Please reply to: - [redacted],
[redacted],
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Telephone: [redacted]

30 April 2012

Mr Robert Fernley
Technology Appraisals Administrator – Committee D
National Institute for Health and Clinical Excellence
Level 1A City Tower
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Dear Mr Fernley,

I am submitting the response on behalf of the British Association for the Study of Headache (BASH) following your communication regards to the Appraisal Consultation Document (ACD) related to the Single Technology Appraisal (STA) for Botulinum Toxin A (Botox) in the prevention of headache associated with Chronic Migraine (CM).

a) Has all of the relevant evidence been taken into account?

BASH agrees that the main trial evidence (PREMPT 1 and 2) has been evaluated. The NICE committee recognised CM as a debilitating condition that affects quality of life. BASH would like to highlight the fact that there is lack of data on both clinical and cost-effectiveness of the other preventative treatments.

BASH feels that more emphasis has been given to the economic aspect of treatment and less on the clinical needs of a group of patients suffering from the most disabling form of headache refractory to currently available treatments. Botulinum Toxin type A (Botox) has a place in the treatment of patients who have failed to respond to at least three first line treatments namely tricyclic antidepressants, beta-blockers and the anti-convulsant Topiramate. In the absence of Botulinum Toxin type A (Botox) the available options include oral medications i.e. Sodium Valproate, Methysergide or invasive treatments i.e. Greater Occipital Nerve Block (GON), Occipital Nerve Stimulator (ONS). The oral medications have unpleasant and intolerable side effects and Methysergide has to be prescribed and monitored in the secondary/tertiary care requiring frequent consultations. GON injection is associated with local side effects and is effective in only 30% for a very short period for which the evidence is not robust; moreover ONS is extremely expensive and require referral to the National Hospital for Nervous Diseases, London.

BASH acknowledges the fact that reduction in headache days (the primary end point) in the Botox arm was modest in the clinical trials and there was a large placebo response (PREEMPT). However, measuring a meaningful response is more than a simple count of the headache days. In clinical practice patients may experience improvement in the duration or intensity of migraine or a reduction in associated symptoms such as nausea, vomiting, sensitivity to light sound, a better quality of life and the ability to return to work or other activities of daily living.

BASH would like to highlight the fact that Botulinum Toxin type A showed a 50% reduction in headache days in 47% of patients compared to 37% for Topiramate; the drug with best available evidence in CM. BASH would like the committee to consider the comparative data for placebo and the active group for 25%, 50% and 75% response rate. BASH acknowledges the fact that a robust response criterion has to be agreed if the treatment is to be recommended by NICE on the National Health Service (NHS) currently faced with a challenge of using resources appropriately

b) Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

Patients with CM are more likely to visit their primary care physician than those with episodic migraine. More patients with CM are referred and re-referred to specialist care (secondary or tertiary) and are less likely to be discharged back to primary care unless a treatment is able to achieve remission. Irrespective of the treatment offered by the specialist, all patients require a consultation for at least 30 minutes. Treatment with Botulinum Toxin is simple and takes 10-15 minutes in addition to a standard consultation. The treatment is delivered in the out-patient setting and once trained can be given by a registrar or specialist headache nurse. The follow ups can be conducted via telephone with patients mailing (or emailing) their diaries beforehand. Patients only need to re-attend the clinic for repeat treatment. BASH feels the treatment can be delivered in the NHS through existing resources except the cost of the drug.

BASH is aware of the financial constraint faced by the NHS and is fully supportive of the fact that treatment be restricted to those who benefit most from it. BASH also acknowledges the fact that a more objective and strict criteria would have to be in place for the start and stoppage of treatment to minimise waste.

BASH recommends that treatment be restricted to those who have failed to respond to adequate trial of three prophylactic medications; the diagnosis of CM is made by physician with special interest and training in headache disorder and the treatment delivered by those trained in the technique; medication overuse must be addressed appropriately and all patients must maintain a headache diary to monitor the response and need for further treatment.

A responder must be defined as one with at least 30% reduction in headache days and those who fail to respond to two treatment cycles should not receive any further treatment (Negative stopping rule). The treatment is repeated to those still fulfilling the criteria for CM but has shown a 30% reduction in headache days. Those with episodic migraine (14 days or less) should not receive further treatment unless they have a relapse (15 or more headache days with 8 or more migraine days for at least three months) (Positive stopping rule). BASH would like to highlight the fact that there is absence of data regards to stopping rules for any preventive treatment in migraine. BASH feels that headache physicians should be able to ensure they use the health resources appropriately and limit the treatment to those benefiting most from it.

c) Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

Botox is the only licensed treatment available for prophylaxis of headache associated with CM. The only other drug with class I evidence is Topiramate which has its limitations of poor tolerability, cognitive and teratogenic side effects. This is important as a large number of CM sufferers are females of child-bearing potential. Botox is often their last hope to continue to live normally and be able to return to work. BASH is disappointed with the draft recommendation of the committee and feels strongly that the decision must be carefully considered.

d) Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?

CM is more common in females at a young age. This is the most productive period of their life both from family and work point of view.

e) Are there any equality-related issues that need special consideration and are not covered in the appraisal consultation document?

Currently the treatment is mainly delivered in the private sector and only those who can afford the treatment are able to receive it. The treatment is commissioned by some Primary Care Trusts in line with the licensed recommendation. The other Primary Care Trust is considering individuals on the basis of exceptionality and has rejected the vast majority of applications through individual funding requests. If the treatment is not recommended on the NHS than it will only be received in the private sector by those who have the ability to pay for it. This is discriminatory as the medication is licensed.

Yours sincerely,