NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Single Technology Appraisal

Daclizumab for treating relapsing-remitting multiple sclerosis [ID827]

Consultee and commentator comment form

Please use this form for submitting your comments on the draft remit, draft scope and provisional matrix of consultees and commentators. It is important that you complete and return this form even if you have no comments otherwise we may chase you for a response.

Enter the name of your organisation here: MS Trust

Comments on the draft remit and draft scope

The draft remit is the brief for a proposed appraisal. Appendix B contains the draft remit. The draft scope, developed from the draft remit outlines the question that the proposed appraisal would answer.

Please submit your comments on the draft remit and draft scope using the table below. **Please take note of any questions that have been highlighted in the draft scope itself** (usually found at the end of the document).

If you have been asked to comment on documents for more than one proposed appraisal, please use a separate comment form for each topic, even if the issues are similar.

Please complete this form and upload it to NICE Docs by Wednesday 24 June 2015. If using NICE docs is not possible please return via email to scopingta@nice.org.uk If you have any questions please contact Michelle Adhemar, Project Manager on 44 (0)20 7045 2239 or at the email address above.

If you do not have any comments to make on the draft remit and draft scope, please state this in the box below.

Comment 1: the draft remit

Section	*Notes*	Your comments
Appropriateness	*It is important that appropriate topics are referred to NICE to ensure that NICE guidance is relevant, timely and addresses priority issues, which will help improve the health of the population. Would it be appropriate to refer this topic to NICE for appraisal?*	Yes, we think this is an appropriate referral though we highlight that a license for daclizumab has yet to be granted by the EMA and so timing of the NICE Technology Appraisal will need to be aligned with the expected timeline from the regulator.
Wording	*Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that*	yes

Section	*Notes*	Your comments
	NICE should consider? If not, please suggest alternative wording.	
Timing Issues	*What is the relative urgency of this proposed appraisal to the NHS?*	As noted above, there is potentially a timing constraint as daclizumab currently does not have market authorisation.
Any additional comments on the draft remit		

Comment 2: the draft scope

Section	*Notes*	Your comments
Background information	*Consider the accuracy and completeness of this information.*	The final paragraph of the background section which describes current pharmacological management of RRMS fails to mention either TA254 (fingolimod) or TA127 (natalizumab). For completeness, these should both be added
The technology/ intervention	*Is the description of the technology or technologies accurate?*	yes
Population	*Is the population defined appropriately? Are there groups within this population that should be considered separately?*	yes, the population is defined correctly, subject to the marketing authorisation, if granted.
Comparators	*Is this (are these) the standard treatment(s) currently used in the NHS with which the technology should be compared? Can this (one of these) be described as 'best alternative care'?*	Yes, the comparators listed represent standard treatment for RRMS in the UK NHS. We would highlight however the no one drug or series of drugs can be described as best alternative care. Choice of DMD is made in partnership between prescribing neurologist and the person living with MS. Treatment selection is increasingly personalised, reflecting clinical and sub-clinical disease activity and any issues regarding drug tolerance as well as patient risk attitudes and their view about the balance of risk, benefit and commitment regarding treatment and monitoring.
Outcomes	*Will these outcome measures capture the most important health related benefits (and harms) of the technology?*	Yes, we agree that these outcome measures capture the most important health benefits, though we highlight the following issues which we believe will need further clarification early in the technology appraisal process: Symptoms - instrument selection for outcome measurement for symptoms such as fatigue and cognition in MS is still an evolving area. Multiple instruments are currently in use

Section	*Notes*	Your comments
		across clinical trials in MS and it will be important to critically consider instrument selection as well as the results they demonstrate in the data submitted. Freedom from disease activity is also an evolving concept in MS and there is not yet a fully settled definition of the term, particularly with respect to the critical measures of sub-clinical disease activity. Some definitions include measurement of total brain volume (TBV) in addition to presence of brain lesions on MRI scans. To be useful in the clinical setting, the exact detail of the outcome measure needs further clarification and definition to guide prescribing and to help people living with MS understand the goals of treatment and help them in making their treatment choices. This may be best facilitated by separating out the measures aggregated in the concept of freedom from disease activity. For instance, number of lesions on MRI scans, as the prime sub-clinical measure may be best treated as a separate measure. The MS Trust supports greater attention to clinical and sub-clinical measures of disease activity in RRMS to inform treatment strategies and a more proactive approach to initiating treament with a DMD early and an escalation strategy if evidence of disease activity is present on current treatment.
Economic analysis	*Comments on aspects such as the appropriate time horizon.*	The draft scope states that costs will be considered from an NHS and Personal Social Services perspective.With more examples of integrated health and social care budgets, economic cases based on a distinction between the two cost domains are less relevant for commissioners and payers. There is greater scope for recognising that costs avoided in social care should be included in analysis of a healthcare intervention. For MS, the impact of reducing the frequency and severity of relapses can have on work presenteeism is also significant, delivering individual and societal benefit that are not taken into account in current economic analyses by NICE.
Equality	*NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics*	no equality issues to highlight

Section	*Notes*	Your comments
	and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope: • *could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;* • *could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;* • *could have any adverse impact on people with a particular disability or disabilities.* *Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.*	
Other considerations	*Suggestions for additional issues to be covered by the proposed appraisal are welcome.*	For completeness, the list of sub-groups should include • patients with previously untreated relapsing-remitting multiple sclerosis We wish to highlight the issue of treatment sequencing. Over specifying sequencing has created perverse 'snakes and ladders' in the use of the current formulary which has in turn created problems for prescribers and patients alike. Within the constraints of any marketing authorisation, we would caution against creating further blockages or impediments to access to any licensed treatments.
Innovation	*Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?* *Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?* *Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these*	Yes, dacluzimab potentially offers greater efficacy than current self-injected agents, appears to be generally well-tolerated by patients (though we note that some patients have had some significant skin reactions to the drug) and its monthly dosing schedule would represent a signicant change from the dosing schedules of all current self-administered DMTs, including the oral agents. As we understand it, the monitoring requirements on initiation and on an ongoing basis would not exceed those required to routinely monitor disease activity, clinical and

Section	*Notes*	Your comments
	benefits.	sub-clinical. Thus, total costs for administration and monitoring, excluding drug costs and initial patient training, would potentially not exceed standard service costs.
Questions for consultation	*Please answer any of the questions for consultation if not covered in the above sections. If appropriate, please include comments on the proposed process this appraisal will follow (please note any changes made to the process are likely to result in changes to the planned time lines).*	Regarding the fit with the NICE pathway for multiple sclerosis, we wish to highlight the point made earlier in the section on comparators. Disease modifying treatment of multiple sclerosis is managed in partnership between the prescribing neurologist and the person living with MS. Many of the sub-groups defined by the regulator and then reflected on in previous technnology appraisals do not match well with the realities of prescribing in the real world clinical setting. In this context prescribing neurologists, supported by MS specialist nurses are assessing disease activity and its impact on the person living with the condition. The person with MS must make their unique nd vital contribution to treatment selection, being able to reflect their attitude to risk, their commitment to longterm administration and monitoring regimes and their personal goals regarding their life with MS.
Any additional comments on the draft scope Related national policy should include the revised (2015) prescribing guidelines for disease modifying therapy from the Association of British Neurologists - we would highlight a change in the treatment paradigm for RRMS, emphasising the importance of early treatment. This is reflected in the revised ABN guideline and has implications for the eligibility criteria for starting disease modifying treatment that currently apply.		

Comment 3: provisional matrix of consultees and commentators

The provisional matrix of consultees and commentators (Appendix C) is a list of organisations that we have identified as being appropriate to participate in this proposed appraisal. If you have any comments on this list, please submit them in the box below.

As NICE is committed to promoting equality and eliminating unlawful discrimination Please let us know if we have missed any important organisations from the lists contained within the matrix, and which organisations we should include that have a particular focus on relevant equality issues.

If you do not have any comments to make on the provisional matrix of consultees and commentators, please cross this box: ☐

Comments on the provisional matrix of consultees and commentators

Comment 4: regulatory issues (to be completed by the company that holds the markets the technology)

Section	*Notes*	Your comments
Remit	*Does the wording of the remit reflect the current or proposed marketing authorisation? If not, please suggest alternative wording.*	
Current or proposed marketing authorisation	*What are the current indications for the technology?*	
	What are the planned indications for the technology?	
	FOR EACH PLANNED INDICATION:	
	Which regulatory process are you following?	
	What is the target date (mm/yyyy) for regulatory submission?	
	What is the anticipated date (mm/yyyy) of CHMP positive opinion (if applicable)	
	What is the anticipated date (mm/yyyy) of regulatory approval?	
	What is the anticipated date (mm/yyyy) of UK launch?	
	Please indicate whether the information you provide concerning the proposed marketing authorisation is in the public domain and if not when it can be released. All commercial in confidence information must be highlighted and underlined.	
Economic model software	*NICE accepts executable economic models using standard software, that is, Excel , DATA, R or WinBUGs. Please indicate which software will be used. If you plan to submit a model in a non-standard package, NICE, in association with the ERG, will investigate whether the requested software is acceptable, and establish if you need to provide NICE and the ERG with temporary licences for the non –standard software for the duration of the appraisal. NICE reserves the right to reject economic models in non-standard software*	

Please complete this form and upload it to NICE Docs by Wednesday 24 June 2015. If using NICE docs is not possible please return via email to scopingta@nice.org.uk If you have any questions please contact Michelle Adhemar, Project Manager on 44 (0)20 7045 2239 or at above the email address.