National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Baricitinib for treating moderate to severe rheumatoid arthritis

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Eli Lilly	Yes, this is an appropriate topic to refer to NICE for appraisal so appropriate and timely advice can be given to the NHS in England and Wales regarding the use of baricitinib within its licensed indication.	Comment noted.
	Pfizer	We consider it appropriate for this topic to be referred to NICE for appraisal.	Comment noted.
Wording	Eli Lilly	Agree.	Comment noted.
	Pfizer	We consider the wording of the remit of this appraisal to be appropriate.	Comment noted.
Timing Issues	Eli Lilly	Advice to the NHS should be as close to marketing authorisation as is feasible within the NICE appraisal programme.	Comment noted.
	Pfizer	We consider the timing of appraisal to be appropriate	Comment noted.
	Eli Lilly	No further comments	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
Additional comments on the draft remit	Pfizer	N/A	

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Eli Lilly	Please also note the following issues: Depression is common in RA and is estimated to occur in 13 to 20% of patients and may even occur in up to 40% of patients. Depression negatively impacts on patient outcomes and is associated with reduced HRQoL, increased risk of mortality, cardiovascular morbidity and disability. The physical and mental effects of RA can often result in a substantial negative impact on patients' ability to work. Impairments in physical function impacts on patients' abilities to carry out daily activities and causes reduced work productivity and disability. Although biologic treatments are not currently approved in the biologic naïve moderate RA population (TA375), all biologics are licensed in the moderate to severe population. In addition, EULAR clinical guidelines emphasise the need to adequately treat patient with moderate disease activity with appropriate treatment. *Reference has been provided but not replicated here.*	Thank you for your comments. The intention of the background section is to introduce the disease and treatments that are available in established NHS clinical practice. Biological treatments are only recommended by NICE for the treatment of severe active RA; they are not considered established clinical practice in the NHS for the treatment of moderate active RA.
	Pfizer	No comments	Comment noted.
	Eli Lilly	Please find further detail on baricitinib below:	Thank you for your comment. The

Section	Consultee/ Commentator	Comments [sic]	Action
The technology/ intervention		Baricitinib (Olumiant®) is a once daily oral selective and reversible janus kinase 1 and 2 (JAK1 and JAK2) inhibitor for the treatment of moderate to severe RA. JAKs are intracellular tyrosine kinases that transduce intracellular signals from cell surface receptors for a number of cytokines and growth factors involved in haematopoiesis, inflammation and immune function. JAKs phosphorylate and activate signal transducers and activators of transcription (STATs), which activate gene expression within the cell. Baricitinib modulates these signalling pathways by partially inhibiting JAK1 and JAK2 enzymatic activity, thereby reducing the phosphorylation and activation of STATs	technology section of the scope has been updated and the brand name of baricitinib has been added. However the intention of this section is to shortly introduce the technology, therefore no further description has been added.
	Pfizer	No comments	Comment noted.
Population	Eli Lilly	Baricitinib has been studied in patients who are treatment naïve, patients who have been treated with conventional DMARDs (including methotrexate) and patients who have been treated with biologic DMARDs.	Thank you for your comment. The scope has been updated and the population section now reads as 'Adults with moderate to severe, active rheumatoid arthritis' to cover the population included the clinical studies. The appraisal committee will only consider the population included in the marketing authorisation.

Section	Consultee/ Commentator	Comments [sic]	Action
	Roche	Roche Products understand the usual treatment approach is conventional DMARDS	Comment noted. No changes to the scope required.
	Pfizer	Pfizer suggests that further clarity should be provided as to when conventional DMARDs or biological DMARDs are being referred to within the population section of the draft scope.	Thank you for your comment. The scope has been updated and the population section now reads as 'Adults with moderate to severe, active rheumatoid arthritis'.
Comparators	Eli Lilly	The patient populations outlined in the 2nd and 3rd paragraphs of the comparators section should include 'For moderate to severe active RA'. Although biologic treatments are not currently approved in the biologic naïve moderate RA population (TA375), all biologics are licensed in the moderate to severe population. [redacted] Additional comparators in the patient population that has not responded adequately to therapy with conventional DMARDs only should include: • Management strategies involving further conventional DMARDs (for example sulfasalazine, leflunomide), NSAIDs and corticosteroids. The other comparators listed in the scope are appropriate.	Thank you for your comment. The scope has been updated so that the comparators for moderate active RA not previously treated with DMARDs and severe active RA (treated and not previously treated) are considered separately. Biological DMARDs are not used to treat moderate active RA in the NHS. They have not been recommended by NICE because they are not cost-effective. The

Section	Consultee/ Commentator	Comments [sic]	Action
			relevant comparator for people with moderate RA with inadequate response to conventional DMARDs is best supportive care.
	Pfizer	• Population omitted: o There are no comparators specified for the treatment of patients with moderate active rheumatoid arthritis that have not responded adequately to therapy with conventional DMARDs only • Missing comparator: o Tocilizumab monotherapy should be included as a treatment option for severe active rheumatoid arthritis that has not responded adequately to therapy with DMARDs including at least one TNF inhibitor when rituximab is contraindicated or withdrawn due to adverse events	Thank you for your comment. The relevant comparator for people with moderate RA with inadequate response to conventional DMARDs is best supportive care. Technology Appraisal guidance 247 does not recommend tocilizumab monotherapy, therefore it is not considered to be in established NHS clinical practice.
Outcomes	Eli Lilly	Other outcomes which could be considered: • Work Productivity and Activity Impairment-Rheumatoid Arthritis (WPAI-RA) • Duration and severity of morning joint stiffness We suggest combining the following outcomes:	Thank you for your comment. Joint damage and radiologic progression were considered as separate outcomes in previous appraisals, therefore for

Section	Consultee/ Commentator	Comments [sic]	Action
		• Joint damage • Radiologic progression As the standard measures of radiologic progression incorporate assessment of joint damage	consistency no changes to the scope required.
	Roche	Roche Products considers the outcomes listed as being appropriate, with importance placed on radiological progression as an indicator of progression	Comment noted. No changes to the scope required.
	Pfizer	No comments	Comment noted.
Economic analysis	Eli Lilly	An economic analysis that addresses the requirements of the NICE reference case will be submitted.	Comment noted.
	Pfizer	No comments	Comment noted.
Equality and Diversity	Eli Lilly	We have not identified any relevant issues.	Comment noted.
	Pfizer	No comments	Comment noted.
Other considerations	Eli Lilly	Please see comments made regarding comparators above.	Comment noted.
	Pfizer	No comments	Comment noted.
Innovation	Eli Lilly	Given the once daily oral formulation and results of the pivotal phase III studies, baricitinib has the potential to be considered an innovative step-change in the RA treatment paradigm. The novel mechanism of action involving the reversible inhibition of JAK1 and JAK2 enzymes represents an innovative treatment approach which will make baricitinib a first-in-class treatment in the EU. The results of the pivotal phase III studies demonstrate	Comment noted. The Appraisal Committee will discuss the potentially innovative nature of this

Section	Consultee/ Commentator	Comments [sic]	Action
		the effectiveness of baricitinib in a broad patient population and highlight its potential use at any stage of the NICE RA treatment pathway. Baricitinib has demonstrated superiority to the most commonly used biologic adalimumab in patients who have had an inadequate response to methotrexate. Baricitinib has also demonstrated substantial improvements in patient reported outcomes (PROs) including pain, fatigue and duration and severity of morning joint stiffness – important factors for patients with RA. In addition, baricitinib provides a rapid onset of efficacy which is seen as early as week 1 and is maintained for up to 52 weeks	technology. No changes to the scope required.
	Pfizer	No comments	Comment noted.
Questions for consultation	Eli Lilly	Q1. 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? The use of baricitinib in patients who have not been treated with conventional DMARDs will be within the anticipated marketing authorisation. We will work with NICE to determine the cost-effectiveness of baricitinib in this patient population. Q2. Have all relevant comparators for baricitinib been included in the scope? Our comments on comparators have been captured above. Q3. Are the outcomes appropriate? Our comments on outcomes have been captured above.	Comment noted. Please see responses and changes to the scope above. Any benefits that have not been captured in the estimate of the QALY and which are supported by evidence, will be considered by the appraisal committee.

Section	Consultee/ Commentator	Comments [sic]	Action
		Q4. 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? Yes. Other potential subgroups include patients who have been previously treated with biologic therapies, including TNF-alpha inhibitors. We will work with NICE to determine the cost-effectiveness of baricitinib in this patient population. Q5. Where do you consider baricitinib will fit into the existing RA NICE pathway The anticipated marketing authorisation for baricitinib will allow use at all stages of the NICE RA treatment pathway. We will work with NICE to determine the cost-effectiveness of baricitinib at these different stages of the RA pathway. Q6. 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)? Our comments on the innovation of baricitinib have been captured above. Q7. 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? Baricitinib has demonstrated substantial clinical benefits in patients with moderate to severe RA that are unlikely to be entirely captured in the QALY	

Section	Consultee/ Commentator	Comments [sic]	Action
		calculation including severity and duration of morning stiffness, fatigue and severity of pain. These health outcomes represent important factors for patients with RA but may not be entirely captured with the QALY calculation. Additionally, it will potentially be the first oral treatment for patients whose only other option may be injectable biologic treatment.	
	Pfizer	No comments	Comment noted.
Additional comments on the draft scope	Eli Lilly	No further comments	Comment noted.
	Pfizer	N/A	

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

- AbbVie Limited
- Royal College of Pathologists
- Merck Sharp and Dohme
- Sanofi
- Department of Health