

Botulinum toxin type A injections for chronic anal fissure

Information for the public

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About this information

This information explains the evidence summary about the off-label use of botulinum toxin type A injections for treating chronic anal fissure. The evidence summary is an overview of the available information about this medicine. It aims to help prescribers and patients when they are considering whether or not to use an unlicensed or off-label treatment. The summary does not contain recommendations from NICE on whether the medicine should be used.

Licensing medicines

In the UK, medicines need to have a licence before they can be marketed. To get a licence, the manufacturer of the medicine has to provide evidence that shows that the medicine works well enough and is safe enough to be used for a specific condition and for a specific group of patients, and that they can manufacture the medicine to the required quality.

Medicines can be prescribed without a licence (an 'unlicensed medicine') if there is no suitable licensed alternative and it is likely to benefit the patient.

A medicine can also be prescribed 'off-label'. This means the prescriber wants to use it in a different way than is set out in the terms of its licence. This could mean using the medicine for a different condition or a different group of patients, or it could mean a change in the dose or that the medicine is taken in a different way. There is more information about licensing medicines on [NHS Choices](#).

What is chronic anal fissure?

An anal fissure is a common and often painful problem caused by a small tear or ulcer (open sore) in the lining of the anus (back passage). This can cause bleeding, local itching and pain with a bowel movement, which can be severe. When someone has an anal fissure the first treatments can include a high-fibre diet, laxatives and applying anaesthetic ointments to the affected area. Anal fissures usually heal within a few weeks but those that have not healed after 4–6 weeks are called chronic fissures.

If someone has a chronic fissure, it is thought that the reason it has not healed is that the ring muscle (sphincter) that goes around the anus (back passage) has become so tense that the flow of blood to the lining of the anus is reduced. That means that not enough oxygen (carried by the blood) gets to the fissure (or tear). Without enough oxygen, the cells which make up the lining can't grow and repair (heal) the fissure (or tear).

A licensed medicine for treating chronic anal fissure in adults (over 18 years of age) is available in the UK. This is a 0.4% glyceryl trinitrate ointment (also called Rectogesic 4 mg/g Rectal Ointment), and is usually tried for a period of 8 weeks. However, treatment with glyceryl trinitrate often causes headache and about 2 in every 10 people using the 0.4% ointment have very bad headaches. These can sometimes be treated successfully with painkillers such as paracetamol but the headache causes some people to stop using the medicine.

If the person has had to stop treatment with 0.4% glyceryl trinitrate or it hasn't worked, there are other treatments that aren't licensed in the UK which may be tried. These include a 0.2% strength of glyceryl trinitrate ointment (see NICE's evidence summary on [0.2% topical glyceryl trinitrate ointment for chronic anal fissure](#)), diltiazem cream or ointment (see NICE's evidence summary on [2% topical diltiazem hydrochloride for chronic anal fissure](#)) or botulinum toxin injections (such as Botox or other brands) into the area around

the anus (back passage). A surgical procedure called sphincterotomy may also be tried.

About botulinum toxin type A injection

When used to treat chronic anal fissure, botulinum toxin type A is usually injected into the muscle around the anus (back passage). The aim is to help reduce excess muscle tension in this muscle, which is thought to help the fissure to heal naturally.

There are 6 brands of botulinum toxin type A (Azzalure, Bocouture, Botox, Dysport, Vistabel and Xeomin) currently licensed in the UK to treat many different medical conditions, including a lot of conditions associated with muscle spasms (uncontrolled muscle contractions). However, no brand of botulinum toxin type A has a UK licence to treat chronic anal fissure. So when it is used to treat chronic anal fissure it is described as being used 'off-label'.

Various different amounts of botulinum toxin type A have been used in studies of chronic anal fissure, injected at various places around the fissure. This usually involves 1 or 2 injections into either only one side of the fissure or in both sides. In the UK, the injections are usually given under a local or general anaesthetic in an operating theatre.

Summary of possible benefits and harms

How well does botulinum toxin type A injection work?

Two reviews looked at a number of different studies of botulinum toxin type A injection when used to treat chronic anal fissure in adults. No studies were found which included children or young people.

Botulinum toxin type A worked much better at healing chronic anal fissures in some studies than others. This variation in whether botulinum toxin healed the fissures can be partly explained by the fact that the studies included in the 2 reviews looked at whether the fissures had healed at different periods of time after the treatment had been given. This ranged from just 1 or 2 months after the treatment to 5 years. This is important because anal fissures can naturally go through temporary periods of being completely healed or only partly healed, only for the fissure to come back later. A lot of the studies

looked at how well the fissures had healed less than 6 months after the treatment was given. This doesn't give a good idea of how well the treatment works over a longer period of time because it doesn't take into account how often the fissure might come back. The studies were not long enough to show this.

There was a large difference between the studies in how often the fissure returned (reoccurred) after it had initially been healed when botulinum toxin type A injection had been used. This is because studies measured this at different points in time.

Despite the large variation between studies, 1 of the reviews found that botulinum toxin type A injection healed chronic anal fissure in around 6 to 7 out of every 10 people who were given the injection. However, botulinum toxin type A injection was found to be no better or worse at healing anal fissures than a dummy treatment with no active ingredient (also called a placebo). This might be because many chronic anal fissures temporarily heal on their own anyway, without treatment.

Overall, the studies also showed that botulinum toxin type A injection was no better or worse at healing fissures than a 0.2% strength of glyceryl trinitrate ointment. Some studies found botulinum toxin type A injection worked better than the ointment, others found it didn't, and others found they were the same. Importantly, the 0.2% strength of glyceryl trinitrate ointment used in the studies is not licensed in the UK. No studies were found that compared botulinum toxin with the 0.4% strength of glyceryl trinitrate ointment, which is currently the only treatment that is licensed in the UK for treating chronic anal fissure.

The studies included in the reviews showed that botulinum toxin did not work as well as surgery (a procedure called 'sphincterotomy') at healing chronic anal fissures. Surgery works well at healing anal fissures but there is a small chance of complications from the surgery. Therefore surgery is usually tried only after other treatments that don't involve surgery, such as glyceryl trinitrate ointment, diltiazem cream or botulinum toxin type A injection, haven't worked.

What are the possible harms or side effects?

One review of studies found that a side effect of using botulinum type A injection was temporary loss of control of flatulence (or passing wind) in about 1 in 10 people who were given the injection. Up to 1 in 20 people who are given the injection may also lose control of their bladder or bowel movements, which usually does not last for long. Potentially serious side effects that can be caused by using botulinum toxin over a long period of time

cannot be ruled out as most of the studies were short and didn't last very long.

If you are receiving any product containing botulinum toxin, you should be aware of the rare, but serious signs and symptoms that the toxin has spread. These include weakness in your muscles or difficulties with breathing. You should see a doctor immediately if you have any of the following symptoms because they may be life-threatening:

- Difficulty breathing.
- Choking.
- Any new difficulties with swallowing or swallowing difficulties that get worse.

Please note that the results of the research evidence only indicate the benefits and harms for the population in the studies. It is not possible to predict what the benefits and harms will be for an individual patient being treated with botulinum toxin.

Prescribing botulinum toxin

If a prescriber wants to use an unlicensed or off-label medicine, they must follow their professional guide, for example for doctors the General Medical Council's [good practice guidelines](#). These include giving information about the treatment and discussing the possible benefits and harms so that the patient has enough information to decide whether or not to have the treatment. This is called giving informed consent.

A [full version of the summary aimed at healthcare professionals](#) is available on the NICE website. The summary for healthcare professionals does not contain recommendations from NICE on whether the medicine should be used.

If your doctor is suggesting that you might try botulinum toxin type A injection for chronic anal fissure, you might like to ask some of the questions below.

Questions to ask

- Why am I being offered an off-label medicine?
- What does the treatment involve?

- What are the benefits I might get?
- How good are my chances of getting those benefits?
- Could having the treatment make me feel worse?
- Are there alternative treatments?
- What are the risks of the treatment?
- Are the risks minor or serious? How likely are they to happen?
- Will this treatment cure my fissure for good, or can it come back?
- What may happen if I don't have the treatment?

More information

The evidence summary and this information for the public were produced for NICE by Bazian Ltd.

NICE has published [information](#) about how evidence summaries for unlicensed and off-label medicines are developed.

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