National Institute for Health and Clinical Excellence

Single Technology Appraisal (STA)

Abatacept 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	Abbott Laboratories	Yes, given the existence of NICE guidance for current therapies available for this patient population.	Comment noted. At the scoping workshop it was considered that an appraisal of abatacept was appropriate.
	Bristol Myers Squibb Pharmaceuticals (BMS)	It is appropriate	Comment noted. At the scoping workshop it was considered that an appraisal of abatacept was appropriate.
	British Health Professionals In Rheumatology (BHPR)	Yes although needs to be considered in the context of other appraisals currently underway in relation to RA	Comment noted. This topic has been referred as an STA in order to provide timely guidance to the NHS.
	Commissioning support appraisals service (CSAS)	Consideration should be given to how this TA will fit with review of the TA for abatacept in its current licensed indication (TA141), which is scheduled for 2010. The review of TA141 appears to be part of the MTA in progress for abatacept (within current license) and other biological therapies after failure of a TNF inhibitor, and is due to be published in June 2010. Review of the existing rheumatoid arthritis guidance is expected February 2012.	Comment noted. This topic has been referred as an STA in order to provide timely guidance to the NHS.

Section	Consultees	Comments	Action
	Royal College of Nursing	This is highly appropriate especially the placing of Abatacept at this point in the pathway. Given the hetrogeneous nature of RA, rapid and effective treatment strategies are required at all points of the pathway, therefore it is important to be able to access a range of treatment options.	Comment noted. At the scoping workshop it was considered that an appraisal of abatacept was appropriate.
	Royal College of Physicians	Royal College of Physicians wishes to endorse the comments submitted by the British Society for Rheumatology on this technology	Comment noted. See responses to the British Society for Rheumatology.
Wording	Abbott Laboratories	Yes	Comment noted. However, the wording in the remit has been revised to better reflect the position of abatacept in the treatment pathway.
	BMS	The wording of the remit should be modified to reflect that abatacept is indicated after the failure of 'conventional disease modifying anti-rheumatic drugs (DMARDs)'	Comment noted. The wording in the draft scope has been amended accordingly.
	BHPR	Yes	Comment noted. However, the wording in the remit has been revised to better reflect the position of abatacept in the treatment pathway.
	CSAS	The wording could be adapted to make it clearer how the scope of this TA differs from that of the existing TA of abatacept (TA141), i.e. consider specifying that this treatment is being considered as second-line therapy after inadequate response to methotrexate and other conventional DMARDs, rather than only third-line as per its current license, i.e. after inadequate response to conventional DMARDs and at least one TNF-α inhibitor	Comment noted. The wording in the scope has been amended to reflect the position of abatacept in the treatment pathway.

Section	Consultees	Comments	Action
	Royal College of Nursing	Given the fact that the licensing indication states failure after two DMARDs and includes failure of one TNF inhibitor, should this not be included in the wording? Reasonably - given that NICE does not address the social impact which tends to produce a rather arbitary cost effectiveness that fails to capture the real costs to society and the health economy related to poor disease control.	Comment noted. This appraisal considers the use of abatacept after the failure of conventional DMARDs. Guidance on the use of abatacept after the failure of TNF inhibitors has been issued in technology appraisal 195. Comment noted. The appraisal will be completed in accordance with the published guide to the methods of technology appraisal. This includes a focus on costs to the NHS and PSS.
Timing Issues	BMS	It would be most appropriate to appraise abatacept in conjunction with the review of TA130 as an MTA.	Comment noted. This topic has been referred as an STA in order to provide timely guidance to the NHS.
	BHPR	It is imperative 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.	Comment noted. This topic has been referred as an STA in order to provide timely guidance to the NHS. Other technologies will be considered as comparators in the appraisal.
	CSAS	The license application was expected to be submitted in September 2009, and launch in 2011.	Comment noted. The appraisal will take into consideration the timing of marketing authorisation.
	Royal College of Nursing	It is important but may have a higher priority if the current appraisal on sequential use fails to allow use of a second TNF inhbitor.	Comment noted. At the scoping workshop it was considered that an appraisal of abatacept was appropriate. This topic has been referred as an STA in order to provide timely guidance to the NHS.

Section	Consultees	Comments	Action
Additional comments on the draft remit	British Society for Rheumatology	We would prefer to see a re appraisal of the clinical and cost effectiveness of Abatacept after failure of DMARDs and anti-TNF therapies. This drug has un-disputed clinical effectiveness and a very favourable toxicity profile (for example with Tocilizumab). As such, the ability to use it in RA patients who fail to respond to DMARDs and anti-TNF drugs would be welcomed.	Comment noted. A review of this guidance was published in August 2010 as technology appraisal 195.
	CSAS	None	Comment noted. No actions required.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	Abbott Laboratories	no comments to add	Comment noted. No actions required.
	BMS	It is accurate.	Comment noted. No actions required.
	BHPR	nil	Comment noted. No actions required.
	British Society for Rheumatology	In this section in paragraph 2, it is stated that RA has a peak age of onset of 70 years. This is not correct, the peak age of incidence is around 55 years. Many individuals between 20 and 60 are affected producing major effects on work, caring, childcare etc. This is an important fact, because it means that RA has the potential to prevent affected individuals from working, and in reality over a third give up their employment because of the RA within 3 years of diagnosis (source ERAN UK cohort 2002 - 2009). This implies that there is a potential to minimise societal cost by preventing work - loss with the use of effective treatments. If DMARD/anti-TNF approaches are unsuccessful then another biologic that can adequately control inflammation and maintain function (including work productivity) is very attractive. In addition, the majority of patients have continuous unremitting disease, not the "flares" separated by low disease activity suggested.	Comment noted. The information in the draft scope has been amended accordingly to accurately reflect the nature of the disease, the population and the age of onset.
	CSAS	This information appears appropriate	Comment noted. No actions required.

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	Royal College of Nursing	The wording below should be changed: 'Rheumatoid arthritis is usually a chronic relapsing condition with flare-ups followed by periods of lower disease activity, but may be constantly progressive in some people.' We would suggest: 'Rheumatoid Arthritis is usually a chronic relapsing condition with flare ups and may then be followed by times where the symptoms of the disease are controlled more effectively. We do not know that the disease is less active in the sense of joint damage and background 'usual level of symptoms' are then coped with. A flare up is when the disease is poorly controlled despite usual attempts to manage the underlying inflammation.'	Comment noted. The information in the scope has been amended to more accurately reflect the nature of the disease.
The technology/ intervention	Abbott Laboratories	yes	Comment noted. However, the scope has been amended to reflect the information in the marketing authorisation.
	BMS	It is accurate.	Comment noted. However, the scope has been amended to reflect the information in the marketing authorisation.
	BHPR	nil	Comment noted. No actions required.
	British Society for Rheumatology	Generally Yes. However, it is important to mention that the therapy has a unique mechanism of action not shared with any other DMARDs or biologcal therapies.	Comment noted. Full information on the mechanism of the technology will be considered in the appraisal. The unique mechanism of action has been recorded in the other considerations section of the scope as an innovative feature of the technology.

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	CSAS	The description of the technology appears accurate. Although abatacept is currently delivered by intravenous infusion, trials of subcutaneous abatacept are ongoing. The scope could clarify whether subcutaneous abatacept will be included in the appraisal	Comment noted. Mode of administration will be considered in accordance with the marketing authorisation.
	Royal College of Nursing	Yes	Comment noted. However, the scope has been amended to reflect the information that is in the marketing authorisation.
Population	Abbott Laboratories	Yes, subgroups will be partly dependent on the anticipated licence wording for the target population	Comment noted. The scope has been amended to include subgroups based on severity of disease activity and antibody status if evidence allows.
	BMS	No comment	Comment noted. No actions required.
	BHPR	nil	Comment noted. No actions required.
	CSAS	Those who have received differing numbers of DMARD treatments, or those who have received different DMARDs could be considered separately	Comment noted. It was agreed at the scoping workshop that stratifying subgroups by number of DMARDs received would not be feasible. However, the scope has been amended to include subgroups based on severity of disease activity and antibody status.
	Royal College of Nursing	The NAO figures should be referred to within this discussion - 580,000 adults The peak age of incidence in the UK - we would again query the evidence for 70 years. Refer to NAO report & ARC assessment of health needs document	Comment noted. The background information in the scope has been amended accordingly.

Section	Consultees	Comments	Action
Comparators	BMS	Rituximab does not currently has a marketing authorisation for this indication. Furthermore, it should not be included as a comparator, as it has been shown to have a limited therapeutic benefit in patients with sero-negative rheumatoid arthritis. The comparator in the economic evaluation should be conventional DMARDs. Methotrexate should not be included as a comparator as patients have already failed on this therapy to become eligible for biological therapies. Currently tocilizumab is undergoing an appraisail with a possibility of a negative recommendation. If there is a negative recommendation it should not be included in this proposed appraisal.	Comment noted. At the scoping workshop it was discussed whether or not rituximab should be included as comparator in this STA. However, as rituximab has not yet received a marketing authorisation for this indication it cannot be considered standard care at the stage at which the evidence submission is provided, and can therefore not be a comparator in this STA. At the scoping workshop it was considered that methotrexate should be included as comparator. However, the marketing authorisation for abatacept states that it should be used after failure of methotrexate. Methotrexate has therefore not been included in the scope as a comparator. At the scoping workshop it was considered that tocilizumab should be considered a comparator subject to the outcome of the ongoing appraisal. TA198 recommends the use of tocilizumab after the failure of TNF inhibitors. This appraisal considers the use of abatacept only after the failure of conventional DMARDs. Tocilizumab has not therefore been included as a comparator in this scope.

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	BHPR	Not clear why the comparator does not mention methotrexate but presume it will include methotrexate.	Comment noted. The marketing authorisation for abatacept states that it should be used after failure of methotrexate. Methotrexate has therefore not been included in the scope as a comparator.
	British Society for Rheumatology	Yes	Comment noted. No actions required.
	CSAS	Some of the treatments suggested as comparators have not yet been licensed for this indication in the UK, and are therefore unlikely to be in use (e.g. golimumab). The relevance of some other comparators is likely to be dependent on the outcome of ongoing NICE appraisals (e.g. tocilizumab). Guidance on certolizumab pegol has now been issued. Existing NICE guidance and licensing indications for rituximab do not currently cover the indication in which abatacept is being assessed, although extension of rituximab to this indication may be being applied for as its use in this indication is being assessed in an ongoing TA.	Comment noted. The appraisal will take into consideration the outcome of relevant technology appraisals.
	Royal College of Nursing	Yes. Methotrexate at a resonable dose, is considered best alternative care against the DMARDs outlined.	Comment noted. The marketing authorisation for abatacept states that it should be used after failure of methotrexate. Methotrexate has therefore not been included in the scope as a comparator.
Outcomes	BMS	No comment	Comment noted. No actions required.

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	BHPR	What about work related issues?	The appraisal will be completed in accordance with the published guide to the methods of technology appraisal. This includes a focus on health related quality of life, and includes for example ability to carry out normal activities.
	British Society for Rheumatology	Amongst outcomes we would suggest thaat the measure of disease activity to be used should be attainment of "low DAS" - i.e. DAS <3.2. We would suggest that work productivity and the summary mental and physical domains of SF-36 be included. Depression (specific scores and SF36) and work related outcomes should also be considered.	Comment noted. Consultees considered that components of DAS would be addressed under disease activity. Components of SF-36 would also be addressed under health related quality of life.
	CSAS	The outcomes appear appropriate. Response or remission could be added (e.g. according to American College of Rheumatology [ACR] or European League Against Rheumatism [EULAR] criteria) as this outcome is often used in clinical trials. Disease activity should be assessed according to a validated composite disease score, e.g. DAS28	Comment noted. Consultees considered that EULAR response and DAS28 could be considered as part of disease activity measures.
	Royal College of Nursing	In the context of what NICE can currently appraise - yes. However, costs related to societal impact are not included and as a result will fail to truly capture the real impact of this disease and potential benefits of improved outcomes to society and health economy	Comment noted. The appraisal will be completed in accordance with the published guide to the methods of technology appraisal. This includes NHS and PSS costs.
Economic analysis	BMS	No comment	Comment noted. No actions required.
	BHPR	Please consider referring to analyses undertaken by the National Audit Office (RA, 2009) - to explore the wider ramifications of poorly controlled disease	Comment noted. The appraisal will consider all evidence submitted by consultees.

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	British Society for Rheumatology	Information will be most readily available for 1 year and 2 years. However, effects over 5+ years should be considered where possible in the setting of a lifelong disease.	Comment noted. The time horizon will address the natural history of the disease. For a chronic disease is this usually life time.
	CSAS	None	Comment noted. No actions required.
	Royal College of Nursing	As this STA will be considering DMARD failures, it is a very important time to consider Abatacept	Comment noted. No actions required.
Equality and Diversity	BMS	No comment	Comment noted. No actions required.
	CSAS	None	Comment noted. No actions required.
	Royal College of Nursing	There are no specific ones in relation to this therapy	Comment noted. No actions required.
Kennedy Report Question – Innovation	BHPR	Patient oriented outcomes should be considered together with indirect healthcare benefits including QoL, return to work and reduction in social care costs.	Comment noted. Factors affecting innovation are those that relate specifically to the technology being considered and not to other technologies currently available. At the scoping workshop it was highlighted that abatacept had a different mechanism of action of the other biologics and that this should be considered innovative.

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	Royal College of Nursing	It will be particularly relevant looking at Abatacept data that the time frames of outcomes are extended compared to usual data as improvements continue to develop over a two year period. Clinical outcomes should also include ability to continue normal valued quality of life factors (e.g. reduction in depression, self efficacy and time taken to undertake tasks). Reduction in surgery or risks related to other co-moribidities directly related to the disease (e.g. Cardiovascular disease) and reduction in the use of drugs such as steroids and NSAIDs. Important to consider the reversible and irreversible aspects of the HAQ. Early HAQ changes may be reversible. (see SmolenJ paper 2010) Ann Rheum Disease in Press. The data available to enable the appraisal committee to take account of the above benefits include: Evidence published as posters and oral presentations in Europe/USA where experience with Abatacept has been greater. Dougasdos M (2009) 68; 484-489 Ann Rheum Disease.	Factors affecting innovation are those that relate specifically to the technology being considered and not to other technologies currently available. At the scoping workshop it was highlighted that abatacept had a different mechanism of action of the other biologics and that this should be considered innovative.
Other considerations	BMS	No comment	Comment noted. No actions required.
	CSAS	None	Comment noted. No actions required.
	Royal College of Nursing	Prompt and rapid access to DMARD therapies - long term benefits need to be considered in the sense of proactive management. Cost effective data often fails to capture the long term outcomes/data. These need to be considered in terms of avoiding joint surgery, periods of hospitalisation, reduction in need for on-going flare management and requests for further GP appointments/treatment changes. The benefits of treatment in reducing the incidence / treatment of co morbid conditons i.e Cardiovascular disease, should also be considered.	Comment noted. The cost effectiveness analysis will address the natural history of the disease and capture the relevant costs associated with management of rheumatoid arthritis. The other considerations section of the scope includes reference to the inclusion of the costs of joint replacement and hospitalisation.

Section	Consultees	Comments	Action
Questions for consultation	Abbott Laboratories	It is important that there is consistency between the comparators, outcomes and economic analysis used in this proposed appraisal and those considered in the appraisal of adalimumab, etanercept and infliximab, as used in TA130 or any subsequent review of the guidance for adalimumab, etanercept and infliximab in the DMARD failure population.	Comment noted. The appraisal will take into consideration comparators and outcomes used in other similar appraisals.
	BMS	Subpopulations: Severe RA, moderate to severe RA, RF negative and positive patients. It would be most approriate to appraise abatacept in an MTA in conjunction with the review of TA130.	Comment noted. The scope has been amended to consider subgroups based on severity of disease activity and antibody status if evidence allows. Comment noted. This topic has been referred as an STA in order to provide timely guidance to the NHS.
	BHPR	nil	Comment noted. No actions required.
	British Society for Rheumatology	1. Yes, the principle comparators should be other DMARDs (mono and combination with and without steroid), ant-TNF therapies with MTX, Rituximab with MTX and Tocilizumab with MTX. 2. No 3. No 4. Not sure	Comment noted. These technologies have been included in the scope as comparators. In relation to the other comments, no actions required.
	CSAS	None	Comment noted. No actions required.
	CSAS	None	Comment noted. No actions required.

Section	Consultees	Comments	Action
Additional comments on the draft scope.	British Society for Rheumatology	The key for rheumatologists and patients is to have access to abatacept for individuals who have failed standard anti-TNF therapy. In the future we may be able to specifically target correct therapy to the correct patient. However, this is difficult at present. There are also concerns regarding the side-effect profiles of other biological therapies that makes the availability of a therapy with a different mechanism of action vital.	Comment noted. A review of this guidance was published in August 2010 as technology appraisal 195.
	CSAS	None	Comment noted. No actions required.
	Roche Products	Rituximab has been referred by the Department of Health and will undergo a STA for the treatment of rheumatoid arthritis after the failure of disease modifying anti-rheumatic drugs. The expected licence will not include patients that are methotrexate naive.	Comments noted. The scope has been updated to reflect the remit referred by the Department of Health.
	Royal College of Nursing	no	Comment noted. No actions required.

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

GlaxoSmithKline
British Pain Society
Department of Health
Pfizer
NHS Quality Improvement Scotland
Public Health Wales NHS Trust
RICE - Research Institute for the Care of Older People
Royal College Of Pathologists
sanofi-aventis
Welsh Assembly Government