National Institute for Health and Clinical Excellence

Single Health Technology Appraisal (STA)
Rituximab for the treatment of rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs

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

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	National Rheumatoid Arthritis Society	The licence application is to use this technology in MTX naïve and post DMARD failure patients. Whilst I think it entirely appropriate that RTX could be used in post DMARD failure patients where the clinician deems it to be more appropriate than using Anti-TNF as first line biologic, I think that patients should be given the opportunity to get their disease under control using combination DMARDs including MTX in line with NICE RA Guidelines unless there is good clinical reason to move straight to a biologic	Following information received from the manufacturer regarding the removal of the methotrexate-naive indication from the licence application, the scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.
	British Society for Rheumatology (comments endorsed by Royal College of Physicians)	Yes	Comment noted. No action required.
	NHS East & North Hertfordshire	This has not been identified as a clinical priority from our dialogue with local specialists and requests received by the PCT. We would question the priority given to this review at this moment in time.	Comment noted. The Institute aims to consider all new technologies, including significant licence extensions to existing technologies. Consultees at the scoping workshop considered that an appraisal of rituximab was appropriate.

Section	Consultees	Comments	Action
	NHS Bradford and Airedale	We are not aware that this is a clinical priority judging from requests so would question priority given to this particular review at this moment in time.	The Institute aims to consider all new technologies and significant licence extensions to existing technologies. Consultees at the scoping workshop considered that an appraisal of rituximab was appropriate.
	Royal College of Nursing	Yes, although needs to be considered in the context of other apppraisals currently underway in relation to RA	As per the Single Technology Appraisal process, any guidance produced will refer only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. However, the use of rituximab at this point in the pathway will be considered in the context of other currently available treatments for RA.
	Royal College of Pathologists	Yes.	Comment noted. No action required.
	Roche Products	Methotrexate-naive rheumatoid arthritis is no longer part of the Roche regulatory submision	The scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.
	Wyeth Pharmaceuticals	No. The use of rituximab (RTX) in methodrexate (MTX) naive rheumatoid arthritis (RA) and of RA after the failure of conventional disease modifying anti-rheumatic drugs (DAMRDs) will not improve the health of the population. The DMARD failure trial for RTX included a high proportion of patients whom have received previous TNF alpha inhibitors, and shows a lower effectiveness when compared to TNF alpha inhibitors.	The Institute aims to consider all new technologies and significant licence extensions to existing technologies. Consultees at the scoping workshop considered that an appraisal of rituximab was appropriate. Please note that following information received from the manufacturer regarding the removal of the methotrexate-naive indication from the licence application, the scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.

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Wording	National Rheumatoid Arthritis Society	I believe so	Comment noted. No action required.
	Royal College of Nursing	Yes	Comment noted. No action required.
	Royal College of Pathologists	YES	Comment noted. No action required.
	Roche Products	Yes, assuming methotrexate treatment naïve wording is taken out	The scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.
	Wyeth Pharmaceuticals	The wording reflects the issues of clinical and cost-effectiveness	Comment noted. No action required.
Timing Issues	National Rheumatoid Arthritis Society	Timing seems appropriate	Comment noted. No action required.
	NHS East & North Hertfordshire	Low on the basis of the requests received and discussions with local clinicians	Comment noted. Consultees at the scoping workshop considered that an appraisal of rituximab was appropriate. Following referral from the Department of Health, this appraisal will proceed following the usual timelines for the Single Technology Appraisal process.
	NHS Bradford and Airedale	Low on basis of our view of current practice	Comment noted. Consultees at the scoping workshop considered that an appraisal of rituximab was appropriate. Following referral from the Department of Health, this appraisal will proceed following the usual timelines for the Single Technology Appraisal process.

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	Royal College of Nursing	It is imperative that there is close working and understanding of other technologies in relation to RA are considered in the context of the overall management options for patients.	As per the Single Technology Appraisal process, any guidance produced will refer only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. However, the use of rituximab at this point in the pathway will be considered in the context of other currently available treatments for RA.
	Royal College of Pathologists	Suggested timing is appropriate	Comment noted. No action required.
	Roche Products	[redacted]	Comment noted. No action required.
	Wyeth Pharmaceuticals	This appraisal is not urgent, as there is already a range of more effective products recommended.	Comment noted. Consultees at the scoping workshop considered that an appraisal of rituximab was appropriate. Following referral from the Department of Health, this appraisal will proceed following the usual timelines for the Single Technology Appraisal process.
Additional comments on the draft remit	No additional comments received on the draft remit.		

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	National Rheumatoid Arthritis Society	No further comments to make	Comment noted. No action required.

Section	Consultees	Comments	Action
	British Society for Rheumatology (comments endorsed by Royal College of Physicians)	I think it would be more accurate to say that RA affects 0.8% of the population. It is more correct to say that NICE guidance (TA 130) recommends the use of TNF inhibitors.... after failure of 2 conventional DMARDS including methotrexate AND A DAS SCORE > 5.1	Comments noted. The scope has been amended accordingly.
	Royal College of Nursing	It is not clear whether Rituximab will be administered with methotrexate as part of this regime - as patients are methotrexate naive before starting - does that mean they start Rituximab + Mtx?	Comment noted. Following information received from the manufacturer regarding the removal of the methotrexate-naive indication from the licence application, the scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.
	Royal College of Pathologists	Satisfactory	Comment noted. No action required.
	Wyeth Pharmaceuticals	Accurate and complete	Comment noted. No action required.
The technology/ intervention	National Rheumatoid Arthritis Society	no further comments to make	Comment noted. No action required.
	British Society for Rheumatology (comments endorsed by Royal College of Physicians)	Rituximab was approved in November 1997 for the treatment of Non- Hodgkin's lymphoma. It has been estimated that probably over one million people have now been given this drug for this indication and thus its safety profile has been well established.	Comment noted. No action required.
	Royal College of Nursing	See comment on background information.	Comment noted. See response above.
	Royal College of Pathologists	Yes	Comment noted. No action required.

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	Roche Products	This technology has also been studied in TNF-IR and it is also indicated in haematological malignances	Comment noted. The rituximab indication subject to this appraisal is its use for the treatment of rheumatoid arthritis after the failure of conventional DMARDs. The use of rituximab after the failure of TNF inhibitors and its use for haematological malignancies have been subject to separate appraisals. No changes made to the scope.
	Wyeth Pharmaceuticals	Accurate	Comment noted. No action required.
Population	National Rheumatoid Arthritis Society	Rituximab has been show to be less effective in sero-negative patient population and therefore should be considered separately in my view	Comment noted. If the evidence allows, the appraisal will consider sub-groups of people defined by their auto-antibody status. This consideration is stated in the scope.

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	NHS East & North Hertfordshire	This treatment is only licensed in combination with methotrexate of severe active rheumatoid arthritis. There is a need for a more explicit patient subgroup (severe active RA) and drug regimen to be covered (ritux [what dose?] We are not clear about how proposed use fits with current pathway. The draft scope is not in line with marketing authorisation i.e. current markrting authorisation is only in combination with methotrexate in patients with severe RA and after DMARD inc. at least 1 anti-TNF. Therefore, our view is that the scope needs to be much clearer identifying the patients to be included and whether ritux is to be used alone or in combination with methotrexate.	As a means of producing guidance for the NHS on the use of technologies as close as is possible to their marketing authorisations, topics are often scoped in advance of their receipt of marketing authorisations. Rituximab is anticipated to receive a marketing authorisation for use after the failure of conventional DMARDs only, which is why it has been scoped for use in this patient population. NICE will only appraise a technology within its licensed indication, which includes licensed dosing regimens. The 'other considerations' section of the scope has been amended to include "If evidence allows, the appraisal will consider the variability in the time to re-treatment with rituximab." Consultees considered that the specification of disease severity to be included in the marketing authorisation would sufficiently define the population for which treatment is indicated. Please note that following information received from the manufacturer regarding the removal of the methotrexate-naive indication from the licence application, the scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.

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	NHS Bradford and Airedale	Our view would be that there is a need to be more explicit about patient group (severe active RA) and drug regimen to be covered (ritux [what dose?] with MTX [as only licensed with MTX]. we are not clear about how proposed use fits with current pathway If review is to be in line with marketing authorisation then this must be in combo with MTX, in patients with severe active disease and after DMARD inc. at least 1 anti-TNF. Scope needs to be more explicit in identifying the patients to be included and whether ritux is to b e used alone or in combo (?with MTX).	As a means of producing guidance for the NHS on the use of technologies s as close as is possible to their marketing authorisations, topics are often scoped in advance of their receipt of marketing authorisations. Rituximab is anticipated to receive a marketing authorisation for use after the failure of conventional DMARDs only, which is why it has been scoped for use in this patient population. NICE will only appraise a technology within its licensed indications, which includes licensed dosing regimens. The 'other considerations' section of the scope has been amended to include "If evidence allows, the appraisal will consider the variability in the time to re-treatment with rituximab." Consultees considered that the specification of disease severity to be included in the marketing authorisation would sufficiently define the population for which treatment is indicated. Please note that following information received from the manufacturer regarding the removal of the methotrexate-naive indication from the licence application, the scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.

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	Primary Care Rheumatology Society	I feel that patients who are unable to use anti-TNF or other biologic therapies because of side effects such as currently having cancer should also be considered as a separate population	At the scoping workshop consultees considered that contraindications to treatment did not need to be specified in the scope. Information about the specific population for whom rituximab may be suitable should be included in any statements or submissions to NICE after the start of the appraisal.
	Royal College of Nursing	Is there any need to consider different treatment strategies based upon age? For example is there a reason that the very young patients who may be receiving this treatment for more than say ten years should also be considered for long term treatment with Rituximab?	Consultees agreed at the scoping workshop that age would not be a sole factor in determining the appropriateness of treatment, and that such a subgroup did not, therefore, need to be specified.
	Royal College of Pathologists	Yes	Comment noted. No action required.
	Roche Products	Population needs to be altered to cover just DMARD-IR.	The scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.
	Wyeth Pharmaceuticals	The population is defined appropriately	Comment noted. No action required.
Comparators	National Rheumatoid Arthritis Society	Best evidence based care would be in line with NICE RA Guidelines	In the identification of comparators, consideration is given specifically to routine and best practice within the NHS, including existing NICE guidance (see section 2.2.4 of the NICE Guide to the methods of technology appraisal.)

Section	Consultees	Comments	Action
	British Society for Rheumatology (comments endorsed by Royal College of Physicians)	BSR's clinical experts were a little confused about some of the information in the "Comparators" section. It refers to: "…people with rheumatoid arthritis who have had an inadequate response to conventional DMARDs" but then goes on to list treatment with biologic agents including several that are not NICE approved such as tocilizumab, certolizumab and golimumab.	The comparators section aims to list those treatments in current standard or best practice which would be used by those in the specified patient population in the absence of rituximab. Golimumab is currently subject to an on-going single technology appraisal in a similar patient population. Certolizumab pegol and tocilizumab were subject to their own single technology appraisals (see NICE technology appraisal guidance 186 and technology appraisal guidance 198 respectively). Certolizumab pegol is included in the scope because it is recommended as an option for the treatment of people with rheumatoid arthritis in the same way as the other tumour necrosis factor (TNF) inhibitor treatments in NICE technology appraisal guidance 130 'Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis'. It has therefore been included in the scope. Tocilizumab has been removed from the scope because NICE guidance does not recommend the use of this technology after only the failure of conventional DMARDs. .

Section	Consultees	Comments	Action
	NHS East & North Hertfordshire	difficult to do as STA - an MTA is really needed now. Under scope, the use of rituximab can only be considered line of its market liscence…..which states that "MabThera in combination with methotrexate is indicated for the treatment of adult patients with severe active rheumatoid arthritis who have had an inadequate response or intolerance to other disease-modifying anti-rheumatic drugs (DMARD) including one or more tumour necrosis factor (TNF) inhibitor therapies." This significantly strengthens the case for consideration of this as a MTA rather than an STA. We view this as critical given the size of the RA population (estimated as 1.5% of the adult pop in england); and the costs involved - a more comprehensive assessement of cost effectivness and budget impact within the context of the broader pathway of treating RA patients is critical. RA requires review of pathway and multiple technologies particularly in view of expanding range of biologics and recommendations for use of drugs like abatacept outside NICE TA Makes most sense to consider RTX in the context of an MTA (i.e. with all the other Anti TNFs) - seems a bit silly to consider in isolation. Should be considered along with all other drugs used in clinical practice in this group of patients.	Please note that following information received from the manufacturer regarding the removal of the methotrexate-naive indication from the licence application, the scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. At the scoping workshop, it was considered that there would be value in doing a single technology appraisal of rituximab in order to provide timely guidance to the NHS. As per the Single Technology Appraisal process, any guidance produced will refer only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. However, consideration will be given specifically to routine and best practice within the NHS (including existing NICE guidance) with regards to the range of available treatments. Please note that the Committee does not consider budget impact in its appraisal of technologies.

Section	Consultees	Comments	Action
	NHS Bradford and Airedale	difficult to do as STA - MTA better. guidance will only consider RTX within line of its market liscence…..which states that "MabThera in combination with methotrexate is indicated for the treatment of adult patients with severe active rheumatoid arthritis who have had an inadequate response or intolerance to other disease-modifying anti-rheumatic drugs (DMARD) including one or more tumour necrosis factor (TNF) inhibitor therapies." This significantly strengthens the case for consideration of this as a MTA rather than an STA. We view this as critical given the size of the RA population (estimated as 1.5% of the adult pop in england); and the costs involved - a more comprehensive assessement of cost effectivness and budget impact within the context of the broader pathway of treating RA patients is critical. RA requires review of pathway and multiple technologies particularly in view of expanding range of biologics and recommendations for use of drugs like abatacept outside NICE TA Makes most sense to consider RTX in the context of an MTA (i.e. with all the other Anti TNFs) - seems a bit silly to consider in isolation. Should be considered along with all other drugs used in clinical practice in this group of patients	Please note that following information received from the manufacturer regarding the removal of the methotrexate-naive indication from the licence application, the scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. At the scoping workshop, it was considered that there would be value in doing a single technology appraisal of rituximab in order to provide timely guidance to the NHS. As per the Single Technology Appraisal process, any guidance produced will refer only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. However, consideration will be given specifically to routine and best practice within the NHS (including existing NICE guidance) with regards to the range of available treatments. Please note that the Committee does not consider budget impact in its appraisal of technologies.
	Royal College of Nursing	It is not clear why the comparator does not allow for methotrexate monotherapy. Does this include methotrexate but oral and subcutaneous route?	Following information received from the manufacturer regarding the removal of the methotrexate-naive indication from the licence application, the scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. "Combination therapy with conventional DMARDs (including methotrexate and at least one other DMARD)" has therefore been removed from the comparators section.

Section	Consultees	Comments	Action
	Royal College of Pathologists	Yes	Comment noted. No action required.
	Roche Products	Comparators should be altered to exclude "For people with rheumatoid arthritis who have not been previously treated with methotrexate", as comparator methotrexate naïve is no longer appropriate. We assume that in the DMARD-IR indication, tocilizumab, certolizumab pegol and golimumab will only become comparators if recommended by NICE	The scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. Yes, this is correct. Please note that certolizumab pegol (technology appraisal 186) has been included in the scope because it is now recommended as an option for the treatment of people with rheumatoid arthritis in the same way as the other tumour necrosis factor (TNF) inhibitor treatments in NICE technology appraisal guidance 130 'Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis'. Tocilizumab (technology appraisal 198) has been removed from the scope because NICE guidance does not recommend the use of this technology after only the failure of conventional DMARDs. Golimumab is currently subject to an ongoing single technology appraisal.
	Wyeth Pharmaceuticals	The comparators are adequate	Comment noted. No action required.
Outcomes	National Rheumatoid Arthritis Society	Work should be included as a health related outcome and is of huge importance to patients of working age (the majority of patients)	As per the NICE reference case (see sections 5.2.7 to 5.2.10 of the NICE methods guide), costs incurred outside the NHS or PSS (i.e., those owing to time away from work) will not be incorporated.

Section	Consultees	Comments	Action
	NHS East & North Hertfordshire	Are fine	Comment noted. No action required.
	NHS Bradford and Airedale	OK	Comment noted. No action required.
	Royal College of Nursing	Should we be measuring any aspects of immunological status?	Consultees agreed at the scoping workshop that immunological status did not need to be specified as an outcome in the scope. The scope stipulates that if evidence allows, the appraisal will consider subgroups of people defined by their auto-antibody status (for example, rheumatoid factor status and CCP antibody status).
	Royal College of Pathologists	Yes	Comment noted. No action required.
	Wyeth Pharmaceuticals	They do	Comment noted. No action required.
Economic analysis	National Rheumatoid Arthritis Society	no further comments to make	Comment noted. No action required.
	NHS East & North Hertfordshire	need to consider dose (although only one licensed so probably can't look at lower dose therapy	NICE will only appraise a technology within its licensed indications.
	NHS Bradford and Airedale	need to consider dose (although only one licensed so probably can't look at lower dose therapy)	NICE will only appraise a technology within its licensed indications.

Section	Consultees	Comments	Action
	Royal College of Nursing	Please consider referring to analyses undertaken by the National Audit Office (RA, 2009) - to explore the wider ramifications of poorly controlled disease	The Committee will consider all evidence submitted by consultees. Please note that as per the NICE reference case (see sections 5.2.7 to 5.2.10 of the NICE methods guide), costs incurred outside the NHS or PSS (i.e., those owing to time away from work) will not be incorporated.
Equality and Diversity	National Rheumatoid Arthritis Society	The only issue here would be to ensure that sero-negative patients are not treat inequitably	NICE has to demonstrate that it has complied with legislation on equalities. The appraisal will consider those groups for whom rituximab is licensed and efficacy data for these groups. As per the Single Technology Appraisal process, any guidance produced will refer only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.
	Royal College of Nursing	Are they any particular sub sets of patients (genetic groups) who would respond more effectively to Rituximab? As per sero-negative group, are there other factors that need to be considered?	The scope stipulates that if evidence allows, the appraisal will consider subgroups of people defined by their auto-antibody status (for example, rheumatoid factor and anti-CCP).
	Wyeth Pharmaceuticals	Accurate.	Comment noted. No action required.
Other considerations	British Society for Rheumatology (comments endorsed by Royal College of Physicians)	The draft scope mentions that the appraisal 'will consider sub-groups of people identified as sero-negative or sero-positive'. Both BSR's clinical experts agree that from extensive experience at University College London Hospitals (the first department to propose and treat RA patients with rituximab and with probably have the world's largest single centre experience of using it in RA and SLE) rituximab really isn't the drug to be thinking of for those patients lacking rheumatoid factor (i.e.. sero negative patients). We would like to underline that in their experience it rarely works for these patients	Comment noted. No change to scope required. This important information should be included in any submissions or statements of evidence for the appraisal.

Section	Consultees	Comments	Action
	NHS East & North Hertfordshire	We presume background to this is desire for ritux to become more 1st/2nd line - this seems fine if it is a cost effective strategy - and more cost effective than cheaper DMARDs.	
		dosing - how different dosing regimens affects clinical and cost effectivness. We have already had discussions with rheumatologists about using half doses etc. Whether this is a clinically or cost effective strategy is a moot point, and probably under researched (if at all) - my sense from the rheumatols was this was emminence based rather than evidence based. This is put forward as a more cost effective strategy.	NICE will only appraise a technology within its licensed indications, which includes licensed dosing regimens. No change to scope required.
		We have picked up that monotherapy is rapidly becoming the norm in clinical practice (i.e. NOT using RTX concurrent with MTX). A substantial economic review undertaken by SCHaRR suggests that this strategy of RTX monotherapy is NOT cost-effective beyond 1st dose	
		Sub groups - differential look at comparative effectiveness in specific sub groups of patients with refractory RA - differential consideration should be given to sero positive / sero negative…….This, in our view, is one of the key considerations in requests for abatacept. While a decision on ritux use in sero neg/pos RA doesn't have a bearing on use of abatacept, it would be good to have view on ritux in both seroneg and sero pos. Clearly the cost of testing will need to be built into the economic analysis.	The scope stipulates that if evidence allows, the appraisal will consider subgroups of people defined by their auto-antibody status (for example, rheumatoid factor status and CCP antibody status).

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	NHS Bradford and Airedale	We presume background to this is desire for ritux to become more 1st/2nd line - this seems fine if it is a cost effective strategy - and more cost effective than cheaper DMARDs.	
		dosing - how different dosing regimens affects clinical and cost effectivness. We have already had discussions with rheumatologists about using half doses etc. Whether this is a clinically or cost effective strategy is a moot point, and probably under researched (if at all) - my sense from the rheumatols was this was emminence based rather than evidence based. This is put forward as a more cost effective strategy.	NICE will only appraise a technology within its licensed indications, which includes licensed dosing regimens. No change to scope required.
		We have picked up that monotherapy is rapidly becoming the norm in clinical practice (i.e. NOT using RTX concurrent with MTX). A substantial economic review undertaken by SCHaRR suggests that this strategy of RTX monotherapy is NOT cost-effective beyond 1st dose	
		Sub groups - differential look at comparative effectiveness in specific sub groups of patients with refractory RA - differential consideration should be given to sero positive / sero negative…….This, in our view, is one of the key considerations in requests for abatacept. While a decision on ritux use in sero neg/pos RA doesn't have a bearing on use of abatacept, it would be good to have view on ritux in both seroneg and sero pos. Clearly the cost of testing will need to be built into the economic analysis.	The scope stipulates that if evidence allows, the appraisal will consider subgroups of people defined by their auto-antibody status (for example, rheumatoid factor status and CCP antibody status).

Section	Consultees	Comments	Action
	Royal College of Nursing	Is there evidence on optimal dosing time and factors that highlight this, for example it appears now that 6 months is optimal rather than 9 months. What are the indicators - rising levels of CD 19 cells or active disease? What are the safe levels and additional factors that need to be considered?	NICE will only appraise a technology within its licensed indications, which includes licensed dosing regimens. The 'other considerations' section of the scope has been amended to include "If evidence allows, the appraisal will consider the variability in the time to re-treatment with rituximab."
	Roche Products	In the interest of obtaining timely advice to the NHS, an STA would be the appropriate way to appraise this technology	Comment noted. No action required.
Questions for consultation	NHS East & North Hertfordshire	If the review makes a final recommendation that changes the current model / clinical practice then recommendations might also be made about disinvestments that could concurrently be made within the same programme area. This may well be outside the scope of the TA process itself but we view that it is ABSOLUTELY critical that NICE also make parallel recommendations for 'in programme' efficiencies.	As per the Single Technology Appraisal process, any guidance produced will refer only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. A series of implementation tools will be produced to support this guidance. No changes to the scope required.
	NHS Bradford and Airedale	if the review makes a final recommendation that changes the current model / clinical practice then recommendations might also be made about disinvestments that could concurrently be made within the same programme area. This may well be outside the scope of the TA process itself but we view that it is ABSOLUTELY critical that NICE also make parallel recommendations for 'in programme' efficiencies	As per the Single Technology Appraisal process, any guidance produced will refer only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. A series of implementation tools will be produced to support this guidance. No changes to the scope required.
	Royal College of Nursing	What is the optimal intravenous administration time that can now be achieved? Is there evidence of treatment without co-prescribing intravenous steroids?	NICE can only make recommendation in accordance with the marketing authorisation of the technologies. This includes guidance on the administration time for rituximab and the co-prescription of steroids. No changes to the scope required.

Section	Consultees	Comments	Action
Additional comments on the draft scope.	NHS East & North Hertfordshire	RA requires review of pathway and multiple technologies particularly in view of expanding range of biologics and recommendations for use of drugs like abatacept outside NICE TA starting and more importantly stopping criterion need to be carefully considered objectively auditable criterion for use need to be set out, and established clearly within the guidance. Time horizon for the cost effectiveness should be relatively long; given the lifelong nature of the condition. Consideration should be given to the long term safety profile of RTX - and the clinical consequences and cost of treating and adverse consequences should be built into the economic evaluation.	As per the Single Technology Appraisal process, any guidance produced will refer only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. However, consideration will be given specifically to routine and best practice within the NHS, (including existing NICE guidance) with regard to range of treatments available. The 'other considerations' section of the scope has been amended to include "If evidence allows, the appraisal will consider the effects of treatment continuation and/or stopping rules." As per the reference case, the scope stipulates that the time horizon will be sufficiently long to reflect any differences in costs and/or outcomes between the technologies being compared. For chronic diseases this is often a life time horizon. Based on the evidence submitted by consultees, the Committee will consider the long term safety profile of rituximab and treatment-related adverse events at the time of appraisal. However, the Committee does not make recommendations solely on the basis of safety data. Regulatory agencies assess the risk-benefit profiles of technologies.

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	NHS Bradford and Airedale	RA requires review of pathway and multiple technologies particularly in view of expanding range of biologics and recommendations for use of drugs like abatacept outside NICE TA starting and more importantly stopping criterion need to be carefully considered objectively auditable criterion for use need to be set out, and established clearly within the guidance. Time horizon for the cost effectiveness should be relatively long; given the lifelong nature of the condition. Consideration should be given to the long term safety profile of RTX - and the clinical consequences and cost of treating and adverse consequences should be built into the economic evaluation.	As per the Single Technology Appraisal process, any guidance produced will refer only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs. However, consideration will be given specifically to routine and best practice within the NHS, (including existing NICE guidance) with regard to range of treatments available. The 'other considerations' section of the scope has been amended to include "If evidence allows, the appraisal will consider the effects of treatment continuation and/or stopping rules." As per the reference case, the scope stipulates that the time horizon will be sufficiently long to reflect any differences in costs and/or outcomes between the technologies being compared. For chronic diseases this is often a life time horizon. Based on the evidence submitted by consultees, the Committee will consider the long term safety profile of rituximab and treatment-related adverse events at the time of appraisal. However, the Committee does not make recommendations solely on the basis of safety data. Regulatory agencies assess the risk benefit profiles of technologies.

Section	Consultees	Comments	Action
	Wyeth Pharmaceuticals	It is not appropriate to reffer this appraisal to NICE, as the use of rituximab (RTX) in methodrexate (MTX) naive rheumatoid arthritis (RA) and of RA after the failure of conventional disease modifying anti-rheumatic drugs (DAMRDs) will not improve the health of the population. The DMARD failure trial for RTX included a high proportion of patients whom have received previous TNF alpha inhibitors, and shows a lower effectiveness when compared to TNF alpha inhibitors.	The Institute aims to consider all new technologies and significant licence extensions to existing technologies. Consultees at the scoping workshop considered that an appraisal of rituximab was appropriate. Please note that following information received from the manufacturer regarding the removal of the methotrexate-naive indication from the licence application, the scope now refers only to the use of rituximab after the failure of disease-modifying anti-rheumatic drugs.

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

NHS Quality Improvement Scotland
Pfizer
RICE - Research Institute for the Care of Older People
Schering-Plough
Welsh Assembly Government
Department of Health
National Public Health Service for Wales
Royal College of Radiologists