Package leaflet: Information for the patient

Prostin® E2 Sterile Solution 10 mg/ml
dinoprostone

[Pfizer logo]

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, nurse or pharmacist.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. see section 4.

What is in this leaflet

1. What Prostin E2 Sterile Solution is and what it is used for

Prostin E2 Sterile Solution contains the prostaglandin dinoprostone and is used to "induce" labour. This means that the medicine will help your uterus (womb) to start contracting and you will go into labour which will end the pregnancy. This is also called termination of pregnancy or an abortion. Dinoprostone is similar to the natural 'E2' type of prostaglandins which are made in your body when labour starts. It is an infusion which will be given into your blood through a vein (intravenous). It will only be given to you in a hospital or clinic which has a specialised obstetric unit.

You could need this treatment for different reasons:
- if your baby has died in your womb
- if it is required to end your pregnancy for health reasons
- if you have an abnormal growth of the placenta called a 'hydatidiform mole'.

2. What you need to know before you are given Prostin E2 Sterile Solution

Most women can be treated with Prostin E2 Sterile Solution. Some women may need extra checks during treatment and for some women a different treatment may be better. Your doctor or nurse will ask you questions before giving you Prostin E2 to make sure it is safe for you. If you do not understand any of the questions, ask your doctor or nurse to explain.

If you are having a pregnancy termination (abortion), it is very important for it to be complete. This is because prostaglandins given at this stage in pregnancy may cause abnormalities in the foetus. If your doctor thinks that the abortion has not worked completely, you will need another treatment, probably an operation.

Do not use Prostin E2 Sterile Solution:
- If you are allergic to dinoprostone or any other prostaglandin or any of the other ingredients of this medicine (listed in section 6). Signs of an allergic reaction include wheezing, breathlessness, swelling of the hands, face, itchy rash or redness of the skin.

Your doctor or nurse will not use Prostin E2 Sterile Solution to start or strengthen your labour in certain circumstances if:

- you have had a Caesarean section or any major surgery to your womb in the past.
- you have been told that you will have an obstructed labour.
- you have an infection of your womb, ovaries or tubes (pelvic inflammatory disease) unless you are receiving treatment for these, or if you have ever had such an infection in the past.
- you have current heart, lung, kidney or liver disease.

Warnings and precautions

Talk to your doctor or nurse before they use this medicine if you have or have had in the past any of the following conditions as they may want to monitor you more closely:

- heart, lung, kidney or liver disease
- glaucoma (raised pressure in the eye)
- epilepsy
- suffered from asthma
- hypertension (high blood pressure) at any time, including during this or any previous pregnancy
- been told you had abnormally strong contractions of your womb during a previous labour
- scarring of your womb from a previous operation
- are you 35 years or older?
- is your pregnancy over 40 weeks?
- do you have any complications related to this pregnancy?
- an increased risk of developing a generalised bleeding disorder, a condition known as post-partum disseminated coagulation.
- if you are having more than one baby
- if your water has broken.

Your doctor or nurse will ask you questions before giving you Prostin E2 Sterile Solution to make sure it is safe for you.

If you do not understand any of the questions, ask your doctor or nurse to explain.

Other medicines and Prostin E2 Sterile Solution

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Prostin E2 Sterile Solution can make you more sensitive to another medicine called oxytocin which is used to strengthen contractions. Medical staff will normally try not to use this medicine at the same time as Prostin E2 Sterile Solution. If used with this medicine in sequence, your doctor or nurse will watch over the womb contractions very carefully.

Pregnancy and breast-feeding

Prostin E2 Sterile Solution will only be given to you in the late stages of pregnancy to induce labour. Prostin E2 Sterile Solution is only used during pregnancy for therapeutic termination of pregnancy, missed abortion and hydatidiform mole.

Although prostaglandins are present in breast-milk, you are not expected to be breast-feeding as this medicine is used to terminate the pregnancy.

Prostin E2 Sterile Solution contains alcohol (ethanol)

Prostin E2 Sterile Solution contains 400 mg alcohol (ethanol) in each 0.5 ml ampoule which is equivalent to 800 mg/ml (80 % w/v). The amount of alcohol in 0.5 ml ampoule is equivalent to less than 10 ml beer or 4 ml wine.

The small amount of alcohol in this medicine will not have any noticeable effects.

Depending on the daily dose given to you this medicinal product will deliver different amounts of ethanol.

Driving and Using Machinery

In view of the indication for Prostin E2 Sterile Solution, this section is not applicable.

3. How Prostin E2 Sterile Solution is given to you

Prostin E2 Sterile Solution will be given to you by a trained professional in a hospital or clinic where facilities for monitoring you and your baby are available. Medical staff will be available at all times.

Prostin E2 Sterile Solution is diluted before use with a salt (saline) or sugar (dextrose) solution and given by an intravenous drip, into a vein.

Medical staff will adjust the dose to suit you. It depends on why you need the treatment and how you react to it. The mixture is made up to contain 5 micrograms/ml of Prostin E2 Sterile Solution and the drip is set to deliver 2.5 micrograms/minute. This is given for 30 minutes, after which the dose is either kept the same or increased to 5 micrograms/minute, depending on how you respond. It could then be increased again after a further four hours if necessary. The doctor or nurse will want to give you enough Prostin E2 Sterile Solution to keep you in labour, but they will want to make sure that the contractions do not become too strong.

The doctor or nurse will keep a very close eye on you during your treatment to make sure that the contractions do not become too strong, as this could cause your uterus to tear. They should be able to act quickly if you have side effects or if your womb reacts too strongly to the dose you are given. You might just need a lower dose, or you might need some other obstetric procedure.

You should not normally be given Prostin E2 Sterile Solution for more than two days at a time.

If you are given more Prostin E2 Sterile Solution than you should
Tell your doctor or nurse if you think you have been given too much Prostin E2 Sterile Solution. Symptoms of this would be excessive contractions of your womb (very strong, frequent and painful contractions) or severe side effects, such as feeling and being sick. If you have such symptoms, the rate at which Prostin E2 Sterile Solution is being given should be reduced, or the treatment should be stopped. If you have a massive overdose, so that the muscles of your womb become very tense and over-active or ruptures, you might need another obstetric procedure.

Your doctor or nurse will do internal checks to make sure that your cervix is opening enough. They will also check your contractions to make sure that they are not too strong.

4. Possible side effects

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

If you have asthma, Prostin E2 Sterile Solution could cause you to have an asthmatic attack by causing a narrowing of your airways (bronchospasm). **You must tell your doctor or nurse if you suffer from asthma or if you start having difficulty in breathing.**

Rare: may affect up to 1 in 1,000 people
Rare but serious side effects which can sometimes happen include the following:

- Tearing or bursting of the wall of your womb (uterine rupture)
- Heart attack
- Allergic/anaphylactic reactions, including anaphylactic shock (serious allergic reactions which can include skin rash, itching, wheezing, shortness of breath, swollen face, lips, hands, fingers, neck and throat, sudden drop in blood pressure, abdominal pain and collapse).

If you get any of these symptoms please tell your doctor or nurse straight away.

Common: may affect up to 1 in 10 people

- Vomiting (being sick)
- Nausea (feeling sick)
- Diarrhoea.

Not known: frequency cannot be estimated from the available data
As prostaglandins make the body go into labour in the same way as it would happen naturally, anything that can happen in a natural labour can also happen if you have been given Prostin E2 Sterile Solution. This includes:

- Vaso-vagal symptoms (flushing, shivering, headache, dizziness, fainting)
- Detached placenta
- Sudden blockage of a blood vessel with amniotic fluid (the fluid which surrounds the baby) or by a blood clot in the lungs. This could cause chest pain and shortness of breath.
- Abnormally strong, frequent or long contractions of the womb
- High blood pressure in the mother
- Very quick opening of the cervix
- Running a high temperature
- Backache
- Rash
- Foetal death, stillbirth and death of the newborn baby (neonatal death); especially following serious events such as tearing of the womb.

Talk to your doctor or nurse about this if you want to know more, as they will be able to give you the information that you need.

In some women the number of white blood cells rises during treatment. This will not cause you any symptoms, but your doctor or nurse may mention this if you have a blood sample taken.

You might have reddening and irritation in the area around the needle for two to five hours after the needle has been removed.

A higher risk of a generalised bleeding disorder following delivery (post-partum disseminated intravascular coagulation-DIC) has been described in women who:

- are aged 35 and above.
- whose pregnancies are more than 40 weeks.
- who have pregnancy-related complications.

Reporting of side effects

If you get any side effects, or you are worried about anything unusual happening during your labour, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Prostin E2 Sterile Solution

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

Prostin E2 Sterile Solution will not be given to you after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

The hospital pharmacist will store this medicine in a refrigerator at 2-8°C before use.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Prostin E2 Sterile Solution contains
The active substance is dinoprostone. Each 1 ml of solution contains 10 mg of dinoprostone.
The other ingredient is ethanol (see section 2 Prostin E2 Sterile Solution contains alcohol (ethanol)).

What Prostin E2 Sterile Solution looks like and contents of the pack
Each pack contains:
- one small, closed glass container (ampoule) containing 0.5 ml of a colourless, sterile solution
- one infusion bag label.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Pfizer Limited
Ramsgate Road
Sandwich
Kent
CT13 9NJ
UK

Manufacturer
Pfizer Manufacturing Belgium NV
Rijksweg 12
B-2870 Puurs
Belgium

For any information on this medicine, please contact Pfizer Medical Information on: 01304 616161.

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The following information is intended for healthcare professionals only:

Prostin® E2 Sterile Solution 10 mg/ml
dinoprostone

[Pfizer logo]

For intravenous use only.

NAME OF THE MEDICINAL PRODUCT

Prostin E2 Sterile Solution 10 mg/ml.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 10 mg dinoprostone (5 mg per ampoule).
Following dilution in accordance with instructions, each ml of the resultant solution for infusion contains 5 micrograms dinoprostone.

Excipient with known effect:
Prostin E2 Sterile Solution 10 mg/ml contains 400 mg anhydrous ethanol in each 0.5 ml ampoule which is equivalent to 800 mg/ml (80% w/v).

PHARMACEUTICAL FORM

Concentrate for solution for infusion (sterile concentrate).

The concentrate is a clear, colourless, alcoholic solution free from particulate matter, for intravenous administration after appropriate dilution.

CLINICAL PARTICULARS

Therapeutic indications

Oxytocic agent. Prostin E2 Sterile Solution 10 mg/ml is indicated for the therapeutic termination of pregnancy, missed abortion and hydatidiform mole by the intravenous route.

Posology and method of administration

Usage is restricted to qualified health care professionals and to hospitals and clinics with specialised obstetric units with facilities for continuous monitoring.

The recommended dose should not be exceeded, and the dosing interval should not be shortened as this increases the risk of uterine hyperstimulation, uterine rupture and uterine haemorrhage.

Posology

Adults

Directions for the Preparation of a Dilute Solution:

For use by IV drip (a drip set delivering 60 drops per ml must be used) or constant rate infusion pump. Withdraw 0.5 ml from the ampoule using an aseptic technique and add to 1,000 ml of sterile normal saline or 5% dextrose. Shake to ensure uniformity.

After dilution, attach the infusion bag label provided. Use dilute solution within 24 hours of preparation and store in a refrigerator at 2-8°C.

The following is a guide to dosage:
A solution of Prostin E2 Sterile Solution in normal saline or 5% dextrose containing 5.0 micrograms per ml should be prepared in accordance with instructions given above. The initial rate of infusion (pump or IV drip delivering 60 drops per ml) will be 2.5 micrograms per minute, and this rate should be maintained for at least the first 30 minutes. If a satisfactory uterine contractility response is produced, this rate should be maintained; if not, the rate should be increased to 5 micrograms per minute. If satisfactory uterine activity is not produced after at least 4 hours at this rate of infusion, the rate may be increased up to 10 micrograms per minute, side-effects permitting, and maintained until abortion occurs or the treatment is considered a failure. If significant side-effects occur, the rate of infusion should be decreased by 50% or discontinued.

If a constant rate infusion pump is used, a different concentration of solution (e.g. 15 micrograms per ml) may be required, dependent on the type of pump, but the dose rates (micrograms per minute) should remain as above.

The appearance of uterine hypertonus requires cessation of therapy until the state returns to normal. The situation should be re-assessed and, if necessary, the infusion can be recommenced, but at lower dosage rates, 50% of the last dose level used.
In all cases the dosage should be adapted to the patient's response. Continuous administration of the drug for more than two days is not recommended.

Elderly

Not applicable.

Paediatric population

Not applicable.

Method of administration

For intravenous administration only.

Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 of SmPC.
Prostin E2 Sterile Solution should not be used where the patient is sensitive to prostaglandins.

Prostin E2 Sterile Solution 10 mg/ml is not recommended in the following circumstances:

- For patients in whom oxytocic drugs are generally contra-indicated or where prolonged contractions of the uterus are considered inappropriate such as:
  - Cases with a history of Caesarean section or major uterine surgery.
  - Cases where there is evidence of a potential for obstructed labour.
- In patients with a past history of, or existing, pelvic inflammatory disease, unless adequate prior treatment has been instituted.
- Patients with active cardiac, pulmonary, renal or hepatic disease.

Special warnings and precautions for use

This product is only available to hospitals and clinics with specialised obstetric units and should only be used where 24-hour resident medical cover is provided.

Use caution in handling this product to prevent contact with skin. Wash hands thoroughly with soap and water after administration.

As with any oxytocic agent, the risk of uterine rupture should be considered. Concomitant medication and maternal status should be taken into consideration in order to minimise the risk of uterine hyperstimulation, uterine rupture and uterine haemorrhage. Careful and regular monitoring of uterine activity should be conducted during use of dinoprostone. Patients who develop uterine hypertonus or hypercontractility should be managed in a manner that addresses the welfare of the mother.

It is advised that Prostin E2 Sterile Solution should not be administered by the intramyometrial route since there have been reports of a possible association between this route of administration and cardiac arrest in severely ill patients.

Caution should be exercised in the administration of Prostin E2 Sterile Solution in patients with:

- asthma or a history of asthma
- epilepsy or a history of epilepsy
- glaucoma or raised intra-ocular pressure
- compromised cardiovascular, hepatic, or renal function
- hypertension
- ruptured chorioamniotic membranes.

Dinoprostone should be used with caution in patients with multiple pregnancy.

Animal studies lasting several weeks at high doses have shown that prostaglandins of the E and F series can induce proliferation of bone. Such effects have also been noted in newborn infants who received prostaglandin E_1 during prolonged treatment. There is no evidence that short-term administration of prostaglandin E_2 can cause similar bone effects.

Women aged 35 years or older, those with complications during pregnancy and those with a gestational age over 40 weeks have been shown to have an increased risk of post-partum disseminated intravascular coagulation. In addition, these factors may further increase the risk associated with labour induction (see section 4.8 of SmPC). Therefore, in these women, use of dinoprostone should be undertaken with caution. Measures should be applied to detect as soon as possible an evolving fibrinolysis in the immediate post-partum phase.

<u>Excipient information:</u>

Ethanol (alcohol)

Each 0.5 ml ampoule of Prostin E2 Sterile Solution 10 mg/ml contains 400 mg anhydrous ethanol (see section 2 of SmPC), which is equivalent to less than 10 ml beer or 4 ml wine.

The small amount of ethanol in this medicine will not have any noticeable effects.

Depending on the daily dose administered this medicinal product will deliver varying amounts of ethanol.

Interaction with other medicinal products and other forms of interaction

The response to oxytocin may be accentuated in the presence of exogenous prostaglandin therapy. Concurrent use with other oxytocic agents is not recommended. A dosing interval of at least 6 hours is recommended in case of oxytocin use is considered necessary following dinoprostone administration. If used in sequence, the patient's uterine activity should be carefully monitored.

Fertility, pregnancy and lactation

Pregnancy

Prostin E2 Sterile Solution 10 mg/ml is only used during pregnancy for therapeutic termination of pregnancy, missed abortion and hydatidiform mole. There has been some evidence in animals of a low order of teratogenic activity, therefore, if abortion does not occur or is suspected to be incomplete as a result of prostaglandin therapy (as in spontaneous abortion, where the process is sometimes incomplete), the appropriate treatment for complete evacuation of the pregnant uterus should be instituted in all instances.

Breast-feeding

Prostaglandins are excreted in breast milk. This is not expected to be a hazard given the circumstances in which the product is used.

Effects on ability to drive and use machines

In view of the indication for Prostin E2 Sterile Solution 10 mg/ml, this section is not applicable.

Undesirable effects

Cardiac disorders: Cardiac arrest
Vascular disorders: Hypertension
Gastrointestinal disorders: Diarrhoea, nausea, vomiting
General disorders and administration site conditions: Fever, local tissue irritation / erythema (injection site), temporary pyrexia, local infections
Immune system disorders: Hypersensitivity reactions such as anaphylactoid reactions and anaphylactic reactions including anaphylactic shock
Investigations: Elevated WBC
Musculoskeletal and connective tissue disorders: Back pain
Nervous system disorders: Transient vasovagal symptoms (flushing, shivering, headache, dizziness)
Pregnancy, puerperium and perinatal conditions: Foetal death, stillbirth, neonatal death* (Frequency not known- cannot be estimated from the available data)

Maternal-related conditions: Uterine hypertonus, uterine rupture, abruptio placenta, pulmonary amniotic fluid embolism, rapid cervical dilatation

*Foetal death, stillbirth, and neonatal death have been reported after application of dinoprostone, especially following the occurrence of serious events such as uterine rupture (see sections 4.2, 4.3 and 4.4 of SmPC).

Respiratory, thoracic and mediastinal disorders: Asthma, bronchospasm
Blood and lymphatic system disorders: An increased risk of post-partum disseminated intravascular coagulation has been described in patients whose labour was induced by pharmacological means, either with dinoprostone or oxytocin (see section 4.4 of SmPC). The frequency of this adverse event, however, appears to be rare (<1 per 1,000 labours).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Overdose

Overdosage may be expressed by uterine hypercontractility and uterine hypertonus. During use, uterine activity and the progression of cervical dilation should be carefully monitored to detect possible evidence of undesired responses, e.g. hypertonus or sustained uterine contractions. Because of the transient nature of prostaglandin E_2 (PGE_2)-induced myometrial hyperstimulation, non-specific, conservative management should be used (rate of infusion should be decreased or discontinued, maternal position change and administration of oxygen). If conservative management is not effective, a tocolytic agent may be used in appropriate patients as a treatment of hyperstimulation following administration of PGE_2 or appropriate measures should be considered.

PHARMACEUTICAL PARTICULARS

List of excipients

Ethanol, anhydrous

Incompatibilities

Not applicable.

Shelf life

2 years.

Special precautions for storage

Store in a refrigerator at 2-8°C.

Once diluted, the diluted solution should be stored in a refrigerator at 2-8°C and used within 24 hours.

Nature and contents of container

Ph. Eur. Type I glass ampoule, containing 0.5 ml sterile solution, packed in a carton.

Special precautions for disposal and other handling

Use caution in handling this product to prevent contact with skin. Wash hands thoroughly with soap and water after administration.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

MARKETING AUTHORISATION HOLDER

Pfizer Limited

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MARKETING AUTHORISATION NUMBER(S)

PL 00057/1027

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