National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Filgotinib for treating moderate to severe rheumatoid arthritis

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	Gilead	It is highly appropriate to refer this topic to NICE for appraisal.	Comment noted.
	National Rheumatoid Arthritis Society (NRAS)	Yes	Response noted.
	AbbVie	AbbVie consider it appropriate to refer to this topic to NICE for appraisal.	Comment noted.
	Roche	No comments	Response noted.
Wording	Gilead	The targeted label is the following: Adult patients with moderately to severely active rheumatoid arthritis who: • Have highly active and early progressive disease and were not previously treated with MTX and for whom treatment with MTX would be inappropriate OR • Have had an inadequate response to, or who are intolerant to one or more DMARDs.	Comment noted. The scope has been amended to reflect this, please see population and comparators sections for further details.

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		However, Gilead will not be making a cost-effectiveness case against the first bullet point i.e. naïve patients for whom methotrexate is inappropriate.	
	NRAS	Yes.	Response noted.
	AbbVie	AbbVie have no comments on the wording of the remit.	Response noted.
	Roche	No comments	Response noted.
Timing Issues	Gilead	• We believe it is necessary for NICE to assess filgotinib in a timely manner, according to NICE's usual timelines. • If NICE does not assess filgotinib with urgency, it is highly likely that CCGs will take a very long time to assess this product or they may not assess it at all. • Delays in local assessment or lack of assessment could be driven by CCGs thinking that they already have JAK inhibitors listed in their formularies, however filgotinib is not the same as currently available JAK inhibitors tofacitinib and baricitinib. • Filgotinib is a next-generation JAK inhibitor that is a potent, highly selective, and reversible inhibitor of JAK-1. • Filgotinib's high selectivity for JAK-1 is expected to result in reduced off-target effects. Clinical data shows low rates of treatment-related adverse events. • Filgotinib is a highly efficacious drug across the treatment pathway from naïve to highly refractory patients. 28-58% of patients have an	Comments noted. No action required.

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		inadequate response to MTX and fail TNF inhibitors as well (Redlich et al 2003). Patients need alternative options to be recommended by NICE and to be made available by the NHS since not all patients will respond adequately to current therapies, will have comorbidities that make them require an alternative treatment and/or may have an intolerance that limits their use of approved therapies.	
	NRAS	There remains unmet need for many people suffering from this painful and debilitating disease and so all new therapies coming to the market are welcomed by patients and patient organisations. We would welcome an appraisal at the earliest stage NICE can accommodate it within its work programme.	Comment noted.
	AbbVie	AbbVie have no comments regarding timing issues related to this proposed appraisal.	Response noted.
	Roche	No comments	Response noted.
Additional comments on the draft remit	Gilead	Nothing further.	Response noted.
	NRAS	No	Response noted.
	AbbVie	No additional comments on the draft remit.	Response noted.
	Roche	No comments	Response noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background	Gilead	• The prevalence section should also reflect the Welsh population which will be covered by this guidance.	Comments noted.

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information		• The background section should cover treat to target strategies from ACR & EULAR and show how most patients will not achieve remission, only 6% achieved remission and only <30% achieved low disease activity (LDA) as per DREAM registry (Johnson et al 2019). So, whilst remission is the main target of treatment, LDA is a more realistic target for many patients and many do not achieve either of these targets, i.e. patients are not flaring as described in this section but are in a constant moderate to high level of disease activity which in turn has a significant impact to their lives. • We suggest changing '*other immunomodulatory therapies*' to targeted synthetic DMARDs, to refer to JAK inhibitors. The term targeted synthetic DMARDs or tsDMARDs covers tofacitinib & baricitinib, as well as the upcoming JAK inhibitors filgotinib and upadicitinib.	The background section is intended as a brief overview of the disease and treatment options available. The committee will consider appropriate treatment targets during the appraisal. The term "immunomodulatory therapies" is consistent with other NICE guidance. No action required.
	NRAS	Not enough attn. is drawn to the impact the disease has on mental health and emotional wellbeing. Anxiety and depression are frequently quoted in our reports and surveys as the top two co-morbidities. We know that inadequately controlled disease and high levels of pain and fatigue in particular have a major impact on emotional wellbeing which in turn impacts things like ability to self-manage an adherence to medication.	Comment noted. The background section is intended as a brief overview, the impact of the disease on patients will be considered further by committee during the appraisal.
	AbbVie	AbbVie have no comments regarding the accuracy and completeness of the background information provided in the draft scope.	Response noted.
	Roche	No comments	Response noted.

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The technology/ intervention	Gilead	• We suggest adding that filgotinib is a potent, selective and reversible JAK-1 inhibitor. • We suggest adding that filgotinib is an oral, once daily medication.	Comments noted. The text has been amended to note that filgotinib is a selective inhibitor of JAK-1.
	NRAS	Yes, to the best of my knowledge However, I had assumed that it would be also be available post failure of cDMARDs as per the other JAK inhibitors but this is not mentioned?	Comment noted. The population includes people who have responded inadequately or are intolerant to one or more DMARDs.
	AbbVie	No comment.	Response noted.
	Roche	No comments	Response noted.
Population	Gilead	• We suggest removing the 'untreated' population. • We have not requested a label for all naïve patients and will not be making a cost-effectiveness argument for the sub-population of naïve patients (MTX intolerant) where a label has been requested.	Comment noted. The untreated population has been removed from the population section.
	NRAS	Yes	Response noted.
	AbbVie	No comment.	Response noted.
	Roche	No comments	Response noted.
Comparators	Gilead	• We suggest removing the untreated population and the comparators	Comment noted.

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		for this population. • All other comparators in the different sub-groups are appropriate.	The untreated population and its comparators have been removed from the comparators section.
	NRAS	Yes Best alternative care would likely be one of the biologics or their biosimilar/s or another JAK with a different pathway (JAK 2/3?)	Comment noted.
	AbbVie	AbbVie suggest that the comparators for severe active rheumatoid arthritis should be categorised depending on the tolerance and intolerance to methotrexate. In particular, AbbVie propose the following amendments in the population and comparators described in the scope: […] For severe active rheumatoid arthritis that has not responded adequately to therapy with conventional DMARDs only **and who tolerate methotrexate and it is not contraindicated**: • Biological DMARDs in combination with methotrexate (adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab, abatacept, **baricitinib, tofacitinib** or sarilumab) **For severe active rheumatoid arthritis that has not responded adequately to therapy with conventional DMARDs only and who do not tolerate methotrexate or it is contraindicated**: • Adalimumab, etanercept, certolizumab pegol, tocilizumab or sarilumab (each as monotherapy) • Tofacitinib or baricitinib (**each as** monotherapy)	Comment noted. The organisation of the comparators has been chosen for consistency with previous scopes and the NICE pathway for rheumatoid arthritis. Some minor amendments to the text have been made for clarity as suggested.

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		For severe active rheumatoid arthritis that has not responded adequately to therapy with **biological** DMARDs**,** including at least one TNF inhibitor**, who tolerate methotrexate and it is not contraindicated**: • Rituximab in combination with methotrexate For severe active rheumatoid arthritis that has not responded adequately to therapy with **biological** DMARDs**,** including at least one TNF inhibitor**, who do not tolerate methotrexate or it is contraindicated**: • **Rituximab as monotherapy** When rituximab is contraindicated or withdrawn due to adverse events **and methotrexate is tolerated and it is not contraindicated**: • Adalimumab, etanercept, infliximab, abatacept, tocilizumab, certolizumab pegol, golimumab or sarilumab, each in combination with methotrexate • Tofacitinib or baricitinib each in combination with methotrexate **When rituximab is contraindicated or withdrawn due to adverse events and methotrexate is not tolerated or it is contraindicated:** • Adalimumab, etanercept, certolizumab pegol, tocilizumab or sarilumab (each as monotherapy) • Tofacitinib or baricitinib (**each as** monotherapy) […]	The use of rituximab as monotherapy is outside of its marketing authorisation indication.
	Roche	Upadacitinib is also currently in review by authorities for marketing authorisation. Depending on how the timeframes compare, there may also be a need to consider this as a relevant comparator.	Comment noted. No action required.
Outcomes	Gilead	• Yes, we believe these outcomes capture the most important health	Comment noted.

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		related benefits.	
	NRAS	Yes.	Response noted.
	AbbVie	No comment.	Response noted.
	Roche	No comments	Response noted.
Economic analysis	Gilead	• No further comments, we agree with the time horizon.	Comment noted.
	NRAS	Nothing further to comment	Response noted.
	AbbVie	No comment.	Response noted.
	Roche	No comments	Response noted.
Equality and Diversity	Gilead	• We do not believe any changes are needed in order to ensure equality	Comment noted.
	NRAS	Nothing to comment	Response noted.
	AbbVie	No comment.	Response noted.
	Roche	No comments	Response noted.
Other considerations	Gilead	No further suggestions.	Comment noted.
	NRAS	No response.	Response noted.
	AbbVie	No comment.	Response noted.
	Roche	Should seropositive/ seronegative patients be included as potential	Comment noted.

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		subgroups, depending on the availability of relevant data?	Clinical data on seropositive and seronegative subgroups may be included as part of a submission if available, but specific economic analyses for these subgroups may not be required
Innovation	Gilead	• Filgotinib is a potent, selective, reversible JAK1 inhibitor. • In cellular assays, filgotinib selectively suppressed JAK1 mediated phosphorylation of STATs with IC50 values of ≥ 179 nM. In cytokine stimulated whole blood assays, filgotinib demonstrated ≥ 14fold selectivity for JAK1 over JAK2. • Many people with RA eventually become unable to work due to chronic disability (Sokka et al 2010). JAK inhibitors have an impact on work productivity not captured by the QALY calculation.	Comments noted. The committee will consider the innovative nature of the technology during the appraisal.
	NRAS	Whilst I don't think that a new JAK could be considered to be a 'step-change' in the management of the condition itself, the JAKs as a class were a step-change. My comments below also apply here, i.e. there are four Jaks, Jak1, Jak2, Jak3, and Tyk2, which selectively bind **different** receptor chains. As RA is a heterogenous disease, even people with seemingly similar disease profiles can react differently to the same drug, so we consider this drug to be an important addition to the range of therapies available to treat moderate to severe RA. The benefits associated with enabling someone to remain working are	Comments noted. The committee will consider the innovative nature of the technology during the appraisal and will consider non-health factors in line with section 6.2.20 of the Guide to Methods of

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		extremely important and yet NICE continue to ignore this important aspect of health related benefit and impact on HE evaluation, so we will continue to advocate for this to be included.	Technology Appraisal 2013.
	AbbVie	No comment.	Response noted.
	Roche	No comments.	Response noted.
Questions for consultation	Gilead	• Gilead is currently assessing the available options, and is considering submitting a fast-track appraisal.	Comment noted.
	NRAS	I imagine that filgotinib will fit into the pathway in same position as other JAK inhibitors. Not aware of any additional monitoring that may be required. The JAK inhibitors as a class should be considered as a 'step-change' in the management of the condition. However, given that there are 2 JAKS already in use by the NHS, a third, even if it is targeting a different step – i.e. JAK 1, I would say that this is not a 'step-change' advancement in therapy.	Comments noted.
	AbbVie	***Have all the relevant comparators for filgotinib been included in the scope?*** Additional comparators for consideration have been outlined in the comparator section above. ***Are the outcomes listed appropriate?*** No comment. ***Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom filgotinib is expected to be more clinically effective and cost-effective or other groups that should be examined separately?***	Comments noted.

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		All appropriate subgroups have been considered. ***Is any additional monitoring anticipated to be required for filgotinib (eg, for risk of pulmonary embolism observed with the other JAK inhibitors)?*** No comment. ***Where do you consider filgotinib will fit into the existing NICE pathway, Rheumatoid arthritis?*** No comment. ***Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.*** No comment.	
	Roche	No response.	Response noted.
Additional comments on the draft scope	Gilead	No further comments.	Response noted.
	NRAS	In regard to being similar in effect to any of the comparators, including the other JAKs, there are four Jaks, Jak1, Jak2, Jak3, and Tyk2, which selectively bind **different** receptor chains. As RA is a heterogenous disease, even people with seemingly similar disease profiles can react differently to the same drug, so we consider this drug to be an important addition to the range of therapies available to treat moderate to severe RA. In regard to its use resulting in any health related benefits unlikely to be included in the QALY calc., we would add work related benefits although we know this is not normally included. Nevertheless, we must continue to advocate for its inclusion.	Comments noted.

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		Do not consider there to be any barriers to adoption of this drug. Think the STA is appropriate for appraising this technology This technology is likely to be similar in its efficacy and resource use to the other JAKs already available. I don't know whether there will be new trials reporting next year.	
	AbbVie	AbbVie do not have any additional comments on the draft scope.	Response noted.
	Roche	No response.	Response noted.

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

Amgen