NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Baricitinib for treating moderate to severe rheumatoid arthritis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of baricitinib within its marketing authorisation for treating 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 is associated with increased mortality and increasing disability, which has a severe impact on quality of life. 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

Baricitinib (brand name unknown, Eli Lilly and Company) is a human tyrosine kinase protein that inhibits Janus kinase 1 and 2 and thereby disrupts mediating signalling pathways involved in inflammatory diseases. It is administered orally.

Baricitinib does not currently have a marketing authorisation in the UK for rheumatoid arthritis. It has been studied in clinical trials as monotherapy or in combination with methotrexate. It has been compared with methotrexate in adults with moderate to severe rheumatoid arthritis who have not received treatment with conventional DMARDs or methotrexate. It has also been compared with placebo in adults with moderate to severe active rheumatoid arthritis, who have been treated with, and whose disease did not respond adequately to, methotrexate. It has also been studied in a clinical trial in combination with methotrexate, compared with adalimumab in combination with methotrexate in adults with moderate to severe active rheumatoid arthritis who have already had methotrexate. It has also been compared with placebo in adults whose disease did not respond adequately to a TNF inhibitor.

Intervention	Baricitinib monotherapy or in combination with methotrexate

Population	Adults with moderate to severe, active rheumatoid arthritis who have not received treatment with DMARDs, or for whom treatment with other DMARDs is not appropriate or whose disease has not responded adequately to DMARDs
Comparators	For moderate active rheumatoid arthritis and for severe active rheumatoid arthritis not previously treated with DMARDs: • Combination therapy with conventional DMARDs (including methotrexate and at least one other DMARD, such as sulfasalazine and leflunomide) • Conventional DMARD monotherapy with dose escalation • Best supportive care (only where conventional DMARDs are not appropriate due to intolerance) For severe active rheumatoid arthritis that has not responded adequately to therapy with conventional DMARDs only: • 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 When rituximab is contraindicated or withdrawn due to adverse events: • Adalimumab, etanercept, infliximab, abatacept or tocilizumab, each in combination with methotrexate • Adalimumab, etanercept (each as monotherapy)

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.
Other considerations	If the evidence allows the following subgroups will be considered. These include people with moderate disease activity (DAS28 between 3.2 and 5.1) and severe active disease (DAS28 greater than 5.1). 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:** Rheumatoid arthritis - adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, abatacept and tocilizumab - review (review of TA guidance 130, 186, 224, 234 and part review of TA guidance 225 and

	247) (2014) NICE Technology Appraisal TA375. Review date: January 2019. Tocilizumab for the treatment of rheumatoid arthritis (rapid review of technology appraisal guidance 198). (2012) NICE technology appraisal TA 247. Guidance on static list Golimumab for the treatment of rheumatoid arthritis after the failure of previous disease modifying anti-rheumatic drugs. (2011) NICE technology appraisal TA 225. Guidance on static list Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor. (2010) NICE technology appraisal TA195. Guidance on static list **Appraisals in development (including suspended appraisals)** Certolizumab pegol for treating rheumatoid arthritis after a TNF inhibitor. Technology Appraisal [ID824]. Publication date: October 2016 Rheumatoid arthritis (after the failure of conventional DMARDs) -rituximab [ID333]. Publication date: July 2011. Status: Suspended – manufacturer is no longer seeking a licence for this indication. Rheumatoid arthritis - tofacitinib [ID526] Technology Appraisal. September 2013 Status: suspended. **Related Guidelines:** Rheumatoid arthritis in adults: the management of rheumatoid arthritis in adults (2009) NICE guideline CG79 Review date: TBC **Related Quality Standards:** Rheumatoid arthritis in over 16s (2013) Quality Standard QS33. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp **Related NICE Pathways:** Rheumatoid arthritis (2015) NICE Pathway
Related National Policy	NHS England (January 2014) 5. Adult highly specialist rheumatology services Manual for prescribed specialised services 2013/14.

	NHS England & BMJ Group. Shared Decision Making Sheets: Rheumatoid Arthritis. NHS England. A13. Specialised Rheumatology. National programmes of care and clinical reference groups. Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1, 2, 3, 4 and 5.. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf

Questions for consultation

In clinical practice, is it anticipated that baricitinib will be used for treating moderate to severe active rheumatoid arthritis that has not been treated with conventional DMARDs?

Have all relevant comparators for baricitinib been included in the scope?

Are the outcomes listed appropriate?

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

Where do you consider baricitinib 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 baricitinib 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 baricitinib 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 baricitinib 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 Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (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'.