Misoprostol for induction of labour after the late death of an unborn baby in the womb

Information for the public
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About this information

This information explains the evidence summary about the off-label use of misoprostol (inserted into the vagina) after oral mifepristone for the induction of labour (starting labour artificially) following the late death of an unborn baby (fetus) in the womb (known as late intrauterine fetal death). In this context, 'late' means the woman is 24 weeks pregnant or more. 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.

If a woman's baby has died in the womb after 24 weeks of pregnancy or more, 1 option that NICE recommends is kick-starting labour using a drug called mifepristone, followed by a drug called a prostaglandin. Misoprostol is a type of prostaglandin. The evidence summary looks at the risks and benefits of misoprostol, particularly the differences between high doses and low doses of this medicine.

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 late intrauterine fetal death?

Intrauterine fetal death is when an unborn baby (fetus) dies inside the womb before birth. This is described as 'late' when it happens in a woman who is 24 weeks pregnant or more, and is estimated to occur in 1% of all pregnancies. In the pregnancies where this happens, if the women were left to go into labour naturally, more than 90% would do so within 3 weeks.

Losing a baby in the womb, whenever it happens, is a traumatic event for the mother, her partner and family. Support is usually offered by healthcare professionals to help them cope with the emotional and physical consequences of the death.

If a woman is physically well and there is no evidence of membrane rupture, infection or bleeding, she is usually offered a choice of having labour induced (starting labour artificially) soon after the diagnosis is made with the aim of reducing complications for the woman, or watchful waiting, during which she is closely monitored. When the diagnosis of late intrauterine fetal death is made, if a woman already has ruptured membranes, infection or bleeding, having labour induced immediately is the preferred option.

About misoprostol

Misoprostol tablets are licensed in the UK to treat ulcers of the stomach and gut (small intestine) and to prevent ulcers associated with taking certain anti-inflammatory pain medication in adults. It is a type of drug called a prostaglandin that is known to cause contractions of the womb, so it is not used for preventing or treating ulcers in women who are pregnant.

Women who chose to have their labour induced after the late death of their unborn baby in the womb (24 weeks pregnant or more) should be offered a drug called mifepristone (which is taken by mouth as a tablet), followed by a drug that acts like the natural hormones that kick-start labour (called a prostaglandin). Misoprostol is a type of prostaglandin and is an option at this point. Prostaglandins should usually be inserted into the vagina as a gel, tablet or pessary.

Misoprostol does not have a UK licence to induce labour, so its use in this way is described as 'off-label'.
Misoprostol comes in the form of a tablet and can be given through the mouth (orally), under the tongue (sublingually) or it can be inserted into the vagina. There are fewer side effects when misoprostol is inserted into the vagina compared with taking it through the mouth. However, when it is inserted into the vagina, the oral tablets may need to be split using a pill cutter to get a lower dose, which can make it difficult to get an exact dose.

This evidence summary has only looked at how well different doses of misoprostol work and how safe they are when inserted into the vagina after taking the drug called mifepristone.

Other licensed drugs for inducing labour under these circumstances include oxytocin and dinoprostone (an alternative prostaglandin).

Summary of possible benefits and harms

**How well does misoprostol work?**

Two studies were found that looked at how well a low dose of misoprostol (inserted into the vagina) worked, compared with a higher dose, when taken after mifepristone for inducing labour in women after the late death of their unborn baby in the womb (24 weeks pregnant or more).

One study compared a low dose of misoprostol (which was inserted into the vagina) with a higher dose of the drug (which was inserted into the vagina and also taken by the mouth) in 47 women. All women were given mifepristone before misoprostol. This study found that the lower dose of misoprostol worked about as well as the higher dose of the drug in reducing the time it took from labour starting until delivery.

The second study compared a combination of mifepristone and a low dose of misoprostol (which was inserted into the vagina) with a higher dose of misoprostol, also inserted into the vagina but used on its own (not after mifepristone) in 130 women. This study found that the lower dose of misoprostol given after mifepristone worked about as well as a higher dose of misoprostol taken on its own (without mifepristone) in reducing the time it took from labour starting until delivery.

**What are the possible harms or side effects?**

The 2 small studies described above gave little evidence on the safety of misoprostol (inserted into the vagina) when given after mifepristone for inducing labour in women after the late death of their unborn baby in the womb (24 weeks pregnant or more).
Overall, few women in the studies had serious complications. Some women did lose a lot of blood (which sometimes meant they needed a blood transfusion) or needed to have the lining of their womb scraped (uterine evacuation). Also, because only 177 women were included in the studies, it is possible that rare or serious problems such as uterine rupture (a tear in the womb) were not detected.

When misoprostol tablets are taken (through the mouth) for treating or preventing ulcers, diarrhoea and rash are very common side effects (seen in 1 or more people in every 10). Other common side effects (seen in between 1 in 100 and 1 in 10 people) include dizziness, headache, stomach pain, constipation, indigestion (dyspepsia), wind (flatulence), feeling sick (nausea) and being sick (vomiting). However, the doses used for late intrauterine fetal death are usually much lower than those used for treating or preventing ulcers.

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

Prescribing misoprostol

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.

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?

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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