Package leaflet: Information for the user

Misodel 200 micrograms vaginal delivery system

Misoprostol

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Misodel is and what it is used for

Misodel contains the active substance misoprostol.
Misodel is used to help start the birth process from 36 weeks of pregnancy.

Misoprostol belongs to a group of medicines called prostaglandins. Prostaglandins have two actions during labour. One is to soften the mouth of the womb (cervix) so that the baby can more easily be born through the vagina. The second is to cause contractions to start, which will help push the baby out of the womb (uterus). There could be several reasons why you might need help to start this process. Ask your doctor if you want more information.

2. What you need to know before you are given Misodel

Do not use Misodel:

- if you are allergic to misoprostol or any of the other ingredients of this medicine (listed in section 6)
- if labour has started
- if your baby is not in good health and/ or is distressed
- if oxytocic drugs (medicines used to facilitate birth) and/or other medicines to induce labour are being given (see “Warnings and precautions” and “Other medicines and Misodel” below)
- if you have had previous cervical or womb surgery including a previous Caesarean birth for any earlier babies
- if you have any womb abnormality such as “heart-shaped” uterus (bicornate uterus)
- if your placenta is covering the birth canal (placenta praevia) or if you have had any unexplained vaginal bleeding after the 24th week of this pregnancy
- if your baby is not in the correct position in the womb to be born naturally (fetal malpresentation)
- if you have any signs or symptoms of inflammation of the waters that surround your baby (chorioamnionitis), unless treatment has already been given
- if you are less than 36 weeks pregnant.

Warnings and precautions
Misodel should only be used under the supervision of an appropriate specialist and where neccessary hospital facilities are readily available.

Your doctor or nurse will carefully monitor womb activity, status of your baby and changes in the neck of the womb (cervix) when Misodel is in place.

Misodel can cause strong womb stimulation if left in place after onset of labour (see "If you use more Misodel than you should" below).

Misodel can cause strong and prolonged womb contractions. When using Misodel the mother and unborn baby will be closely monitored to ensure that Misodel is removed timely. Sometimes it is necessary to add another medication (tocolytic treatment), which in most cases will resolve the contractions.

The effects of Misodel have not been studied in women with severe pre-eclampsia (a condition where the pregnant women suffer from high blood pressure, protein in the urine and possibly other complications).

Misodel has not been studied in women whose waters have been broken for more than 48 hours prior to insertion of Misodel. Please tell your doctor or if you think your waters might have broken (premature rupture of your membranes).

If you have an infection (Group B Streptococcus) that requires preventive antibiotic therapy, the antibiotic treatment may be given to you at the same time as Misodel or earlier so that you and your baby are treated before birth. If you know you have an infection, please tell your doctor or nurse.

If your doctor finds that treatment with oxytocin (medicine used to facilitate birth) should be started, Misodel must be removed by the doctor or nurse at least 30 minutes prior to oxytocin adminstration (see "Do not use Misodel" above and "Other medicines and Misodel" below).

A second dose of Misodel is not recommended, as the effects of a second dose have not been studied.

An increased risk of disseminated intravascular coagulation (severe bleeding) after delivery has been described in patients whose labour has been induced by any method.

There is no experience with the use of Misodel to start the birth process in women who are pregnant with more than one baby and there is no experience with the use of Misodel in women who have had more than 3 previous babies delivered vaginally after 24 weeks of pregnancy.

Misodel is only used if you have a medical reason for needing help to start the birth process.

Other medicines and Misodel
Tell your doctor or nurse if you are using, have recently used or might use any other medicines. Some other medicines may influence the effect of Misodel.

Misodel must not be given at the same time as oxytocic drugs (medicines used to facilitate birth) and/or other medicines to help start labour (see "Do not use Misodel" and "Warnings and precautions" above).

Pregnancy and breast-feeding
Misodel is used to help start labour from week 36 of the pregnancy. Misodel should not be used at other phases of pregnancy.

Misoprostol acid may be excreted in colostrum (the fluid excreted by the breasts for the first 3 – 4 days after delivery) and breast milk, but the level and duration is expected to be very limited and should not hinder breast-feeding.

Fertility
Fertility will not be affected by use of Misodel to help start the birth process from 36 weeks of pregnancy.

Misodel contains Butylated hydroxyanisole
Misodel contains butylated hydroxyanisole which is used as an antioxidant that preserves the product. It is only present in trace amounts. Butylated hydroxyanisole can cause skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

3. How you are given Misodel

The recommended dose is one Misodel vaginal delivery system which contains 200 micrograms of misoprostol. The active ingredient, misoprostol, is released at an average rate of approximately 7 micrograms per hour over a 24 hour period.

Your doctor or nurse will place one Misodel in your vagina next to the neck of your womb (cervix). You will not do this yourself. Your doctor or nurse may coat Misodel with a small amount of lubricating jelly before putting it in place. Misodel can easily be pulled out by the doctor or nurse when it is time to remove it.

You will be lying down during this procedure and you will have to stay that way for about 30 minutes after insertion of Misodel.

Once placed in the vagina, Misodel takes up moisture and slowly releases misoprostol.

When using the toilet, please use caution to avoid removing Misodel by mistake. Tell the doctor or nurse if Misodel falls out at any time.

The doctor or nurse will decide how long Misodel will be kept in place, depending on your progress. Misodel can be left in place for up to 24 hours.

Your doctor or nurse will remove Misodel
- when labour starts when contractions are becoming regular
- in case of irregular contractions that are too strong, prolonged or too frequent and/or changes in the neck of the womb
- if your baby becomes distressed
- if 24 hours have elapsed since insertion

If Misodel falls out, it will not be replaced.

On removal of the product from the vagina, Misodel will have swollen to 2-3 times of its original size and be flexible.

Use in children and adolescents
Misodel has not been studied in pregnant women less than 18 years of age.

If you use more Misodel than you should
If Misodel is left in place after onset of active labour it may lead to increasing contractions or the baby may become distressed. Misodel will then be removed immediately by your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Very common: may affect more than 1 in 10 people:

- The unborn baby's heart rate changes during labour which may be a reason for concern (foetal heart rate disorder)
- The mother's womb contracts too frequently with and without affecting the newborn which may be a reason for concern (uterine contractions abnormal)
- The mother's womb contracts too frequently and the unborn baby's heart rate may be affected which may be a reason for concern (abnormal labour affecting foetus)
- The baby has a bowel movement in the womb which may be a reason for concern (meconium in amniotic fluid)

Common: may affect up to 1 in 10 people:

- The baby has difficulty in breathing immediately after birth (neonatal respiratory depression; transient tachypnoea of the newborn)
- Excessive vaginal bleeding after birth (postpartum haemorrhage)
- A contraction that lasts too long and may be a reason for concern (uterine hypertonus)
- Overall newborn condition depressed at birth (apgar score low)
- Increased acidity in the baby's blood (foetal acidosis)

Uncommon: may affect up to 1 in 100 people:

- Brain affected in the baby due to not enough oxygen (hypoxic-ischaemic encephalopathy)
- Nausea
- Vomiting
- Rash
- Unexpected bleeding from the vagina before delivery (antepartum haemorrhage)
- The placenta separates from the wall of the womb before the birth of the baby (premature separation of placenta)
- Itching of the genital area (pruritus genital)
- Increase in blood pressure
- Tearing of the womb (uterine rupture).

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any side effects not listed in this leaflet. You can also report side effects directly via <the national reporting system> <[to be completed nationally]>. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Misodel

Keep this medicine out of the sight and reach of children.

Store in a freezer (-10 to -25°C). No thawing is required prior to use.

Do not use this medicine after the expiry date which is stated on the foil and the carton after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Your doctor or nurse should throw away or dispose of medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Misodel contains

- The active substance is misoprostol.
  Each vaginal delivery system contains 200 micrograms of misoprostol and releases misoprostol at a mean rate of approximately 7 micrograms/hour over 24 hours..

- The other excipients are:
  Cross-linked hydrogel polymer (comprised of macrogol, 1,2,6- hexanetriol and dicyclohexyl-methane-4,4'-diisocyanate)

  butylated hydroxyanisole

  polyester retrieval system (knitted polyester yarn)

What Misodel looks like and contents of the pack
Misodel contains a reservoir of 200 micrograms misoprostol. Misodel is a small rectangular shaped piece of plastic contained in a cloth mesh retrieval system. The plastic is a hydrogel polymer which swells in the presence of moisture to release a contolled amount of misoprostol. The retrieval system has a long tape which allows the doctor or nurse to remove it when they need to.

1 x 200 micrograms vaginal delivery system
5 x 200 micrograms vaginal delivery system
5 x 200 micrograms vaginal delivery system (multipack).

Each vaginal delivery system is contained within an individual foil sachet produced from an aluminium foil laminated strip containing a desiccant and packed in a carton.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

To be completed nationally

Manufacturer
Ferring Controlled Therapeutics Limited
1 Redwood Place
Peel Park Campus
East Kilbride
Scotland G74 5PB

This medicinal product is authorised in the Member States of the EEA under the following names:

<{Name of the Member State}> <{Name of the medicinal product}>
<{Name of the Member State}> <{Name of the medicinal product}>

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The following information is intended for healthcare professionals only.

Misodel is supplied in an individual aluminium foil sachet. There is a “tear mark” on one side of the foil sachet. Open the package along the tear mark across the top of the sachet. Do not use scissors or other sharp objects which may cut the retrieval system.

Place Misodel high in the posterior vaginal fornix (Figure a). To ensure that Misodel remains *in situ*, it should be turned 90° so that it lies transversely in the posterior fornix of the vagina (Figure b). Water-soluble lubricants may be used to aid insertion when necessary.

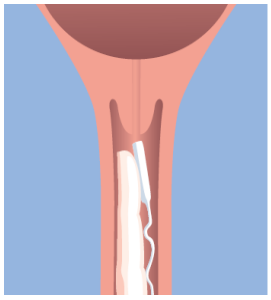

Figure a.

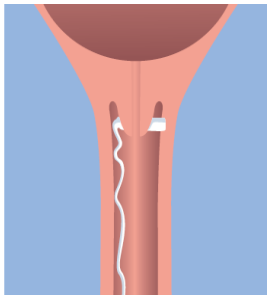

Figure b.

Figure c.

After Misodel has been inserted, the withdrawal tape may be cut with scissors always ensuring there is sufficient tape outside the vagina to allow removal.
The patient is to remain in bed for 30 minutes after insertion, but may be ambulatory thereafter. Take care not to inadvertently remove Misodel during toileting and vaginal examinations. Misodel is removed by gently pulling the tail of the retrieval system (Figure c).
The vaginal delivery system should NEVER be removed from the retrieval system.
Misodel is a controlled release formulation that swells in the presence of moisture, causing drug release to occur. During insertion, Misodel will swell to 2-3 times its original size and be pliable. After removal, ensure that the entire product (insert and retrieval system) has been removed from the vagina.