National Institute for Health and Clinical Excellence

Golimumab for the treatment of rheumatoid arthritis after failure of previous disease-modifying antirheumatic drugs

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	RCN	Yes.	Comments noted. It was agreed at the scoping workshop that an appraisal of golimumab was appropriate.
	Roche	High level of non-responding patients within this disease area therefore rapid referral appropriate.	Comments noted. It was agreed at the scoping workshop that an appraisal of golimumab was appropriate.
	Schering-Plough	Yes, we believe this is an important topic and it should be referred to NICE for appraisal.	Comments noted. It was agreed at the scoping workshop that an appraisal of golimumab was appropriate.
	British Health Professionals in Rheumatology	Yes.	Comments noted. It was agreed at the scoping workshop that an appraisal of golimumab was appropriate.
	Wyeth Pharmaceuticals	In the event golimumab gains a marketing authorisation for rheumatoid arthritis in the United Kingdom it would be appropriate to refer this topic to NICE. However, as there are already four biologic therapies for the treatment of these patients recommended by NICE, and this product appeas not to offer any incremental health gains, it would be appropriate to include golimumab into the review of TA130.	Comment noted. It was agreed at the scoping workshop that an appraisal of golimumab was urgent.
Wording	RCN	Yes.	Comments noted no action required.
	Schering-Plough	Yes.	Comments noted, no action required.

Section	Consultees	Comments	Action
	British Health Professionals in Rheumatology	Yes.	Comments noted, no action required.
	Wyeth Pharmaceuticals	The remit reflects the decision problem.	Comments noted, no action required.
Timing Issues	RCN	It depends upon the outcome of the current appraisals in process. It is also important to have clarity with where the RA guidelines sit in advising on the treatment pathways for these therapies.	Comment noted. The NICE rheumatoid arthritis guideline will incorporate any relevant technology appraisal guidance published at the time of publication of the clinical guideline.
	Schering-Plough	This topic should be regarded as urgent – **Comercial in confidence information removed.**	Comment noted. Following the final referral from the Department of Health, the appraisal will be planned into the technology appraisal schedule to allow as timely as possible guidance to the NHS.
	British Health Professionals in Rheumatology	It is apporopriate but needs to be into the RA guidelines that are currently in process.	Comment noted. The NICE rheumatoid arthritis guideline will incorporate any relevant technology appraisal guidance published at the time of publication of the clinical guideline.
	Wyeth Pharmaceuticals	As there are already four biologic therapies for the treatment of these patients are recommended by NICE, and the similar profile of golimumab to the already available therapies, the relative urgency of this proposed appraisal is low. It would be appropriate to include golimumab into the review of TA130.	Comment noted. It was agreed at the scoping workshop that an appraisal of golimumab was urgent.

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Additional comments on the draft remit	RCN	Learnings from recent appraisals are vital. The wider co-morbidities and costs attributed need to be thoroughly and adequately considered. Radiological progression of the newer therapies are increasingly showing significant benefits and much be adequately scoped in sense of cost effectiveness (reductions in surgical interventions that don't just rely on hip or knee -but other orthopaedic interventions such as small joint replacements and stabilisation of cervical spine etc and quality of life issues - for example co-morbidities as outlined but also depression related to chronic pain related to poorly managed disease, osteoporosis etc.	Comment noted. It was agreed at the scoping workshop that the appraisal should consider radiological progression as an outcome and if evidence allows the appraisal should consider the costs associated with joint replacement and hospital stays.
	British Health Professionals in Rheumatology	The economic model needs to take into consideration the costs of surgical interventions in a much more meaningful and transparent way.	Comment noted. It was agreed at the scoping workshop that if the evidence allows the appraisal will consider the cost of joint replacement therapy and the costs associated with hospital stays.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	RCN	Accurate.	Comments noted, no actions required.
	Roche	NICE recommendation for TNF inhibitors is mentioned however the recommendation of rituximab for patients who have failed a TNF inhibitor is not mentioned. Roche suggest this should be added to provide a more accurate reflection of current NICE recommended clinical practice.	Comments noted. The scope has been amended accordingly.
	British Health Professionals in Rheumatology	Yes - accurate.	Comments noted, no actions required.
	Wyeth Pharmaceuticals	Accurate.	Comments noted, no actions required.
The technology/ intervention	RCN	Yes.	Comments noted, no actions required.
	Schering-Plough	This section should be amended slightly - while it is correct that golimumab is being developed with both subcutaneous and IV formulations, it should be pointed out that only the subcutaneous formulation is expected to be avialable at launch.	Comments noted. The scope has been amended accordingly.
	British Health Professionals in Rheumatology	Yes.	Comments noted, no actions required.
	Wyeth Pharmaceuticals	Accurate.	Comments noted, no actions required.
Population	RCN	Yes.	Comments noted, no actions required.

Section	Consultees	Comments	Action
	Roche	Appropriate assuming it reflects the population currently included within phase III registration studies.	Comment noted. This technology has been referred to NICE as two separate appraisals. To reflect the population under appraisal, the scope has been amended to state people who have had an inadequate response to DMARDs.
	Schering-Plough	The population should be amended to reflect the expected wording in the SPC which is as follows: • the treatment of active rheumatoid arthritis in adult patients when the response to disease modifying anti rheumatic drug (DMARD) therapy including MTX has been inadequate. • the treatment of active rheumatoid arthritis in adult patients not previously treated with MTX. Golimumab can be used in patients previously treated with one or more TNF inhibitor(s).	Comments noted. This technology has been referred to NICE as two separate appraisals. To reflect the population under appraisal, the scope has been amended to state people who have had an inadequate response to DMARDs.
	British Health Professionals in Rheumatology	Yes.	Comments noted, no actions required.
	Wyeth Pharmaceuticals	Accurate.	Comments noted, no actions required.
Comparators	RCN	Need to be compared against second TNF as well as against first use of TNF in sub groups of patients who failed first TNF due to toxicity and those that failed due to side effects if FAD on sequential use is implemented.	Comment noted. The list of comparators includes TNF inhibitors.
	Roche	Tocilizumab may also be included as it is currently scheduled for NICE review and may potentially have endorsement at time of submission	Comments noted. The scope has been amended accordingly.

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	Schering-Plough	The list of comparators appears accurate. Perhaps rather than distinguishing between biologic and non-biologic options, it would be helpful to indicate that the comparator is likely to be determined according to the line of therapy.	Comment noted. It was agreed at the scoping workshop that the list of comparators was appropriate.
	British Health Professionals in Rheumatology	Compare to Tnf and Rituximab and also when second tnf used prior to Rituximab in the economic modelling.	Comment noted. TNF inhibitors and rituximab are included in the list of comparators.
	Wyeth Pharmaceuticals	Standard treatments currently used in the NHS to treat rheumatoid arthritis are conventional DMARDS, and biological agents.	Comment noted. The scope has been amended accordingly
Outcomes	RCN	This should include radiological progression - e.g. DMARDs versus golimumab Depression, Independence - e.g. particularly meaningful functional benefit to the individual. Self efficacy, reduction in pain and fatigue, well being. Use of healthcare resources (community and specialist) Patient perceived ability to self manage	Comments noted. It was agreed at the scoping workshop that the outcome radiological progression should be included in the scope. It was also agreed at the scoping workshop that depression, independence, self efficacy, self management and well being would be covered by HRQOL.
	Roche	Yes.	Comment noted, no actions required.
	Schering-Plough	List of outcomes should be extended to reflect other outcomes that are available in the trials - including cardiovascular endpoints - MI, stroke and death.	Comment noted. It was agreed at the scoping workshop that the extra-articular manifestations of RA should be included in the scope.

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	Schering-Plough	It would be useful to add some detail to 'adverse events of treatment' by including an example - injection site reactions	Comment noted. It was agreed at the scoping workshop that injection site reaction is adequately covered by the existing outcome adverse events.
	British Health Professionals in Rheumatology	Yes.	Comment noted, no actions required.
	Wyeth Pharmaceuticals	They do.	Comment noted, no actions required.
Economic analysis	RCN	Time horizons should ensure there is sufficient data capture on radiological benefits and reduction in co-morbidities and surgical interventions	Comment noted. The appraisal has been referred as an STA. Therefore the manufacturer will provide the main submission of evidence for the appraisal.
	British Health Professionals in Rheumatology	Ensure data is enough to capture the benfits of the treatment.	Comment noted. The appraisal has been referred as an STA. Therefore the manufacturer will provide the main submission of evidence for the appraisal.
	Wyeth Pharmaceuticals	The description of the economic analysis is appropriate.	Comment noted, no actions required.

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Equality	RCN	It is essential to consider aspects of choice in route of administration and cost effectiveness issues. The cost benefit issues in relation to receiving nursing support whilst receiving treatment include educational, and social psychological support & are an important factor for the patient. In future the benefit of patient centered approach to care needs to be factored in at a point in the delivery of care - it should be integral to these therapies too - and if so benefits of such should also be captured.	Comments noted. The appraisal will be completed in accordance with the NICE guide to the methods of technology appraisal.
	British Health Professionals in Rheumatology	Ensure patient choice as this will promote equality for treatment.	Comment noted. The NICE social value judgements recognise the importance of patient choice, but states that this should not override economic factors.
Other considerations	RCN	Consider the overall benefits of the suggested treatment pathway that is transparent to the patient and health economy. Aspects of the wider social impact are not usually considered but there is an ongoing challenge about how a proactive treatment pathway can enable people to maintain their work and remain independent. Consequences of those who loose work and become 'chronic patients' include; depression, pain, fatigue, poor self esteem and poor self efficacy - with a heavy reliance on healthcare resources particularly primary care - much of the activity data related to these patients in primary care is not captured at present.	Comments noted. The appraisal will be completed in accordance with the NICE guide to the methods of technology appraisal.
	British Health Professionals in Rheumatology	Suggest look at loss of work and impact on patients with RA.	Comments noted. The appraisal will be completed in accordance with the NICE guide to the methods of technology appraisal.

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Questions for consideration	RCN	At present it is difficult to identify the exact patient groups who would benefit from this therapy pending the sequential use of TNFa inhibitors. But likely to be for TNF failures. However there is an increasing need now to have transparency for the patients on what their treatment pathway and their options are in controlling their disease.	Comments noted, no actions required.
	RCN	We are unable to review the specific remit for a Multiple Technology Appraisal versus a STA as could not find any specific documents outlining the basis for MTA versus a STA on the website. The link given only leads to an overview discussion without any detailed explanation.	Comments noted. The appraisal has been referred as an STA.
	Roche	Position driven by licensed indication.	Comment noted, no actions required.
	Schering-Plough	The comparators for golimumab vary according to the position in the pathway of care that is under consideration. Separate phase III data are available for methotrexate naïve patients, patients who have already failed DMARDs including methotrexate, and patients who have previously received treatment with a TNF-α inhibitor. There are therefore several potential places for golimumab in the pathway of care and these should all be considered in the appraisal.	Comments noted. This technology has been referred as two appraisals: one appraising golimumab for the treatment of rheumatoid arthritis after failure of DMARDs and one appraising goimumab for the treatment of rheumatoid arthritis in people who are DMARD naïve.

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	Schering-Plough	Trial analyses will be available that consider the impact of disease severity on outcomes - for example, baseline severity measured by swollen/tender joint counts.	It was agreed at the scoping workshop that the scope should specify that the appraisal should consider subgroups of people based on their baseline disease severity.
	Schering-Plough	The single technology appraisal process would be preferable for this topic as this would ensure guidance is available to the NHS as soon as possible after the technology receives marketing authorisation.	Comment noted. The appraisal has been referred as an STA.
	British Health Professionals in Rheumatology	We can't target patients according to which treatment they will respond to, yet patients need access to treatments to ensure they can continue as normal a life as possible.	Comment noted, no actions required.
	Wyeth Pharmaceuticals	The most appropriate comparators have been included.	Comment noted, no actions required.
Any additional comments on the draft scope	RCN	There is a problem that we do not have a clear patient treatment pathway for patients who have aggressive disease - this plus other appraisals need to be cohesively reviewed and considered to ensure that patients can look positively to a return to normal life that includes social participation and reduced use of healthcare resources with a high level of self management. This cannot be achieved if a short term individual approach to each of these drugs is applied - patients cannot plan their lives and assume their disease will be effectively controlled adding to a continuing life time stressor.	Comment noted. The scope of a technology appraisal is to examine the clinical and cost effectiveness of healthcare technologies. The examination of patient treatment pathways is more appropriately considered as part of a clinical guideline.

Comment 4: Regulatory issues

Section	Consultees	Comments	Action
Remit	Schering-Plough	Yes - however, a more detailed wording has been suggested above with regard to the proposed population for this appraisal.	Comment noted. The remit referred to the Institute is 'to appraise the clinical and cost-effectiveness of golimumab within its licensed indication for the treatment of rheumatoid arthritis after failure of previous disease-modifying antirheumatic drugs'. A separate appraisal has been referred to consider the use of golimumab in people who are DMARD naïve.
Current or proposed marketing authorisation	Schering-Plough	Golimumab does not have marketing authorisation for any indication at the present time Planned indication for the technology: rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis Target date for regulatory submission: **CIC information removed** Regulatory procedure followed: centralised procedure Anticipated date of regulatory approval: **CIC information removed**	Comment noted, no actions required.

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

Abbott Laboratories Ltd
RICE - The Research Institute for the Care of Older People
NHS Quality Improvement Scotland
British Society for Rheumatology
NPHS
Royal Pharmaceutical Society
GlaxoSmithKline