

2% Topical diltiazem hydrochloride for chronic anal fissure

Information for the public

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About this information

This information explains the evidence summary about the unlicensed use of 2% diltiazem hydrochloride cream or ointment for treating chronic anal fissure in children, young people and adults. 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 a 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: glyceryl trinitrate ointment (also called Rectogesic 4 mg/g Rectal Ointment). Glyceryl trinitrate is commonly abbreviated to GTN. GTN ointment is applied to the affected area twice a day and is used to relieve pain caused by the fissure. The GTN helps the ring muscle (sphincter) to relax which allows more blood to flow to the lining of the anus (back passage) so that the cells which make up the lining can heal the fissure (or tear).

Treatment with GTN often causes headache and about 20 in every 100 people using it have very bad headaches. These can be treated with pain-killers such as paracetamol but the headache causes some people to stop using the medicine.

If the person has had to stop treatment with GTN, or the fissure hasn't healed or has come back, other treatments can be tried. These include botulinum toxin injections (such as

Botox or other brands) into the area around the anus (back passage) or a surgical procedure called spincterotomy. Both these treatments help the ring muscle (sphincter) to relax and allow more blood to flow to the lining of the anus (back passage). Diltiazem hydrochloride cream or ointment can also be tried. It is also sometimes used in children; there is no licensed medicine for treating chronic anal fissures in children.

About topical diltiazem hydrochloride

Topical diltiazem hydrochloride is not licensed in the UK for treating chronic anal fissure. Topical diltiazem hydrochloride typically comes as a 2% cream or ointment. Topical means that the medicine is applied to the surface of the body, in this case, just inside the anus (back passage). The 2% figure gives an indication of the strength of the medicine because it tells us the amount of active ingredient present in the cream (in this case, the amount of diltiazem hydrochloride).

A small amount of the diltiazem cream or ointment is applied to the affected area twice a day. The medicine is thought to work by helping the ring muscle (sphincter) that goes around the anus (back passage) to relax and allow blood to flow to the lining of the anus (back passage). This aids the healing process and relieves the pain (see '[What is a chronic anal fissure?](#)').

Summary of possible benefits and harms

How well does topical diltiazem hydrochloride work?

In all, 9 studies have looked at how well diltiazem cream or ointment works for treating anal fissures.

Only 1 of these studies looked at how well it worked compared with using no treatment. The anal fissure healed completely in 24 out of 30 adults who were using the diltiazem ointment compared with 10 out of 30 adults who were not using anything. The study had only a small number of people so this finding may not be accurate. Adults who were using the diltiazem ointment also had less pain than those who weren't receiving any treatment.

Out of the 9 studies, 7 compared diltiazem cream or ointment with GTN. Overall, these

studies showed that the diltiazem cream or ointment worked about as well as GTN at both healing fissures and relieving pain. Other studies have found that, on average, about 49 people in every 100 who used GTN had their anal fissure healed, compared with about 36 people in every 100 who used dummy cream or ointment. One of the studies compared diltiazem cream with botulinum toxin injection. The diltiazem cream worked about as well as botulinum toxin injection at both healing fissures and relieving pain. However, the study had only a small number of people so this finding may not be accurate.

Two of the studies compared diltiazem ointment with surgery. Fewer people using diltiazem ointment had their fissures healed than people who had surgery (32 people out of 40 using diltiazem ointment compared with 38 out of 40 who had surgery in 1 study; and 63 out of 91 using diltiazem ointment compared with 93 out of 97 who had surgery in the other study). These studies had only small numbers of people so these findings may not be accurate.

Only 1 of the studies of diltiazem was in children. The average age of the children in this study was about 3 years. The study suggested that diltiazem ointment was better than GTN at healing anal fissures in children (23 out of 28 using diltiazem were healed compared with 11 out of 28 using GTN). However, the study had only a small number of children so this finding may not be accurate.

What are the possible harms or side effects?

Based on the studies, diltiazem cream or ointment does not appear to cause significant harm or side effects in adults using it in the short term. Most studies looked at use for around 3 months or less. It is not known what possible harms or side effects the treatment may cause if it is used for longer than this. However, diltiazem cream or ointment is not usually used for long periods.

A few adults in the studies had itchiness or irritation around the place where the diltiazem cream or ointment was applied. Some people had mild headaches while using it. Because of the small number of people in the studies, it is not possible to draw firm conclusions on how common these side effects are. But fewer people using diltiazem cream or ointment got headache compared with people using GTN (although some did). The 1 study in children was too small to draw conclusions about what side effects may occur when diltiazem cream or ointment is used to treat anal fissures in children, or how common they are.

Please note that the results of the research studies 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 the diltiazem cream or ointment.

Prescribing topical diltiazem hydrochloride

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.

The full version of the summary aimed at healthcare professionals is available at <http://publications.nice.org.uk/esuom3-chronic-anal-fissure-2-topical-diltiazem-hydrochloride-esuom3/> 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 topical 2% diltiazem hydrochloride (as a cream or ointment) for chronic anal fissure, you might like to ask some of the questions below.

Questions to ask

- Why am I being offered an unlicensed 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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