NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Sarilumab for previously treated moderate to severe active rheumatoid arthritis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of sarilumab within its marketing authorisation for previously treated moderate to severe active rheumatoid arthritis.

Background

Rheumatoid arthritis is an inflammatory autoimmune disease that typically affects the synovial tissue of the small joints of the hands and feet but can affect any synovial joint, causing swelling, stiffness, pain and progressive joint destruction. It is a systemic disease and can affect the whole body, including the lungs, heart and eyes. Rheumatoid arthritis is usually a chronic relapsing condition which has a pattern of flare-ups followed by periods of lower disease activity; however, for some people, the disease is constantly progressive. Rheumatoid arthritis has a severe impact on quality of life and it is estimated that approximately one-third of people stop work within 2 years because of the disease, and this prevalence increases thereafter. Severity of disease can be classified into 3 categories, based on the disease activity score (DAS28) scoring system. A DAS28 greater than 5.1 indicates high disease activity or severe disease, between 3.2 and 5.1 indicates moderate disease activity, and less than 3.2 indicates low disease activity.

The prevalence of rheumatoid arthritis in the UK is estimated to be 0.44% in males and 1.16% in females[1]; which is approximately 520,000 people in England (140,000 males and 380,500 females)[1,2]. There are approximately 17,500 people diagnosed with rheumatoid arthritis every year in England[3]. It can develop at any age, but the peak age of onset in the UK is about 45–75 years[1].

There is no cure for rheumatoid arthritis and treatment aims to improve quality of life and to prevent or reduce joint damage. The main aim of management in early disease is to suppress disease activity and induce disease remission, prevent loss of function, control joint damage, maintain pain control and enhance self-management. For people with newly diagnosed rheumatoid arthritis, NICE clinical guideline 79 ('Rheumatoid arthritis: the management of rheumatoid arthritis in adults') recommends a combination of conventional disease modifying anti-rheumatic drugs (DMARDs; including methotrexate, leflunomide and sulfasalazine) as first-line treatment, ideally beginning within 3 months of the onset of persistent symptoms. Where combination therapies are not appropriate (for example where there are comorbidities or pregnancy)

DMARD monotherapy is recommended. Where the disease has not responded to intensive combination therapy with conventional DMARDs, NICE Technology appraisal guidance 375 recommends biological DMARDs (adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept) in combination with methotrexate for severe rheumatoid arthritis only. For those people with severe rheumatoid arthritis who cannot take methotrexate because it is contraindicated or because of intolerance, the guidance recommends that adalimumab, etanercept, certolizumab pegol or tocilizumab monotherapy can be used.

Where the disease has not responded adequately or in the case of intolerance to other DMARDs, including at least one TNF inhibitor, rituximab in combination with methotrexate is recommended for severe active disease only (NICE Technology appraisal guidance 195). Where rituximab is contraindicated or withdrawn because of an adverse event, adalimumab, etanercept, infliximab, abatacept, golimumab, tocilizumab and certolizumab pegol each in combination with methotrexate are recommended as options (NICE Technology appraisal guidance 195, 225, 247 and 415). Where rituximab therapy cannot be given because methotrexate is contraindicated or has been withdrawn due to an adverse event, adalimumab, etanercept and certolizumab pegol, each as a monotherapy, are recommended as options (NICE Technology appraisal guidance 195 and 415). Tocilizumab is a treatment option for people whose disease has not responded to one or more TNF inhibitors and rituximab (NICE technology appraisal guidance 247).

The technology

Sarilumab (Kevzara, Sanofi) is a fully human anti-interleukin 6 receptor α monoclonal antibody that blocks the IL-6 immune and inflammatory responses. It is administered subcutaneously.

Sarilumab does not currently have a marketing authorisation in the UK for the treatment of moderate to severe active rheumatoid arthritis. It has been studied in randomised controlled trials as monotherapy or in combination with methotrexate or conventional DMARDs in adults with moderate to severe active rheumatoid arthritis. Sarilumab in combination with methotrexate has been compared with placebo in combination with methotrexate in adults whose disease did not respond adequately to methotrexate. It has also been compared in combination with conventional DMARDs with placebo alone and with tociluzumab in combination with conventional DMARDs in adults whose disease did not respond adequately to, or who are intolerant of TNF inhibitors. Sarilumab monotherapy has also been compared with adalimumab monotherapy in adults whose disease did not respond adequately to, or who are intolerant of methotrexate.

Intervention(s)	Sarilumab monotherapy or in combination with conventional DMARDs

Population(s)	Adults with moderate to severe, active rheumatoid arthritis, whose disease has not responded adequately to, or who are intolerant of conventional or biological DMARDs
Comparators	People with moderate active rheumatoid arthritis that has not responded adequately to, or who are intolerant of therapy with conventional DMARDs • Best supportive care People with severe active rheumatoid arthritis that has not responded adequately or who are intolerant to therapy with conventional DMARDs: • Biological DMARDs in combination with methotrexate (adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab, abatacept) • Adalimumab, etanercept, certolizumab pegol or tocilizumab (each as monotherapy) People with severe active rheumatoid arthritis that has not responded adequately to, or who are intolerant of therapy with DMARDs including at least one TNF inhibitor: • Rituximab in combination with methotrexate • When rituximab is contraindicated or withdrawn due to adverse events: - Abatacept, adalimumab, certolizumab pegol, etanercept, infliximab, tocilizumab, or golimumab, each in combination with methotrexate - Adalimumab, etanercept or certolizumab pegol (each as monotherapy) People with severe, active disease despite treatment with biological DMARDs recommended according to NICE guidance: • Tocilizumab in combination with methotrexate • Best supportive care

Outcomes	The outcome measures to be considered include: • disease activity • physical function • joint damage • pain • mortality • fatigue • radiological progression • extra-articular manifestations of the disease • 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 will be taken into account. The availability and cost of biosimilar products should be taken into account.

Other considerations	If evidence allows, the appraisal will consider subgroups of people identified as: • having had primary or secondary failure of response to the first TNF inhibitor; or • having seronegative or seropositive antibody status • people with moderate disease activity (DAS28 between 3.2 and 5.1) and severe active disease (DAS28 greater than 5.1). If the evidence allows, the appraisal will include the costs of joint replacement therapy and hospital admissions. 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:** 'Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed' (2016). Technology appraisal 375. Review date January 2019. 'Tocilizumab for the treatment of rheumatoid arthritis (rapid review of technology appraisal guidance 198)' (2012). Technology Appraisal 247. Part updated in 2016 within technology appraisal 375. 'Golimumab for the treatment of rheumatoid arthritis after the failure of previous disease-modifying anti-rheumatic drugs' (2011). Technology Appraisal 225. Part updated in 2016 within technology appraisal 375. 'Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor' (2010). Technology Appraisal 195. Transferred to the static list in September 2013. 'Certolizumab pegol for treating rheumatoid arthritis after inadequate response to a TNF-alpha inhibitor' (2016). Technology appraisal 415. Review date October 2019.

	Appraisals in development: 'Tofacitinib for the treatment of moderate to severe active rheumatoid arthritis' NICE technology appraisal [ID 526]. Publication expected December 2017. 'Baricitinib for treating moderate to severe rheumatoid arthritis'. NICE technology appraisal [ID 979]. Publication expected September 2017. **Related Guidelines:** 'Rheumatoid arthritis in adults: management' (2009). NICE guideline 79. Partially updated in December 2015. Anticipated publication of full update August 2018. **Related Quality Standards:** 'Rheumatoid arthritis in over 16s' (2013). NICE quality standard 33. Review Proposal Date unknown. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp **Related NICE Pathways:** 'Rheumatoid arthritis' (2013). http://pathways.nice.org.uk/pathways/rheumatoid-arthritis
Related National Policy	NHS England Manual for prescribed specialised services 2016/17. Section 5: Adult highly specialist rheumatology services. NHS England & BMJ Group. Shared Decision Making Sheets: Rheumatoid Arthritis. NHS England. A13. Specialised Rheumatology. National programmes of care and clinical reference groups. National Service Frameworks: Policy: Older People Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 2 to 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf

References

1. Arthritis Research UK (2015) 'How common is rheumatoid arthritis?' Accessed March 2016.

2. Office for National Statistics (2015) 'Population Estimates by Age and Sex'. Accessed September 2015

3. NICE (2013) 'Support for commissioning for rheumatoid arthritis'.