NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Sirukumab for previously treated moderate to severe active rheumatoid arthritis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of sirukumab 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 and tocilizumab each in combination with methotrexate are recommended as options (NICE technology appraisal guidance 195, 225 and 247). Where rituximab therapy cannot be given because methotrexate is contraindicated or has been withdrawn due to an adverse event, NICE technology appraisal guidance 195 recommends that adalimumab and etanercept, each as a monotherapy, can be used.

The technology

Sirukumab (brand name unknown, Janssen) is a fully human monoclonal antibody with a high affinity and specificity for interleukin-6 (IL-6). It is administered subcutaneously.

Sirukumab does not currently have a marketing authorisation in the UK for rheumatoid arthritis. It has been studied in 1 randomised controlled trial compared with adalimumab in people whose moderate or severe rheumatoid arthritis was intolerant to or had an inadequate response to methotrexate. Sirukumab has also been studied in 2 randomised controlled trials compared with placebo in patients with moderate to severe rheumatoid arthritis whose disease had an inadequate response to disease-modifying anti-rheumatic drugs or an inadequate response or intolerant response to TNF inhibitors.

Intervention(s)	Sirukumab plus methotrexate or as monotherapy
Population(s)	Adults with moderate to severe, active arthritis, whose disease has not responded adequately to conventional DMARDs or TNF inhibitors
Comparators	For moderate active rheumatoid arthritis that has not responded adequately to therapy with conventional DMARDs • Best supportive care

	For severe active rheumatoid arthritis that has not responded adequately 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) For severe active rheumatoid arthritis that has not responded adequately to therapy with DMARDs including at least one TNF inhibitor: • Rituximab in combination with methotrexate • Certolizumab pegol (subject to on-going NICE appraisal) When rituximab is contraindicated or withdrawn : • Abatacept, adalimumab, etanercept, golimumab, infliximab, or tocilizumab, each in combination with methotrexate • Certolizumab pegol in combination with methotrexate (subject to on-going NICE appraisal) For adults for whom rituximab therapy cannot be given because methotrexate is contraindicated or withdrawn • Adalimumab monotherapy, etanercept monotherapy or tocilizumab monotherapy • Certolizumab pegol monotherapy (subject to on-going NICE appraisal) For people with severe, active disease despite treatment with biological DMARDs recommended according to NICE guidance: • Tocilizumab in combination with methotrexate • Best supportive care • Certolizumab pegol (subject to on-going NICE appraisal)

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 should 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). NICE technology appraisal guidance 375. Review date January 2019. 'Tocilizumab for the treatment of rheumatoid arthritis (rapid review of technology appraisal guidance 198)' (2012). NICE technology appraisal guidance 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). NICE technology appraisal guidance 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. **Appraisals in development:** 'Rheumatoid arthritis - certolizumab pegol (after TNF

	inhibitor)' [ID 824]. Publication expected October 2016. **Related Guidelines:** 'Rheumatoid arthritis in adults: management' (2009). NICE guideline 79. Partially updated in December 2015. Anticipated publication date TBC. **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: NHS England Manual for prescribed specialised services 2016/147. 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

Questions for consultation

Have all relevant comparators for sirukumab been included in the scope for the different populations?

Which treatments are considered to be established clinical practice in the NHS in England for moderately active rheumatoid arthritis after conventional DMARDs or TNF inhibitors?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom sirukumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider sirukumab will fit into the existing NICE pathway, Rheumatoid arthritis?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which sirukumab will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider sirukumab 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 sirukumab 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 Technology Appraisal Process. NICE has just consulted on an additional technology appraisal

process known as the Abbreviated Appraisal Process (ATA). More information on the consultation is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/abbreviated-technology-appraisal-process-consultation. We welcome comments on the appropriateness and suitability of considering the new ATA process for appraising this topic. Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

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'.