

Botulinum Toxin

Why has my doctor recommended a preventative drug?

Preventative drugs are recommended for people who have frequent attacks of migraine that are not effectively controlled with symptomatic treatment alone. Preventative drugs are unlikely to stop ALL attacks but they do help to reduce the frequency of attacks and may also enable symptomatic treatment be more effective. However, frequent headaches often result from overuse of drugs to treat the symptoms of headache for headache. It is important to treat the medication-overuse first as, if effective, it may mean that preventative drugs are unnecessary.

What is botulinum toxin?

Botulinum toxin is a protein produced by the bacterium *Clostridium botulinum*. This toxin is responsible for the condition botulism that can result from eating contaminated food. It has powerful effects on the nervous system, paralysing muscles. Scientists realised that controlled doses of the toxin can relax muscles and treat certain medical conditions in which the muscles are overactive.

Can it be used for migraine?

BOTOX®, a specific brand of botulinum toxin type a, is licensed for the treatment of 'chronic migraine', defined as headache in patients who have at least 15 days of headache a month, of which at least 8 days are migraine. Other brands of botulinum toxin type a including Azzalure®, Bocouture®, Dysport®, Vistabel® and Xeomin® are not licensed for migraine.

How does it work in migraine?

It is not known how botulinum toxin controls frequent headache but it has been suggested that it may work by blocking pain signals within the brain.

What else it is used for?

Botulinum toxin is used for treatment of persistent muscle contraction disorders including blepharospasm (spasm of the eyelid muscle) and torticollis (spasm of the neck muscles). It is also used to control excessive underarm sweating. It is popular as a cosmetic treatment to smooth facial wrinkles.

How is it given?

Botulinum toxin is given as a series of small injections under the skin or into the muscles of the forehead, above the ears, and into the neck and shoulders. For headache, the usual number of injections is 31 to 39, although fewer injections may be effective for some people. The injections can be repeated every 12 weeks. The clinical effect usually lasts 2-6 months.

How effective is it?

Most people with migraine will not benefit from botulinum toxin, as it does not affect episodic migraine attacks i.e., less than 15 headache days a month. However, studies show that BOTOX® can reduce the frequency of days with headache in patients who have at least 15 days of headache a month, of which at least 8 days are migraine. Three clinical trials have been published, with similar results. Patients were treated with either BOTOX® or saline injections. Each group started with an average of 20 days of headaches a month (study 1: 20 days in the BOTOX® group versus 19.8 in saline group; study 2: 19.9 days versus 19.7; study 3: 19.9 days versus 19.8). By the end of 24 weeks of treatment (2 courses), patients given BOTOX® had fewer headache days per month than patients treated with saline. The results were statistically significant but the absolute difference was small (study 1: 12.2 days in the BOTOX® group versus 13.4 in saline group; study 2: 10.9 days versus 13; study 3: 11.5 days versus 13.2).



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What side effects might I get?

Side effects are uncommon. In the trials, 5.9-8.7% of patients receiving BOTOX®, reported neck pain and 5.2-5.9% reported muscle weakness. Other effects included eyelid drooping, muscle aches and muscle stiffness. These resolved spontaneously over several weeks. Occasionally pain and bleeding at the injection sites can occur. Uncommon side effects have included difficulty in swallowing. In most cases this has been mild. If you experience any difficulty in breathing, swallowing, or speaking following botulinum toxin injections, you should seek medical help immediately.

How long do I have to take before I notice any benefit?

It can take a couple of weeks before you notice improvement. The effects usually last several months. If the effect wears off you can have repeat injections provided that they are not given more often than every 12 weeks.

How long can I use it for?

Clinical trials show that up to five BOTOX® treatment courses at 12-weekly intervals were safe and well tolerated. A few people develop neutralizing proteins known as antibodies that stop botulinum toxin working. Some studies have shown that this is more likely to happen in people who have high treatment doses at more frequent intervals than is generally recommended. You are less likely to develop antibodies if you use the lowest effective number of injections of BOTOX® and do not repeat the courses too frequently.

Further reading:

1. Aurora SK, Dodick DW, Turkel CC, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 1 trial. *Cephalalgia* 2010;30(7):793-803.
2. Diener H, Dodick D, Aurora S, et al. OnabotulinumtoxinA for treatment of chronic migraine: Results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. *Cephalalgia* 2010;30(7):804-14.
3. Dodick DW, Turkel CC, DeGryse RE, et al. OnabotulinumtoxinA for treatment of chronic migraine: pooled results from the double-blind, randomized, placebo-controlled phases of the PREEMPT clinical program. *Headache* 2010;50(6):921-36.

Does it interact with any other drugs that I might be taking?

Certain antibiotics may increase the effect of botulinum toxin. These include gentamicin, neomycin, spectinomycin, streptomycin and tobramycin. If possible, avoid aspirin in the week before treatment, to minimize bleeding at the injection sites. Please make your doctor aware of any other drugs you are taking when botulinum toxin is prescribed.

What if I want to become pregnant?

Seek advice from your doctor. Because botulinum toxin has not been proven to be safe in pregnancy or during breastfeeding, it is not generally recommended unless the benefits of treatment are considered by your doctor to outweigh any potential risk.

Who cannot use it?

In addition to pregnant or breastfeeding women, botulinum toxin should not be used by people who have previously had an allergic reaction to the toxin. People with muscle weakening conditions such as myasthenia gravis, may find that the botulinum toxin injections are more potent than expected. Please let the doctor know of any other medical problems you have now or have suffered from in the past.

This information is provided as a general guide only and is not a comprehensive overview of prescribing information. If you have any queries or concerns about your headaches or medications please discuss them with your GP or the doctor you see at the City of London Migraine Clinic.

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