Healthcare professional group/clinical specialist statement

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name:

Name of your organisation (if applicable): Association of British Neurologists

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? YES
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? YES
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?
- other? (please specify)

Professor of Clinical Neurology, Institute of Neurology, University College London
Honorary Consultant Neurologist, National Hospital for Neurology & Neurosurgery, University College London Hospitals Trust

What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS?. Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

The licensed disease modifying treatments – beta interferon and glatiramer acetate – are currently used to treat patients with clinically active relapsing MS according to the 2001 Association of British Neurologists (ABN) guidelines and through the Department of Health Risk Sharing Scheme. These agents reduce relapse rate by one third; it is unclear what effect they have on the long term course of MS. The main limitation of these therapies is their modest efficacy: many patients will continue to experience relapses and/or develop disability. I am not aware of major geographical variations in practice. There is, however, a considerable range of views amongst neurologists as to how effective these treatments are and who should be treated.

Natalizumab is more effective in suppressing relapses – by two thirds. It has a risk for progressive multifocal leucoencephalopathy that is estimated at 1 per 1000 after 18 months of treatment. In my view, natalizumab would be most appropriately used to treat patients with frequent and severe (disabling) relapses and an active MRI scan (showing new and/or enhancing lesions), especially if these occur in spite of treatment with beta interferon or glatiramer acetate. Currently, such patients are sometimes treated with mitoxantrone or Campath-1H, but neither of these therapies is licensed and both can have significant adverse effects.

Natalizumab is given by intravenous administration once per month. It should be provided by an experienced MS service at a regional neuroscience centre; the MS team should include a consultant neurologist and MS nurse.

As far as I know, natalizumab is not being used in the NHS, as funding is unlikely to be provided prior to the NICE review.

The ABN is developing a comprehensive guideline for the treatment of relapsing MS with natalizumab

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

Most of these questions will be addressed in the forthcoming ABN guidelines, which will consider the evidence, recommend starting and stopping criteria and give practical advice on delivery of treatment and patient monitoring while being treated.

The phase 3 natalizumab trials studied patients with relapsing remitting MS who are relevant to UK clinical practice. The trials showed clear efficacy on appropriate relapse and disability endpoints and on MRI lesion activity. The risk of hypersensitivity reactions (~4%) including anaphylaxis (~1%) mandate that treatment is provided in a clinic or ward setting with full resuscitation facilities to hand. Because of the risk of progressive multifocal leucoencephalopathy (estimated 1 per 1000 after 18 months treatment), it is appropriate to focus treatment for those who have the greatest benefit-to-risk ratio, i.e. patients who have frequent and severe (disabling) relapses and an active MRI scan, particularly when beta interferon or glatiramer acetate is not effective.

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

It should be provided by an experienced MS service, probably in a limited number of centres.

Already well established MS services – some having developed since the Risk Sharing Scheme started – should be able to accommodate natalizumab treatment for a subgroup of patients with frequent and severe relapses. An infusion suite and some additional staff support (e.g. nurse) may be required in some centres.