NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

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

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of botulinum toxin type A within its licensed indication for the prophylaxis of headaches associated with chronic migraine.

Background

Migraine is primarily a headache disorder manifesting as recurring attacks usually lasting for 4–72 hours involving throbbing head pain of moderate to severe intensity. It is often accompanied by nausea, sometimes vomiting, sensitivity to light, sensitivity to sound, and/or other sensory stimuli. Some people can have warning symptoms called an aura, before the start of a headache. Factors that can trigger attacks in people susceptible to migraines include stress, change in sleep pattern, overtiredness, consumption of caffeine or alcohol, climatic conditions and use of visual display units.

Chronic migraine is defined by the International Headache Society as the occurrence of headaches on 15 days or more per month for at least 3 months where the attacks fulfil criteria for pain and associated symptoms of migraine without aura on at least 8 days per month for at least 3 months, where there is no medication overuse, and where the headaches are not attributable to another causative disorder. To fulfil the criteria for chronic migraine, a person must previously have had at least five attacks fulfilling the International Headache Society's criteria for migraine without aura. Despite these criteria, in clinical practice, there is a lack of consensus regarding the definition of chronic migraine.

It is estimated that there are 190,000 migraine attacks experienced every day in England and 6 million people suffer from migraine in the UK. Prevalence has been reported to be 5–25% in women and 2–10% in men. Prevalence of chronic migraine in the UK is not known, although some clinicians consider the rate could be 1 in 1000 people.

Preventative (also called prophylactic) treatment of migraines can be an important component of chronic migraine management. The goals of preventive therapy are to reduce the frequency, painfulness, and/or duration of migraines, and to increase the effectiveness of medication that is taken at the earliest signs of a migraine headache (known as abortive therapy). Preventative treatment of migraines may also help to avoid medication overuse headache, otherwise known as rebound headache, which is linked to

overuse of pain medications, and is a common problem among people with migraines.

Preventative interventions can take many forms including nutritional supplements, lifestyle alterations such as increased exercise and avoidance of migraine triggers, and prophylactic migraine medications. Prophylactic chronic migraine medications are generally considered for people who have at least two attacks a month, whose attacks are increasing in frequency, whose attacks cause significant disability despite abortive treatment, or who cannot take abortive treatment for migraine attacks. Prophylactic migraine medications include betablockers (propranolol, atenolol,metoprolol, nadolol and timolol), valproic acid, sodium valproate, topiramate, antidepressants (amitriptyline, nortriptyline, imipramine, desipramine), pizotifen, gabapentin and cyproheptadine.

The technology

Botulinum toxin type A (Botox, Allergan) is a purified neurotoxin complex which produces seven neurotoxins that are structurally similar but immunologically distinct, and has neuromuscular transmitter blocking effects.

Botulinum toxin type A (Botox) has a UK marketing authorisation for the prophylaxis of headaches in adults with chronic migraine (headaches on at least 15 days per month of which at least 8 days are with migraine). It is administered by intramuscular injection to between 31 and 39 sites around the head and back of the neck. Repeated treatments are recommended every 12 weeks.

Intervention(s)	Botulinum toxin type A (Botox)
Population(s)	Adults with headaches on at least 15 days per month of which at least 8 days are associated with chronic migraine and • whose condition has failed to respond to at least three prior pharmacological prophylaxis therapies and • medication overuse has been appropriately managed.
Comparators	Standard management without botulinum toxin type A excluding invasive procedures

Outcomes	The outcome measures to be considered include: • frequency of headache days per month • frequency of migraine days per month • severity of headaches and migraines • number of cumulative hours of headache or migraine on headache or migraine days • reduction in acute pharmacological medication • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If evidence allows, the presence or absence of medication overuse should be considered as a subgroup.
Related NICE recommendations	Related Guidelines: Clinical Guideline in preparation, 'Diagnosis and management of headaches in young people and adults'. Earliest anticipated date of publication December 2012. Related Interventional Procedures: Interventional Procedure Guidance No. 370, December 2010, 'Percutaneous closure of patent foramen ovale for recurrent migraine'. Review date tbc. Interventional Procedure Guide No. 381, March 2011, 'Deep brain stimulation for intractable trigeminal autonomic cephalalgias'. Review date tbc.