NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA260; Botulinum toxin type A for the prophylaxis of headaches associated with chronic migraine

Final recommendation post consultation
The guidance should be moved to the 'static guidance' list.

1. Background

This guidance was issued in June 2012.

At the GE meeting of 16 June 2015 it was agreed that we would consult on the recommendations made in the GE proposal paper. A four week consultation has been conducted with consultees and commentators and the responses are presented below.

2. Proposal put to consultees and commentators

The guidance should be transferred to the 'static guidance' list.

3. Rationale for selecting this proposal

No significant new evidence has been identified that would be likely to change the current recommendation in TA260. It is therefore appropriate to transfer this guidance to the 'static guidance list'.

4. Summary of consultee and commentator responses

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Respondent: Cochrane Pain, Palliative Care and Supportive Care Group **Response to proposal:** Notification of additional evidence • We note that the International Headache Society is not on the list of stakeholders, and we suggest they are contacted for feedback. • We published the Cochrane protocol, Botulinum toxins for the prevention of migraine in adults (March 2015). Review development is on-going, with the aim of publishing within 2 years. Citation: Herd CP, Sinclair A, Ives N, Rick C, Edwards J, Clarke CE. Botulinum toxins for the prevention of migraine in adults (Protocol). Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD011616. DOI: 10.1002/14651858.CD011616. Link to Cochrane Library: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011616/abstract.	**Comment from Technology Appraisals** The International Headache Society does not meet our criteria to be included as a stakeholder; however, their UK affiliate, British Association for the Study of Headache, does meet our criteria and has responded separately.

Respondent: British Association for the Study of Headache **Response to proposal:** Not stated 1. Definition of Responder: NICE has defined responder as one with at least 30% reduction in headache days. However, many patients report reduction in severity of their headache (migraine days) with improvement in Quality of Life score measured through Headache Impact Test 6 (HIT-6). Such patients may show no or little change in the total number of headache days. Khalil et al (2014)[1] have highlighted the importance of measuring severity. The number of patients who achieved 50% reduction in migraine days were 50% compared to headache days (32%) suggesting migraine reduction is more sensitive in evaluating responder. Given severity of headache drives disability, it seems important for patients that its reduction is acknowledged and indeed encouraged as an endpoint. The clinical commissioning groups (CCG) have insisted on following NICE guidelines and many patients showing response through reduction in migraine and severity of headache have been declined the treatment and had to go through exceptional treatment panel. We invite the Committee to seek expert patient input on this issue.	**Comment from Technology Appraisals** The recommendations were based on the negative stopping rule that was applied in the company's base case economic model (that is, less than 30% reduction in headache days per month). This outcome was chosen in the model because reduction in frequency of headache days was the primary endpoint of the two large phase III trials that were the focus of the company's submission (PREEMPT 1 and 2). In line with expert and company opinion, the Committee concluded that a 30% reduction in the number of headache days per month after two cycles of treatment was the most clinically relevant and reasonable negative stopping rule on which to base its

We would like to propose that responder be defined as one with 30% reduction in either headache or migraine days. 2. Medication Overuse: The International Classification for Headache Disorder (2004)[2] defined chronic migraine as those with headaches on > 15 days per month for > 3 months, of which > 8 days meet criteria for migraine without aura or respond to migraine-specific treatment in the absence of medication overuse. When medication overuse is present, this may be the cause of persistent headache. The new International Headache Society Classification (ICHD 3 beta)[3] recognises chronic migraine with or without medication overuse as two third of patients with chronic migraine seen in specialist headache clinics have medication overuse[4]. There has been no difference in the response to Botox in those with or without medication overuse[5]. <u>References</u>: 1. Khalil M, Zafar H W, Quarshie V, Ahmed F (2014). Prospective analysis of the use of OnabotulinumtoxinA (BOTOX) in the treatment of chronic migraine; real-life data in 254 patients from Hull, UK. The Journal of Headache and Pain 15:54. 2. IHS (2004) The International Classification of Headache Disorders; 2nd edition. Cephalalgia 24:9-160. 3. IHS (2013) The International Classification of Headache Disorders; 3 beta. Cephalalgia 33;9:627-808. 4. Straube A, Pfaffenrath V, Ladwig KH, Meisinger C, Hoffman W, Fendrich K, Vennemann M, Berger K (2010) Prevalence of chronic migraine and medication overuse headache in German – the German DMKG headache study. Cephalalgia 30:207-13. 5. Khalil M, Zafar HW, Ahmed F (2014) Does medication overuse matter in treating patients with chronic migraine with OnabotulinumtoxinA. Abstract – European Headache and Migraine Trust Congress (EHMTIC), Copenhagen.	decision, which was also considered to be cost-effective. NICE acknowledges the importance of different outcomes, including headache severity, and is aware that this outcome (in addition to headache frequency and duration), helps to describe the overall burden of illness that is not captured by the measurement of frequency of headache days alone. However, we don't believe that, on this basis, a review of this appraisal would add value to the NHS given no significant new published evidence has been identified which would lead to a change in the recommendations. Thank you for the information regarding the new ICHD 3 beta definition of chronic migraine in recognising people with medication overuse. During the original appraisal, the Committee heard from clinical experts that people considered for treatment with botulinum toxin type A are assessed for medication overuse before treatment starts, and that this is monitored during treatment. The guidance states that botulinum toxin type A is recommended as an option for the prophylaxis of headaches in adults with chronic migraine whose condition is appropriately managed for medication overuse.

Respondent: Allergan **Response to proposal:** Agree We agree with the proposal to move TA260 to the static list.	**Comment from Technology Appraisals** Comment noted.

Paper signed off by: Helen Knight, 23 December 2015

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