Comparators</b>	<p>For people aged 2 years and older with active systemic juvenile idiopathic arthritis whose disease has responded inadequately to previous therapy with NSAIDs and systemic corticosteroids:</p> <ul style="list-style-type: none"> <li>• methotrexate</li> </ul> <p>For people aged 2 years and older with active systemic juvenile arthritis whose disease has responded inadequately to previous therapy with NSAIDs, systemic corticosteroids and methotrexate:</p> <ul style="list-style-type: none"> <li>• anakinra</li> <li>• tocilizumab</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• disease activity</li> <li>• physical function</li> <li>• joint damage</li> </ul>

	<ul style="list-style-type: none"> <li>• growth</li> <li>• bone health</li> <li>• pain</li> <li>• fever</li> <li>• corticosteroid sparing</li> <li>• mortality</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>
<b>Other considerations</b>	Guidance will only be issued in accordance with the marketing authorisation.
<b>Related NICE recommendations and NICE pathways</b>	<p>Related Technology Appraisals:</p> <p>Technology Appraisal No.238, December 2011, 'Tocilizumab for the treatment of systemic juvenile idiopathic arthritis'. Review proposal date: December 2014.</p>
<b>Related NHS England policy</b>	<p>Service specification for paediatric medicine rheumatology:</p> <p><a href="http://www.england.nhs.uk/wp-content/uploads/2013/06/e03-paedi-medi-rheum.pdf">http://www.england.nhs.uk/wp-content/uploads/2013/06/e03-paedi-medi-rheum.pdf</a></p>