Health Technology Briefing
October 2023

Botulinum toxin type A for preventing episodic migraine

Company/Developer	AbbVie

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 33809	NICE TSID: Not available	UKPS ID: 670977

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Botulinum toxin type A (an active constituent in BOTOX) is currently in clinical development for the prevention of episodic migraine. Migraine is a debilitating neurological condition that commonly causes extremely painful headaches. Episodic migraine is defined as a headache which occurs on less than 15 days per month. Migraines may be triggered by any of the following: stress or anxiety, bright or flashing lights, sleep changes, weather changes, excess caffeine, and tobacco. Symptoms of a migraine usually manifest as, throbs with a pulse and is made worse by physical activity. People often lose their appetite during a migraine attack, and nausea is a common symptom, which sometimes progresses to vomiting. After the worse of the attack is over, sufferers often feel 'washed out'. Preventative (prophylactic) treatment of migraine is used to reduce the number of migraines, severity, and duration of migraines a patient may experience. There is currently no cure for migraines.

Botulinum toxin type A is a type of nerve toxin which can paralyse muscles. It can reduce migraine attacks by blocking certain chemicals that cause the pain of migraine. Botulinum toxin type A is administered as an intramuscular injection. If licensed for episodic migraine, Botulinum toxin A would offer an additional preventative treatment option for patients with episodic migraines.

Proposed Indication

Botulinum toxin type A for the prevention of episodic migraines (EM) in adults.[1]

Technology

Description

Botulinum toxin type A (BOTOX) is a purified neurotoxin complex, which is derived from the bacterium *Clostridium botulinum*. It has neuromuscular transmitter blocking effects.[2] Botulinum toxin type A enters nerve endings at neuromuscular junctions (NMJs) where, by cleaving soluble N-ethylmaleimide-sensitive factor-attachment protein receptors (SNARE) proteins, they prevent the vesicular release of acetylcholine (ACh) from the synaptic terminal, causing muscle relaxation and flaccid paralysis.[3]

Botulinum toxin type A is currently in clinical development for patients who experience EM. In the phase III clinical trial (NCT05028569), participants will receive either dose A or B of botulinum toxin type A, or placebo administered intramuscularly on week 0 and week 12. Eligible participants will receive BOTOX Dose A on Week 24 and Week 36.[1]

Key Innovation

There is no cure for EM, therefore, patients must rely on preventive therapy to reduce frequency, duration, or severity of attacks.[4,5] Botulinum toxin type A is approved for use on the NHS for the treatment of chronic migraine in adults.[6] Botulinum toxin type A was discovered as effective for people with chronic migraine while being used for cosmetics treatment. It was then found that people who had botox experienced fewer headaches.[7] If licensed for EM, botulinum toxin type A will offer an additional treatment option for adult patients suffering from EM.

Regulatory & Development Status

Botulinum toxin type A is licensed in the UK for treatment of the following indications in adults: [8]

- focal spasticity
- overactive bladder
- neurogenic detrusor overactivity
- hyperhidrosis of the axillae
- blepharospasm
- hemifacial spasm
- idiopathic cervical dystonia
- prophylaxis of chronic migraine

Botulinum toxin type A is ccurrently in phase II and III clinical development for several indications including:[9]

- upper limb spasticity
- ventral hernia
- upper limb essential tremor
- chronic migraine
- post-operative atrial fibrillation
- temporomandibular disorders
- drug-resistant focal seizure
- interstitial cystitis/bladder pain syndrome (IC/BPS)

Patient Group

Disease Area and Clinical Need

Migraine is a debilitating neurological condition that commonly causes extremely painful headaches.[4] Migraine can be further categorised according to the frequency of attacks.[1] Patients who suffer from EM have headaches which occur on less than 15 days per month.[10] Migraines include symptoms such as nausea, or a sensitivity to light and sound. Migraine can be one-sided, but it is also common for the pain to be on both sides. Patients may experience throbs with a pulse and may lose their appetite during migraine attack.[11] Migraine is caused by the activation of a mechanism deep in the brain that leads to release of pain-producing inflammatory substances around the nerves and blood vessels of the head.[11] The cause of this mechanism is unknown. However, it is expected that those who have a close family member who suffers from migraines are more likely to also experience them. Certain triggers causing migraines include: beginning of menstrual cycle, anxiety and depression, tiredness, irregular eating patterns, caffeine excess an lack of exercise.[12]

Migraine is common with a global prevalence of around 1 in 7 people, especially in women. It affects about 1 in 5 women and 1 in 15 men.[11,13] Migraine can occur at any age but is most common between 25 to 55 years.[13] Episodic migraine is more common than chronic migraine.[14] In England (2022/2023), there were 29,970 hospital admissions, with primary diagnosis of migraine (ICD-10: G43) and 36,048 finished consultant episodes (FCE), resulting in 26,412 FCE bed days and 9,073 day cases.[15]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends the following prophylactic treatment options for adult patients with EM:[16-20]

- Galcanezumab
- Erenumab
- Fremanezumab
- Rimegepant
- Eptinezumab

Clinical Trial Information

Trial	NCT05028569; Phase 3 Multicenter, Randomized, Double-blind, Placebo-controlled Study of BOTOX (Botulinum Toxin Type A) for the Prevention of Migraine in Subjects with Episodic Migraine **Phase III** – Recruiting **Location(s):** 5 EU countries, UK, USA, Canada, and Israel. **Primary completion date**: June 2024
Trial Design	Randomised, parallel assignment, quadruple masking
Population	N=777; adults with history of migraine headache disorder meeting International Classification of Headache Disorders (ICHD)-3 diagnostic criteria for migraine with aura or migraine without aura for >= 12 months; aged 18 years to 65 years
Intervention(s)	Intramuscular Injection of botulinum Toxin Type A (dose A) Intramuscular Injection of botulinum Toxin Type A (dose B)
Comparator(s)	Intramuscular Injection (placebo)

Outcome(s)	Primary outcome(s): Change from baseline in the frequency of monthly migraine days (i.e., migraine or probable migraine headache days) will be assessed See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Botulinum toxin type A is already marketed in the UK for the treatment of chronic migraine in adults; a 200-unit vial is £276.40. The manufacturer estimates that the administration cost is £73 per treatment, based on a total treatment time of less than 30 minutes. The total cost for treatment and administration of treatment per 12-week cycle, assuming no vial sharing, is therefore expected by the manufacturer to be £349.40. Costs may vary in different settings because of negotiated procurement discounts.[21]

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Rimegepant for preventing migraine (TA906). July 2023
- NICE technology appraisal. Eptinezumab for preventing migraine (TA871). March 2023
- NICE technology appraisal. Fremanezumab for preventing migraine (TA764). February 2022
- NICE technology appraisal. Erenumab for preventing migraine (TA682). March 2021
- NICE technology appraisal. Galcanezumab for preventing migraine (TA659). November 2020
- NICE clinical guideline. Headaches in over 12s: diagnosis and management (CG150). September 2012

NHS England (Policy/Commissioning) Guidance

- NHS England. NHS Standard Contract for Specialised Pain. D08/S/a.
- NHS England. NHS Standard Contract for Neurosurgery. D03/S/a.
- NHS England. Clinical Commissioning Policy: Occipital Nerve Stimulation for Adults with Intractable Chronic Migraines and Medically Refractory Chronic Cluster Headaches. D08/P/c. July 2015.

Other Guidance

- Scottish Intercollegiate Guidelines Network. Pharmacological management of migraine. 2018.[22]

Additional Information

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NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.