

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal

## Baricitinib for treating moderate to severe rheumatoid arthritis

## Final scope

**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<sup>1</sup>; which is approximately 441,000 people in England (119,000 males and 322,000 females)<sup>1,2</sup>. There are approximately 17,500 people diagnosed with rheumatoid arthritis every year in England<sup>3</sup>. It can develop at any age, but the peak age of onset in the UK is about 45–75 years<sup>1</sup>.

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: management') 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 (a subgroup of biological DMARDs), 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, can be used (NICE Technology appraisal guidance [195](#) and [415](#)).

### The technology

Baricitinib (Olumiant, 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.

<b>Intervention</b>	Baricitinib monotherapy or in combination with methotrexate
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<b>Population</b>	Adults with moderate to severe, active rheumatoid arthritis whose disease has responded inadequately to, or who are intolerant of one or more disease modifying anti-rheumatic drugs (DMARDs), including conventional or biologic DMARDs.
<b>Comparators</b>	<p>People with moderate active rheumatoid arthritis:</p> <ul style="list-style-type: none"> <li>• Combination therapy with conventional DMARDs (including methotrexate and at least one other DMARD, such as sulfasalazine and leflunomide)</li> <li>• Conventional DMARD monotherapy with dose escalation</li> <li>• Best supportive care (only where conventional DMARDs are not appropriate due to intolerance)</li> </ul> <p>People with severe active rheumatoid arthritis that has not responded adequately to therapy with conventional DMARDs only:</p> <ul style="list-style-type: none"> <li>• Biological DMARDs in combination with methotrexate (adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab, abatacept)</li> <li>• Adalimumab, etanercept, certolizumab pegol, or tocilizumab (each as monotherapy)</li> </ul> <p>People with severe active rheumatoid arthritis that has not responded adequately to therapy with DMARDs including at least one TNF inhibitor:</p> <ul style="list-style-type: none"> <li>• Rituximab in combination with methotrexate</li> <li>• When rituximab is contraindicated or withdrawn due to adverse events: <ul style="list-style-type: none"> <li>- Abatacept, adalimumab, certolizumab pegol, etanercept, infliximab, tocilizumab, or golimumab, each in combination with methotrexate</li> <li>- Adalimumab, etanercept or certolizumab pegol (each as monotherapy)</li> </ul> </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> <li>• pain</li> <li>• mortality</li> <li>• fatigue</li> <li>• radiological progression</li> <li>• extra-articular manifestations of the disease</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 will be taken into account.</p> <p>The availability and cost of biosimilar products of etanercept, infliximab and rituximab should be taken into account.</p>
<b>Other considerations</b>	<p>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).</p> <p>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.</p>
<b>Related NICE recommendations</b>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">Certolizumab pegol for treating rheumatoid arthritis after</a></p>

<p><b>and NICE Pathways</b></p>	<p><a href="#">inadequate response to a TNF-alpha inhibitor</a> (2016) NICE Technology Appraisal TA415. Review date: October 2019.</p> <p><a href="#">Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed (review of TA guidance 130, 186, 224, 234 and part review of TA guidance 225 and 247)</a> (2016) NICE Technology Appraisal TA375. Review date: January 2019.</p> <p><a href="#">Tocilizumab for the treatment of rheumatoid arthritis (rapid review of technology appraisal guidance 198)</a> (2012) NICE technology appraisal TA247. Guidance on static list.</p> <p><a href="#">Golimumab for the treatment of rheumatoid arthritis after the failure of previous disease modifying anti-rheumatic drugs</a> (2011) NICE technology appraisal TA225. Guidance on static list.</p> <p><a href="#">Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor</a> (2010) NICE technology appraisal TA195. Guidance on static list.</p> <p><b>Appraisals in development (including suspended appraisals)</b></p> <p><a href="#">Rheumatoid arthritis (after the failure of conventional DMARDs) -rituximab</a>. Technology Appraisal [ID333]. Status March 2011: Suspended – manufacturer is no longer seeking a licence for this indication.</p> <p><a href="#">Rheumatoid arthritis - tofacitinib</a>. Technology Appraisal [ID526]. Publication date: January 2018.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">Rheumatoid arthritis in adults: management</a> (2009) NICE guideline CG79. Review date: August 2018.</p> <p><b>Related Quality Standards:</b></p> <p><a href="#">Rheumatoid arthritis in over 16s</a> (2013) Quality Standard QS33.</p> <p><b>Related NICE Pathways:</b></p> <p><a href="#">Rheumatoid arthritis</a> (2015) NICE Pathway.</p>
<p><b>Related National Policy</b></p>	<p>NHS England (2016) <a href="#">Manual for prescribed specialised services 2016/17</a>. 5. Adult highly specialist rheumatology services.</p>

	<p>NHS England &amp; BMJ Group (2012) <a href="#">Shared Decision Making Sheets: Rheumatoid Arthritis</a>.</p> <p>NHS England (2013) <a href="#">A13. Specialised Rheumatology</a>. National programmes of care and clinical reference groups.</p> <p>Department of Health (2016) <a href="#">NHS Outcomes Framework 2016 to 2017</a>. Domains 1, 2, 3, 4 and 5.</p>
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**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. National Institute for Health and Care Excellence (2013) [Rheumatoid arthritis: commissioning guide](#). Accessed November 2016.