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]

Name of your organisation ; Migraine in Primary Care Advisors

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? Yes. Used Botox in Migraine for >10 years . 700+ treatments given. National trainer for use of Botox in CM
- 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.)? [redacted]
- other?.

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

How is the condition currently treated in the NHS?
There are no licensed drugs apart from Botox however antidepressants, antiepileptics and other drugs are used prophylactically. Avoidance of caffeine and analgesia is a key part of management
Is there significant geographical variation in current practice?
There are very few tertiary Headache clinics and they are spread across the UK. Most patients are referred within the secondary care framework to Neurology.
There are even fewer intermediate care options.
Most sufferers are not referred but managed by their own GP.
Are there differences of opinion between professionals as to what current practice should be?
Some feel services should be concentrated within Regional centres. Although this is a valuable resource all Neurologists and primary care professionals would benefit from a heightened skill level in headache.
What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?
Drug approaches are considered good if 50% of patients reduce frequency of migraine by 50% and many accepted treatments do not achieve this level. They also typically have unwanted side effects. This combination leads to low adherence.

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient?
1% Chronic headache have New Daily Persistent Headache which predicts a bigger therapeutic challenge. Another 1% Hemicrania Continua that requires a trail if Indomethacin.
Some feel that a squeezing element to the pain or eye involvement predicts better outcome to Botox.
Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology? No

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics?
By professionals who are trained in CM, Botox evidence and application of Botox specifically in CM..
Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)? No

If the technology is already available, is there variation in how it is being used in the NHS? No.
Is it always used within its licensed indications? If not, under what circumstances does this occur? Used in Cervical Dystonia which can occur in CM but not in Preempt or any other paradigm for CM.

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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.
Migraine Trust and BASH statement supports use of Botox. MIPCA guidelines are supported by Medline evidence search and revision is in press at present. It supports use of Botox in CM by trained providers.

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?
Botox is simple to apply once a professional is trained – it takes 10-15 mins in experienced hands. 2 applications , 3 months apart usually is enough to see if the treatment is effective. Side effects are usually local and fade with the metabolism of the drug.

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.
It is usual to offer Botox to individuals who have failed at least 2 preventative treatments for migraine. B blockers and Topiramate are the only licensed agents at present and although other drugs are used commonly, it is felt ethically not appropriate to require failure of more drug families than are licensed. Failure is defined as lack of efficacy or emergent intolerability

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.
Reasonably similar. In private practice the strict 12 weekly injections are usually more flexible. After 2 series of injections, 12 weeks apart (not 4 series as in Preempt) efficacy is usually able to be predicted.
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?
It is possible that the population chosen in the studies does not quite represent the group of CM patients in the UK. The baseline Preempt average was about 18 days of headache , all of which is migraine. Our experience is for more headache days and a proportion only to be migraine. CM is defined as 15 days or more of headache and 8 days or more migraine. Some patients break the cycle of headache after 1 or 2 injection series and do not need more. Others reduce migraine only and need repeated injections to maintain control.
What, in your view, are the most important outcomes, and were they measured in the trials?
Reduction in migraine days (other headache days not disabling) , reduction of rescue medication usage and a global assessment by the patient.
Pattern of treatment series not measured in studies is important to predict service requirement.

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NB . An International study is currently in progress to identify the best questions to identify a need to review preventative treatment strategy in an individual.
If surrogate measures of outcome were used, do they adequately predict long-term outcomes?
No. The study only covers 1 year.
In my experience however Botox either is ineffective over the first few series (and can be suspended), breaks the cycle (may be needed intermittently in the future) or builds up effect over the first few cycles and is then consistent in its action. It is always hard to predict longterm outcomes in CM because of the number of confounding issues eg stress, whiplash injury etc

What is the relative significance of any side effects or adverse reactions?
These are minimal and rarely cause patients to withdraw from treatment
In what ways do these affect the management of the condition and the patient's quality of life?
Many patients attend because they have side effects with systemic drugs coupled with low efficacy. This makes Botox more attractive.
Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?
No

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.
There are many Investigator sponsored studies but no other high grade placebo controlled studies in CM.
I have published a clinical audit style study using upto 4 treatment cycles in a year, if it would be helpful. The study endpoints were reduction of migraine days, use of rescue medication , changes to measures of quality of life and pattern of Botox usage over time.

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

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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?
Over 100 professionals have been trained on the CM and Preempt since its license by MHRA in July 2010. Furthur training will be available for those in geographical areas with a paucity of potential providers.
Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?
Providers should be appropriately trained . Yes- appropriate training.The injections are an outpatient procedure requiring normal saline, syringes, needles and a freezer to store Botox.

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?
None