National Institute for Health and Care Excellence

Single Technology Appraisal (STA/MTA)

Sirukumab for previously treated moderate to severe active rheumatoid arthritis

Response to consultee and commentator comments on the draft remit and draft scope

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	Janssen	We consider it appropriate for this topic to be referred to NICE for appraisal. Sirukumab is a human interleukin-6 (IL-6) monoclonal antibody, but unlike the existing IL-6 inhibitor (tocilizumab), sirukumab selectively binds to the cytokine rather than the receptor protein. Sirukumab therefore provides an additional mode of action and treatment option to existing biologic disease modifying anti-rheumatic drugs (DMARDs) for the treatment of moderate to severe rheumatoid arthritis.	Comments noted
	MSD	Yes	Comment noted
	Pfizer	No comments	No comments noted
	UK Clinical Pharmacy Association	Yes	Comment noted

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Wording	Janssen	To allow for specific patient population eligible for sirukumab as per the pending EMA license in moderate to severe rheumatoid arthritis, we request that wording 'previously treated' be removed from the remit. We would suggest that the alternative wording should be: 'To appraise the clinical and cost effectiveness of sirukumab within its licensed indication for the treatment of moderate to severe rheumatoid arthritis.' This is consistent with the final scope for tocilizumab for the treatment of moderate and severe rheumatoid arthritis (TA 247)	Comment noted. It is noted that the eligibility for all of the trials for sirukumab stipulated a prior treatment. The remit is considered broad enough to not exclude anyone who may be eligible for sirukumab in the treatment pathway for rheumatoid arthritis. No changes made
	Pfizer	No comments	'No comments' noted
	UK Clinical Pharmacy Association	Yes	Comment noted
Timing Issues	Janssen	We suggest that the final guidance for sirukumab should be published as close to the date of market authorisation as possible.	Comment noted.
	Pfizer	No comments	'No comments' noted
	UK Clinical Pharmacy Association	It is not hugely urgent as other treatments for RA are in place. However, only one other treatment has the same mode of action therefore this could be an important advance for a cohort of patients who are refractory to/ intolerant of other treatments such as TNF inhibitors.	Comment noted

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Additional comments on the draft remit	UK Clinical Pharmacy Association	Patients are only eligible for other biologics in RA when their RA is severely active. Should sirukumab only be considered for severe RA? If the eligibility for biologics will in future be based on a lower DAS28 (so that patients with moderately active RA are eligible), this may be appropriate.	Comment noted. The clinical trials included people with moderate to severe rheumatoid arthritis. The recommendations will be in line with the population covered by the marketing authorisation for sirukumab.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Janssen	We noted that NICE technology appraisal 415 certolizumab pegol for treating rheumatoid arthritis after inadequate response to a TNF-inhibitor has been published and should be added to the background information. We also suggest that the background information describes that tocilizumab in combination with methotrexate can be used when the disease has responded inadequately to one or more TNF inhibitors and rituximab, as stated in NICE TA 247.	Comments noted, the recommendations from NICE technology appraisal 415 have been added to the background section of the scope. The text "tocilizumab is a treatment option for people whose disease has not responded to one or more TNF inhibitors and rituximab

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			(NICE technology appraisal guidance 247)" has been added to the background section of the scope.
	Pfizer	No comments	No comments noted
	UK Clinical Pharmacy Association	Should it instead read… 'stop work within two years *of diagnosis/of symptom onset*'? Should it read 'a DAS28 greater than *or equal* to 5.1 indicates…' and similarly for DAS 'less than *or equal to* 3.2'?	Comment noted. The scope background has been revised.
The technology/ intervention	Janssen	We would suggest that a description of the cytokine IL-6 is also included, as used in the NICE scope for TA 247 tocilizumab for the treatment of rheumatoid arthritis: 'IL-6 is a pro-inflammatory mediator and reducing the activity of IL-6 may reduce inflammation of the joints, prevent long-term damage QoL and function and relieve certain systemic effects of RA.'	Comment noted. 'The technology section has been updated with a short description of IL-6: 'IL-6 is a pro-inflammatory mediator and reducing the activity of IL-6 may reduce inflammation of the joints and relieve certain systemic effects of rheumatoid arthritis.'
	Pfizer	No comments	No comments noted

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	UK Clinical Pharmacy Association	Yes but include a sentence on what IL-6 does/why it is targeted? The comparator adalimumab is used in England and Wales for *severe* RA so is the RCT relevant if we are including people with moderate RA? Are there any trials using sirukumab with methotrexate if this could be a proposed intervention?	'The technology section has been updated with a short description of IL-6: 'IL-6 is a pro-inflammatory mediator and reducing the activity of IL-6 may reduce inflammation of the joints and relieve certain systemic effects of rheumatoid arthritis.' Adalimumab is listed in the scope as a comparator for people with severe rheumatoid arthritis who may be treated with sirukumab
Population	Janssen	Sirukumab has been studied in people with moderate to severe rheumatoid arthritis who have inadequate response to TNF inhibitors and other biologics DMARDs (for example rituximab and tocilizumab). We therefore request that population of the scope is changed to: 'Adults with moderate to severe, active arthritis whose disease has not responded adequately to conventional DMARDs or biological DMARDs.'	Comments noted. The population in the scope has been updated to: 'Adults with moderate to severe, active rheumatoid arthritis, whose disease has not responded adequately to, or who are intolerant of one or more disease modifying anti-

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			rheumatic drugs (DMARDs), including conventional or biological DMARDs'
	Pfizer	Could NICE please consider our suggestion of a more detailed description of the population; "*Adults with moderate to severe, active rheumatoid arthritis, whose disease has not responded adequately to one or more conventional disease modifying anti-rheumatic drugs (cDMARDs) or TNF inhibitors"*	Comment noted. The population is defined broadly before the marketing authorisation for sirukumab is granted. NICE recommendations will be in line with the marketing authorisation wording. The population in the scope has been updated to: 'Adults with moderate to severe, active rheumatoid arthritis, whose disease has not responded adequately to, or who are intolerant of one or more disease modifying anti-rheumatic drugs (DMARDs), including conventional or biological DMARDs'

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	Roche	Roche suggest the population for this appraisal should be 'adults with moderate to severe, active **rheumatoid** arthritis, whose disease has not responded adequately to conventional DMARDs and/or TNF inhibitors'	'Rheumatoid' has been added to the scope
	UK Clinical Pharmacy Association	Again, should it be used in moderate RA? Needs to state '*rheumatoid* arthritis'. Not just 'arthritis'. Is it still appropriate that the medication should be trialled after use of a TNF inhibitor? As tocilizumab (probably wouldn't then want to then trial sirukumab as same mode of action) or abatacept can also be used first line as per NICE TA375.	Comment noted. 'rheumatoid' has been added to the population. The comparator groups have been outlined based on the information of the eligible populations in the clinical trials of sirukumab.
Comparators	Janssen	We agree with the comparators included in the draft scope. However, we note that final guidance for treating rheumatoid arthritis after an inadequate response to a TNF inhibitor has now been published (NICE TA 415). We request that certolizumab pegol is included as a comparator, as per the populations for which it is recommended in NICE TA 415	Comment noted. Certolizumab pegol is a comparator in the scope
	MSD	In the absence of a positive technology appraisal, certolizumab pegol should not be listed as a comparator in the two populations below: 1) For severe active rheumatoid arthritis that has not responded adequately to therapy with DMARDS including at least one TNF inhibitor 2) For people with severe, active disease despite treatment with biological DMARDs recommended according to NICE guidance	Comment noted. Certolizumab pegol is now recommended as a treatment option for rheumatoid arthritis in NICE technology appraisal guidance 415

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	Pfizer	Could NICE please consider our suggestion of defining the moderate RA comparators for this section; *"For moderate active rheumatoid arthritis that has not responded adequately to therapy with one or more conventional DMARDs:* • *Best supportive care* • *Combination therapy with cDMARDs (including methotrexate and at least one other cDMARD, such as sulfasalazine and leflunomide)* • *cDMARD monotherapy with dose escalation"* In addition, Certolizumab pegol [TA415] has now been formally recommended by NICE. Could NICE therefore please acknowledge its recommendation remit of Certolizumab pegol within the Sirukumab [ID1002] scope?	Comments noted. The comparator section has been revised to include "Combination therapy with cDMARDs (including methotrexate and at least one other cDMARD), cDMARD monotherapy with dose escalation, Tofacitinib [subject to ongoing appraisal], and Best supportive care (only where conventional DMARDs are not appropriate due to intolerance)" Certolizumab pegol is listed as a comparator in the scope
	Roche	Roche suggest clarifying the patient group described as having 'severe, active disease despite treatment with biological DMARDs recommended according to NICE guidance'. It is unclear whether this patient group are those with an inadequate response to rituximab or a different population.	Comment noted. The patient group described as having 'severe, active disease despite treatment with biological DMARDs recommended according to NICE guidance' has been

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			revised to “For people with severe, active disease that has not responded adequately to one or more TNF inhibitor treatments and to rituximab”, in line with the wording of the recommendations of TA247.
	UK Clinical Pharmacy Association	Does ‘Best supportive care’ cover physiotherapy/occupational therapy and analgesia? Alternative care: consider acupuncture? NICE TA415 has now been published (certolizumab pegol post TNF inhibitor).	Comment noted. It is noted that best supportive care could cover a range of treatments and care. It is anticipated that the best supportive care in clinical practice in England would be determined during the appraisal and therefore it is not defined in the scope. Certolizumab pegol is a comparator in the scope
Outcomes	Janssen	Yes	Comment noted
	MSD	Yes	Comment noted

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	Pfizer	No comments	'No comments' noted
	UK Clinical Pharmacy Association	Is any therapeutic drug monitoring required?	The costs and impact on patients of any monitoring are assessed during the appraisal
Economic analysis	Janssen	PAS for other comparators are not published in the public domain and therefore we will explore a range of different discounts within our analysis, as per the NICE 'guide to the processes of technology appraisal 2014'.	Comment noted
	Pfizer	No comments	'No comments' noted
	UK Clinical Pharmacy association	Should the 'reference case' be described in more detail? Are there any additional costs or monitoring costs?	Comments noted. The reference case is described in more detail in the NICE methods for technology appraisal.
Equality and Diversity	Janssen	No comments	'No comments' noted
	Pfizer	No comments	'No comments' noted
	UK Clinical Pharmacy association	It is not apparent that this will discriminate against any particular groups.	Comment noted
	Janssen	No comments	'No comments' noted

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Other considerations	Pfizer	No comments	'No comments' noted
	UK Clinical Pharmacy Association	Are there any benefits of its use over tocilizumab? (Also targets IL-6). Route of administration.	It is anticipated that this question will be addressed in the appraisal
Innovation	Janssen	Sirukumab is a human IL-6 monoclonal antibody, but unlike the existing IL-6 inhibitor (tocilizumab), sirukumab selectively binds to the cytokine rather than the receptor protein. Sirukumab therefore provides a novel mode of action and a valuable additional treatment option for the management of moderate to severe rheumatoid arthritis	Comment noted
	Pfizer	No comments	'No comments' noted
	UK Clinical Pharmacy Association	This would be only the second drug available with this mode of action. There are some side effects associated with tocilizumab. It would be particularly useful if the same side effects do not occur with sirukumab although they may be a class effect.	Comment noted. The side effect profile of technologies and the impact on patients' quality of life is taken into account in all technology appraisals.
Questions for consultation	Janssen	We believe that all relevant subgroups and outcomes have been included in the current NICE scope. We request that certolizumab pegol is included as a comparator, as per the populations for which it is recommended in NICE TA 415 We believe sirukumab will fit into similar positions to tocilizumab monotherapy and tocilizumab in combination with MTX within treatment pathways. As with	Comments noted

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		tocilizumab, sirukumab provides an additional option to patients who have failed existing conventional DMARDs and/or biological DMARDs. In addition sirukumab potentially provides a valuable option for patients who have failed tocilizumab due to a difference in how IL-6 cytokine is inhibited. We believe that sirukumab in combination with MTX or monotherapy would be appropriate and suitable for the new ATA process. Sirukumab has been studied in the SURROUD-H study, which has compared sirukumab monotherapy to adalimumab monotherapy. Initial results have demonstrated that sirukumab monotherapy has similar or improved efficacy compared to adalimumab monotherapy. It is anticipated that sirukumab will also demonstrate similar or equivalent effectiveness to existing biologic DMARDs and therefore an ATA would be appropriate to appraise sirukumab.	
	Pfizer	No questions	'No questions' noted
	UK Clinical Pharmacy Association	I think it is important to assess those with moderate and severe disease activity separately when calculating the QALY to ensure a fair comparison to current treatments. Sirukumab could be included in NICE pathways first line if TNF inhibitors are contra-indicated, or If a TNF inhibitor is ineffective or withdrawn due to an adverse event, or If both TNF inhibitors and rituximab have been trialled but had to be withdrawn due to inefficacy or adverse events. However this is all dependent on a review of the evidence and calculated QALY.	Comments noted.

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		If sirukumab is shown to be similarly effective to tocilizumab / current treatments and the cost is similar or lower, the ATA may be appropriate for this medication. This may also be appropriate as we are already familiar with a different medication of the same mode of action.	
Additional comments on the draft scope	Pfizer	none	Noted.
	Roche	As per Roche's response to the Abbreviated Technology Appraisal (ATA) consultation, we have concerns regarding the lack of clinician and patient input into the currently proposed ATA process. Moreover, Roche does not support the current ATA proposal that comparator manufacturers will only receive a summary of the submitting manufacturer's documents. Additionally, it is unclear what the most appropriate comparator would be for sirukumab to be appraised against via the ATA route.	Comments noted.
	UK Clinical Pharmacy Association	If sirukumab is recommended for treatment it will add to the tocilizumab's competition therefore may help to keep costs competitive.	Comment noted.

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

AbbVie, BMS