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:
Fayyaz Ahmed

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 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 clinical community agrees that patients with more headache days than without them are classed as Chronic Daily Headaches. Those with more than 8 days of migraine headaches are defined as a separate category and the International Headache Society (IHS) has given the name of 'Chronic Migraine' (CM) to these patients. A large proportion of CM patients overuse painkillers as defined by the IHS and it remains unclear whether this is the cause or outcome of CM. IHS in their definition excludes such patients from their definition of CM. In actual practice it is difficult to identify many patients with CM who do not overuse painkillers. There is consensus that patients with CM should be treated with prophylactic agents such as beta-blockers, tricyclic antidepressants and anticonvulsants, although there is very little published evidence in the literature for their efficacy in CM compared to episodic migraine patients. Topiramate has the best evidence but the side effects of cognitive dysfunction, paraesthesia, weight loss and interaction with the contraceptive pills limits its use in young females which comprise a large chunk of CM patients. Those who fail on these agents are given the choice of sodium valproate, methysergide, pizotifen; all have significant side effect profile and given alternative choice, not many patients would like to take these drugs. Methysergide is prescribed only in secondary care due to the required monitoring for renal and liver function and the long term side effect of retroperitoneal and cardiac valve fibrosis. Greater occipital nerve block with local anaesthetic with or without corticosteroids provides only a temporary relief in less than a third of patient and its long term use is associated with

local side effects of cutaneous atrophy and localised baldness. The use of Occipital Nerve Stimulator (ONS) is expensive and is in an early stage for its use in CM patients as most of the experience is in patients with Cluster Headache and other Trigeminal Autonomic Cephalalgias. Treatment of medication overuse often leaves patients with disabling migraine per se and a simultaneous need for preventive treatment is used by most of the headache experts in CM.
Treatment of CM with Botulinum Toxin type A (Botox) brings an alternative prophylactic option for intractable migraine sufferers who fail to respond to the first line agents. Although it involves injections in different head and neck muscles, the procedure is simple, well tolerated and side effects, if any, are purely local and transient. The treatment is out-patient based and does not take longer than an ordinary headache consultation. As studies in undefined chronic daily headaches, episodic migraine and other headache types with Botulinum Toxin Type A (Botox) have been negative, it is extremely important that the treatment be given to the right patient and accurate diagnosis of CM by a physician with interest and experience in headache patients is mandatory. The treatment with Botulinum Toxin Type A (Botox) is, therefore, restricted to dedicated headache clinics and given by those who have received training in this procedure. The treatment can be given by the specialist nurses and specialist registrars can also deliver this treatment under supervision.
The treatment should be given within the licensed indication to those who failed to improve with at least three classes of prophylactic medications.

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?

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The treatment with Botulinum Toxin Type A (Botox) is currently given in the private sector to those who are self funded or given approval through individual funding request via exceptional treatment panel of the primary care trusts (PCT). The patients have had tried the first line agents and remain unresponsive; patients prefer to receive Botox than sodium valproate, methysergide and the greater occipital nerve block. It is a much preferred option than referral to the National Hospital for Nervous Diseases for ONS both in terms of cost and the invasive nature of treatment.
The treatment with Botulinum Toxin Type A (Botox) can be delivered within existing resources and require no additional equipment considering that the drug is excluded from payment by result (PbR).
I have been injecting Botox for intractable CM patients who failed 3-4 prophylactic agents. Since the license was granted by the MHRA, I have injected 72 patients with 45 showing a good response with 50% or more reduction on either the headache or migraine days or the severity of the attacks. Some patients had a remarkable response with more than 75% reduction in headache days. Those who do not respond to two cycles of injection are not given further treatment cycles. In my experience most patients show an incremental response with subsequent treatment cycle and I envisage that at least 5 cycles of treatment be allowed based on the published data (PREEMPT) as the need for long term therapy remains unknown. A considerable proportion of patients with migraine require 12-18 months of oral prophylactic agents which may well be the case with treatment with Botulinum Toxin Type A (Botox).
Patients with medication overuse should be regarded as a sub-type of CM as pure medication overuse is rarely seen. In actual clinical practice preventive treatment is offered to most of these patients irrespective of medication overuse and the patients included in the clinical trial reflect what is seen in real life. The outcome of treatment should also include patients' own assessment of Quality of Life in addition to the diary data on headache/migraine days, severity of attacks and the consumption of oral or other painkillers.
In my experience I have yet to see any systemic side effects of the treatment. Pain and discomfort on the injection site and mild weakness of the neck muscles with temporary exacerbation of headache is seen in some patients. There are risks of ptosis and double vision although the dose injected in the forehead muscles is small enough to cause such effects. Patients preferred the side effects of Botox compared to what they experienced with some of the 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.

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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)?

The injection technique is simple and quick to learn and teach. There are neurologists with expertise in delivering such treatment for other neurological disorders such as dystonia, spasticiy, hyperhidrosis etc. Those with interest in headache have been involved in clinical trials and to my knowledge; most of the headache physicians have already received training to this procedure. No additional equipment is required although if recommended by NICE, the centres may need additional headache specialist nurses to administer the treatment. Patients are usually followed by on the telephone with the migraine diary posted before the consultation to assess the response. Physical attendance for follow up is rarely necessary as no examination is required on these patients.