NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Anakinra for treating Still's disease

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of anakinra within its marketing authorisation for treating Still's disease.

Background

Still's disease is a rare systemic inflammatory disorder which can affect adults (adult-onset Still's disease) or children (systemic juvenile idiopathic arthritis). The symptoms of Still's disease can develop quickly or over time and include a daily fever which usually peaks in the late afternoon or early evening, joint and muscle pain and swelling (commonly in the knees, wrists and ankles) and a pink rash. Signs and symptoms are highly variable between individuals. Adult-onset Still's disease can take 2 forms, systemic or arthritis-predominant. In the systemic form, the predominant symptoms are acute onset characterised by fever, weight loss and other systemic manifestations. The arthritis-predominant form is characterised by slow onset and symptoms mainly affecting the joints. Macrophage Activation Syndrome is an uncommon but potentially fatal complication of the disease. The cause of Still's disease is unknown although it is thought that abnormalities in a particular part of the immune system causes episodes of inflammation to occur in the body. It may be difficult to diagnose Still's disease because diagnosis is usually based on clinical evaluation, patient history, identification of characteristic findings, and exclusion of other possible disorders, rather than specific tests or laboratory findings that may differentiate it from similar disorders.

Still's disease affects between 400 and 800 adults[1] and around 1,000 children in England.[2] Adult-onset Still's disease primarily affects young adults[3] while systemic idiopathic juvenile arthritis affects children under 16 years old, with onset usually between 3–5 years old, and the disease resolving before adulthood in about 50% of patients.[4]

Treatment aims to induce and maintain remission of symptoms; controlling pain, fever and inflammation, and reducing joint damage, disability and loss of function, thereby improving quality of life. Still's disease, including adult-onset Still's disease and systemic juvenile idiopathic arthritis, is treated initially with combinations of non-steroidal anti-inflammatory drugs (NSAIDs), analgesics and corticosteroids, before progressing to non-biological disease modifying anti-rheumatic drugs (DMARDs) such as methotrexate. If symptoms are not adequately controlled with non-biological DMARDs, biological therapies such as tocilizumab may be used.

In systemic juvenile idiopathic arthritis, NICE technology appraisal guidance 238 recommends tocilizumab (monotherapy or in combination with methotrexate) for children and young people aged 2 years and older whose disease has responded inadequately to NSAIDs, systemic corticosteroids and methotrexate. It is not recommended when the disease continues to respond to methotrexate or has not yet been treated with methotrexate. An NHS England clinical commissioning policy recommends anakinra for systemic juvenile idiopathic arthritis that does not respond to tocilizumab and for macrophage activation syndrome. There is no NICE technology appraisal guidance for adult-onset Still's disease. An NHS England clinical commissioning policy recommends anakinra for adult-onset Still's disease that is refractory to second-line therapy.

The technology

Anakinra (Kineret, Swedish Orphan Biovitrum) is a recombinant Interleukin-1 receptor antagonist (IL-1Ra) that blocks the biological activity of cytokine IL-1, thereby controlling active inflammation. It is administered by subcutaneous injection.

Anakinra has a marketing authorisation in the UK for treating Still's disease. It is indicated 'in adults, adolescents, children and infants aged 8 months and older with a body weight of 10 kg or above for the treatment of Still's disease, including Systemic Juvenile Idiopathic Arthritis (SJIA) and Adult-Onset Still's Disease (AOSD), with active systemic features of moderate to high disease activity, or in patients with continued disease activity after treatment with non-steroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids.' Anakinra can be given as monotherapy or in combination with other anti-inflammatory drugs and disease-modifying anti-rheumatic drugs (DMARDs).

Anakinra also has a marketing authorisation in the UK for treating rheumatoid arthritis and cryopyrin-associated period syndromes (CAPS).

Interventions	Anakinra as monotherapy or in combination with other anti-inflammatory drugs and DMARDs
Population	People with Still's disease (including Systemic Juvenile Idiopathic Arthritis and Adult-Onset Still's Disease).
Comparators	For previously untreated disease: • NSAIDs and systemic corticosteroids For disease previously treated with NSAIDs or systemic corticosteroids • DMARDs For disease previously treated with DMARDs: • Tocilizumab (only for systemic juvenile idiopathic arthritis that has responded inadequately to

	methotrexate) • Canakinumab
Outcomes	The outcome measures to be considered include: • disease activity (including disease flares and remission) • fever • physical function • blood markers (including markers for inflammation) • glucocorticoid tapering • rash • 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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	If the evidence allows, the following subgroups will be considered: • People with systemic juvenile idiopathic arthritis or adult-onset Still's disease • People with Macrophage Activation Syndrome • Level of disease activity 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** 'Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis' (2015). NICE Technology Appraisal 373. Review date December 2018. 'Tocilizumab for the treatment of systemic juvenile idiopathic arthritis' (2011). NICE Technology Appraisal 238. Currently under review. **Terminated appraisals** 'Canakinumab for treating systemic juvenile idiopathic arthritis' (2013). NICE Technology Appraisal 302. **Appraisals in development (including suspended appraisals)** 'Canakinumab and tocilizumab for treating systemic juvenile idiopathic arthritis' NICE technology appraisals guidance [ID983]. Suspended. **Related Guidelines** 'Rheumatoid arthritis in adults: management' (July 20185). NICE guideline NG100. Review date to be confirmed. **Related NICE evidence summaries** 'Systemic juvenile idiopathic arthritis: canakinumab' (2014). NICE evidence summary: new medicines 36. **Related NICE Pathways** Musculoskeletal conditions (2019) NICE pathway http://pathways.nice.org.uk/pathways/musculoskeletal-conditions
Related National Policy	NHS England (2018) Clinical Commissioning Policy: Anakinra/tocilizumab for the treatment of Adult Onset Still's Disease refractory to second-line therapy (adults). https://www.england.nhs.uk/wp-content/uploads/2018/07/1609-anakinra-and-tocilizumab-for-aosd.pdf NHS England (2018) Manual for Prescribed Specialised Services 2018/19. Chapter 138: Stem cell transplantation service for juvenile idiopathic arthritis and related connective tissue disorders (children). https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual.pdf Department of Health and Social Care (2016) NHS

	Outcomes Framework 2016-2017: Domains 2, 3 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2015) Clinical Commissioning Policy Statement: Biologic Therapies for the treatment of Juvenile Idiopathic Arthritis (JIA) and Appendix A. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/10/e03pd-bio-therapies-jia-oct15.pdf and https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/07/appx-a-jia-e03Pd.pdf NHS England (2013) A13/S/a 2013/14 NHS standard contract for specialised rheumatology services (adult). https://www.england.nhs.uk/wp-content/uploads/2013/06/a13-spec-rheumatology.pdf NHS England (2013) B09/S/a 2013/14 NHS standard contract for specialised immunology (all ages). https://www.england.nhs.uk/wp-content/uploads/2013/06/b09-spec-immun.pdf

References

[1] NHS England (2018) Clinical Commissioning Policy: Anakinra/tocilizumab for the treatment of Adult-Onset Still's Disease refractory to second-line therapy (adults). Accessed July 2018.
[2] NICE Evidence Summary: New Medicines 36 (2014) Systemic juvenile idiopathic arthritis: canakinumab. Accessed July 2018.
[3] Orphanet Adult-onset Still disease. Accessed July 2018.
[4] Ophanet Systemic-onset juvenile idiopathic arthritis. Accessed July 2018.