NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Botulinum toxin type A for the prophylaxis of headaches associated with chronic migraine

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:
[redacted] **is submitting the Statement on behalf of the Organisation; The British Association for the Study of Headache**

Name of your organisation:
British Association for the Study of Headache

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.)? Yes
- other? (please specify)

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

How the condition is 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.

Chronic Migraine (CM) is the most disabling form of the disorder with a prevalence of 1.5 – 3 % in the general population. The International Headache Society (IHS) defines the disorder as headaches on 15 or more days of which at least 8 or more days are with migraine headaches for at least three months. The current definition excludes patients with medication overuse, although a significant number of patients with CM (50-80%) overuse acute medications. As to when one should address medication overuse: prior to or contemporaneous with starting a preventive, remains a topic for discussion. However, such patients represent what is seen in real life practice and hence these patients were included in clinical trials for CM. Preventive treatments used for episodic migraine that have been used for CM include beta-blockers, tricyclic antidepressants and anti-convulsants. However, Topiramate is the only agent with published evidence of efficacy and although it is useful in some patients, the side effects of cognitive dysfunction, paraesthesia and teratogenecity limits its use in young females that comprise a large proportion of CM patients. There is little difference in the choice of preventive treatments in different headache and neurology centres in the UK. If patients fail to respond to these agents the alternatives including drugs such as sodium valproate, methysergide, are associated with a range of side effects including significant weight gain, drowsiness and with methysergide monitoring in secondary care. Another alternative is greater occipital nerve (GON) block with local anaesthetic and or corticosteroid for which there is response in one third of the patients and the treatment is required every two to three months. Subsequently, some patients are referred for consideration for an Occipital Nerve Stimulator (ONS) which is an invasive and fairly expensive option currently only done at the National Hospital, London. It could be argued that patients with

significant medication overuse may be classed as a different sub-group of CM patients where medication overuse needs to be addressed at the same time.
The treatment with Botulinum Toxin type A (Botox) is new and requires injections to different head and neck muscles; it is important that such treatment is received by those who benefit most and is given by those who have expertise in the diagnosis and management of headache disorders. It should, therefore, be restricted to secondary care headache clinics, although the treatment may be given by the headache specialist nurses once the diagnosis is confirmed and the suitability of treatment is ascertained by the physician. The treatment is given in the normal out-patient setting and takes no longer than 30 minutes to administer. The British Association for the Study of Headache has advocated for the use of Botulinum Toxin type A in patients within the licensed indication in those who failed to improve with at least three classes of preventive treatments currently available. This is based on the fact that alternatives would be more expensive and invasive, and medically refractory CM patients should be given the choice of a licensed and less expensive treatment with relatively few adverse events.

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?

The treatment with Botulinum Toxin Type A (Botox) will be considered in those that have failed the first line treatments. The treatment will be available, given and monitored locally that would prevent referral to centres in London, or elsewhere, for alternative treatments. The technique is relatively straightforward in its use by a trained headache specialist, and will not require additional equipment or personnel.

The follow ups can be conducted through telephone consultations. The treatment is well tolerated in comparison to some of the current oral treatment and with a reduction in acute treatments will have a positive impact on QoL.

The organisation has endorsed that suitably identified patients be given at least two cycles of treatment three months apart and those who fail to respond should not receive the third cycle. There is lack of data beyond one year and hence those who respond may be given five cycles of treatment in the first instance.

The clinical trial included patients with CM with and without medication overuse and reflect what is seen in real clinical practice. The results were statistically significant with reduction of two days of headache in the active group. This average decrease masks the clinically very important groups of responders with 47% of patients having a fifty per cent or greater reduction in headache days, and 23% of patients having a seventy-five per cent or greater reduction; this should be compared to a 38% fifty per cent response for topiramate in chronic migraine.

The impact of treatment should be measured as outlined in the final scoping document in addition to a global view of the patients' own assessment of perceived improvement in QoL.

The adverse events are fairly mild and restricted locally to site of injections. Systemic side effects are rare. The treatment is well tolerated compared to some of the existing oral treatments.

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.

None

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.

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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)?

Botox is currently given in various NHS hospitals by Neurologists for dystonia, spasticity; by Dermatologists and Plastic Surgeons for hyperhidrosis and cosmetic reason; by General Surgeon for anal fissure; by ENT surgeons for laryngeal dystonia; by Ophthalmologists for strabismus and by Urologist for neurogenic bladder. The drug is available in virtually every hospital. The drug is payment by result excluded and hence the main cost of the treatment will be the drug itself. Various headache centres who participated in phase II and III trials over the last ten years are already trained in the technique. Since licensing, the manufacturers have organised sessions to train additional physicians and specialist nurses interested in headaches. A number of headache physicians are already providing this treatment in the private sector to people who are self-funded and those that are approved by the Exceptional treatment panel of the Primary Care Trust. If recommended by NICE the treatment will be available in the existing headache centres. The most important issue is to get the right diagnosis and evaluate the suitability of a patient that benefits most from this treatment. No particular equipment or facility will be needed. The lead physician in the centre will be training the Specialist registrars and most of the new treatment will be absorbed in the existing services.

Equality

Are there any issues that require special attention in light of the NICE's duties to have due regard to the need to eliminate unlawful discrimination and promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others?

No issues