Package leaflet: Information for the patient

Prostin® E2 Sterile Solution 1 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, midwife or pharmacist. If you get any side effects, talk to your doctor, midwife 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. 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.

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 midwife 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 midwife to explain.

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 midwife 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.
- you have been told that your baby is too big for your pelvis, is lying awkwardly or may be physically stressed.
- your baby is not lying with his or her head down.
- there has been or there is suspected foetal distress (your baby is short of oxygen).
- you had a difficult labour or traumatic delivery in a previous pregnancy.

- you had any abnormal contractions of your womb that were too strong or went on for too long during a previous 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 been told that you have or might have placenta praevia (where the placenta lies across the entrance to the womb, rather than being high up and out of the way during birth). This causes bleeding from the vagina during pregnancy and may require that your baby is delivered by Caesarean section.
- during your pregnancy you have had bleeding from the vagina or spotting at any time during months four to nine (second and third trimester) of your pregnancy.
- you have current heart, lung, kidney or liver disease.

Warnings and precautions
Tell your doctor or midwife 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 midwife 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 midwife 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 midwife 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.

Although prostaglandins are present in breast-milk they will not harm your baby and you may breast-feed as normal after delivery.

Prostin E2 Sterile Solution contains alcohol (ethanol)

Prostin E2 Sterile Solution contains 600 mg alcohol (ethanol) in each 0.75 ml ampoule which is equivalent to 800 mg/ml (80 % w/v). The amount of alcohol in 0.75 ml ampoule is equivalent to less than 15 ml beer or 6 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. Prostin E2 Sterile Solution is given by an intravenous drip, into a vein. It is always diluted before use with a saline (salt) or dextrose (sugar) solution. Your doctor or midwife will adjust the dose to suit you.

The mixture is made up to contain 1.5 micrograms/ml of Prostin E2 Sterile Solution and the drip is set to deliver 0.25 micrograms/minute for 30 minutes. This dose is then either kept the same or increased. (If the baby has died (a 'still birth'), a higher dose may be needed so the drip may be set to deliver 0.5 micrograms/minute and this may be adjusted hourly).

Your doctor or midwife will be keeping a very close eye on you during your treatment. They should be able to act quickly if you have side effects. If your baby becomes distressed or the muscles of your womb become very tense (uterine hypertonus), or your contractions become very strong and painful your doctor or midwife will stop your treatment temporarily. When the muscles of your womb have relaxed and your baby is not distressed any more your doctor or midwife may start your treatment again with half the last dose used. If your doctor or midwife stops your treatment temporarily and your condition does not return to normal then he or she may deliver your baby by Caesarean section.

If labour does not start within the first 12 to 24 hours of you being given prostaglandin E_2, your doctor or midwife will stop treatment.

Your doctor or midwife 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) and your baby (to make sure he or she does not get distressed).

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 midwife if you suffer from asthma or if you start having difficulty in breathing.**

Very common: may affect more than 1 in 10 people
- Vomiting (being sick)
- Nausea (feeling sick)
- Diarrhoea

- Irritation and/or reddening of the skin at the site of injection
- Slowing or quickening of the baby's heart rate and distress in the baby
- Low Apgar score – a baby born with an Apgar score lower than seven. The Apgar score, which is measured on a scale of one to ten, is used to describe the baby's condition at birth. A low Apgar score means that the baby's heart or lungs are not working properly

Common: may affect up to 1 in 10 people
- Vasovagal symptoms (flushing, shivering, headache, dizziness)
- High blood pressure
- Problems (distress) for the unborn child
- Abnormally strong, frequent or long contractions of the womb

Uncommon: may affect up to 1 in 100 people
- Excessive contraction of the airway muscles causing breathing difficulty (bronchospasm)
- Placenta becoming detached
- High body temperature (fever)

Rare: may affect up to 1 in 1 000 people
- Abnormal blood clotting throughout the body's blood vessels

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:
- Serious allergic (hypersensitive) reactions with widespread effects such as shortness of breath, skin rashes and low blood pressure including anaphylactic shock - sudden, severe allergic reaction with breathing difficulty, swelling, lightheadedness, fast heartbeat, sweating and loss of consciousness
- Heart attack (cardiac arrest)
- Asthma
- Back pain
- Tearing of the womb
- Sudden blockage of a blood vessel with amniotic fluid (the fluid which surrounds the baby) or by blood clots in the lungs. This could cause chest pain and shortness of breath
- Very quick opening of the cervix
- Breathing problems for the baby (neonatal distress)
- Foetal death, stillbirth and death of the newborn baby (neonatal death); especially following serious events such as tearing of the womb
- Local infections
- Increased amount of white blood cells

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

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

Studies have shown proliferation (thickening) of bone in new-born infants who have been treated with prostaglandins for a long time. There is no evidence that this occurs following short-term treatment with Prostin E2 Sterile Solution.

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, midwife 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 1 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 0.75 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
2870 Puurs-Sint-Amands
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 1 mg/ml
dinoprostone

[Pfizer logo]

NAME OF THE MEDICINAL PRODUCT

Prostin E2 Sterile Solution 1 mg/ml.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 1 mg dinoprostone (750 micrograms per ampoule).
Following dilution in accordance with instructions, each ml of the resultant solution for infusion contains 1.5 micrograms dinoprostone.

Excipient with known effect:

Prostin E2 Sterile Solution 1 mg/ml contains 600 mg anhydrous ethanol in each 0.75 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, which after appropriate dilution is intended for intravenous administration to human beings.

CLINICAL PARTICULARS

Therapeutic indications

Oxytocic agent. Prostin E2 Sterile Solution 1 mg/ml is indicated for the induction of labour 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, uterine haemorrhage, foetal and neonatal death.

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 0.75 ml from the ampoule using an aseptic technique and add to 500 ml sterile normal saline or 5% dextrose. Shake to ensure uniformity.
After dilution attach label provided. Use dilute solution within 24 hours of preparation and store in a refrigerator at 2-8°C.
The dose of Prostin E2 Sterile Solution used, normally depends not only upon the indication, but also on patient response.

The following is a guide to dosage:
Dilute with normal saline or 5% dextrose to produce a 1.5 micrograms/ml solution. The 1.5 micrograms/ml solution is infused at 0.25 micrograms/minute for 30 minutes and then maintained or increased. Cases of foetal death *in utero* may require higher doses. An initial rate of 0.5 micrograms/minute may be used with stepwise increases, at intervals of not less than one hour.
The appearance of foetal distress or 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.
If no response is seen within the first 12-24 hours of treatment, the medication should be discontinued.

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 1 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 cephalopelvic disproportion.
  - Cases in which foetal malpresentation is present.
  - Cases where there is clinical suspicion or definite evidence of pre-existing foetal distress.
  - Cases in which there is a history of difficult labour and/or traumatic delivery.
- In patients with a past history of, or existing, pelvic inflammatory disease, unless adequate prior treatment has been instituted.
- In patients where there is clinical suspicion or definite evidence of placenta praevia or unexplained vaginal bleeding during this pregnancy.
- 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, maternal and foetal status should be taken into consideration in order to minimise the risk of uterine hyperstimulation, uterine rupture, uterine haemorrhage, foetal and neonatal death. Careful and regular monitoring of uterine activity and foetal heart rate should be conducted during use of dinoprostone. Patients who develop uterine hypertonus or hypercontractility, or in whom unusual foetal heart rate patterns develop, should be managed in a manner that addresses the welfare of the foetus and 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 1 mg/ml for the induction of labour 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.

In labour induction, cephalopelvic relationships should be carefully evaluated before use of Prostin E2 Sterile Solution. During use, uterine activity, foetal status and the progression of cervical dilation should be carefully monitored to detect possible evidence of undesired responses, e.g. hypertonus, sustained uterine contractions, or foetal distress.

In cases where there is a known history of hypertonic uterine contractility or tetanic uterine contractions, it is recommended that uterine activity and the state of the foetus (where applicable) should be continuously monitored throughout labour. The possibility of uterine rupture should be borne in mind where high-tone uterine contractions are sustained.

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.

Excipient Information

Ethanol (alcohol)

Each 0.75 ml ampoule of Prostin E2 Sterile Solution 1 mg/ml contains 600 mg anhydrous ethanol (see section 2), which is equivalent to less than 15 ml beer or 6 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 1 mg/ml is only used during pregnancy, to induce labour.

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 1 mg/ml, this section is not applicable.

Undesirable effects

System Organ Class	**Very Common ≥1/10**	**Common ≥1/100 to <1/10**	**Uncommon ≥1/1 000 to <1/100**	**Rare ≥1/10 000 to <1/1 000**	**Very Rare <1/10 000**	**Frequency Not Known (Cannot Be Estimated From Available Data)**
Blood and lymphatic system disorders				Disseminated intravascular coagulation		
Immune system disorders						Hypersensitivity, Anaphylactoid reaction, Anaphylactic reaction, Anaphylactic shock

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1 000 to <1/100	Rare ≥1/10 000 to <1/1 000	Very Rare <1/10 000	Frequency Not Known (Cannot Be Estimated From Available Data)
Nervous system disorders		Vasovagal symptoms (flushing, shivering, headache, dizziness)				
Cardiac disorders						Cardiac arrest
Vascular disorders		Hypertension				
Respiratory, thoracic and mediastinal disorders			Bronchospasm			Asthma
Gastrointestinal disorders	Diarrhoea, Nausea, Vomiting					
Musculoskeletal and connective tissue disorders						Back pain
Pregnancy, Puerperium and Perinatal conditions		Foetal distress syndrome, Uterine hypertonus, Uterine contractions abnormal	Premature separation of placenta			Uterine rupture, Anaphylactoid syndrome of pregnancy, Rapid cervical dilatation, Neonatal distress, Death neonatal, Stillbirth, Foetal death
General disorders and administration site conditions	Injection site irritation, Injection site erythema		Pyrexia			Local infections
Investigations	Apgar score low, Foetal heart rate abnormal					White blood cell count increased

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

Over dosage may be expressed by uterine hypercontractility and uterine hypertonus. During use, uterine activity, foetal status and the progression of cervical dilation should be carefully monitored to detect possible evidence of undesired responses, e.g. hypertonus, sustained uterine contractions, or foetal distress. Because of the transient nature of prostaglandin E_2 (PGE_2)-induced myometrial hyperstimulation, non-specific, conservative management was found to be effective in the vast majority of cases: i.e. maternal position change and administration of oxygen to the mother. If conservative management is not effective, ß-adrenergic drugs may be used as a treatment of hyperstimulation following administration of PGE_2 for cervical ripening, in appropriate patients.

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 0.75 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
Ramsgate Road
Sandwich
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CT13 9NJ
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MARKETING AUTHORISATION NUMBER(S)

PL 00057/1028

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