Prostin ® E2 1 mg and 2 mg Vaginal Gels
dinoprostone

PHYSICIAN LEAFLET

Prostin® E2 1 mg and 2 mg Vaginal Gels
(dinoprostone)

Presentation
Translucent, thixotropic gel containing 1 or 2 mg dinoprostone per 3 g (2.5 ml).

Uses
Oxytocic. Prostin E2 Vaginal Gel is indicated for induction of labour, when there are no foetal or maternal contraindications.

Dosage and 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.

In primigravida patients with unfavourable induction features (Bishop score of 4 or less), an initial dose of 2 mg should be administered vaginally. In other patients an initial dose of 1 mg should be administered vaginally.

In both groups of patients, a second dose of 1 mg or 2 mg may be administered after 6 hours as follows:
1 mg should be used where uterine activity is insufficient for satisfactory progress of labour.

2 mg may be used where response to the initial dose has been minimal.

Maximum dose 4 mg in unfavourable primigravida patients or 3 mg in other patients (see section 4.4 of SmPC).

The gel should be inserted high into the posterior fornix avoiding administration into the cervical canal. The patient should be instructed to remain recumbent for at least 30 minutes.

Contraindications, warnings, etc.
Contraindications:
Prostin E2 Vaginal Gel should not be used where the patient is sensitive to prostaglandins or other constituents of the gel.

Prostin E2 Vaginal Gel is not recommended in the following circumstances:

1. For patients in whom oxytocic drugs are generally contraindicated 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;
- Multiple gestation;
- Engagement of the head has not taken place;

- Obstetric conditions where either maternal or foetal benefit / risk ratio favours surgical intervention.

2. In patients with a past history of, or existing, pelvic inflammatory disease, unless adequate prior treatment has been instituted.

3. In patients where there is clinical suspicion or definite evidence of placenta praevia or unexplained vaginal discharge and /or abnormal bleeding during this pregnancy.

4. Patients with active cardiac, pulmonary, renal or hepatic disease.

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.

The Clinician should be alert that the intracervical placement of dinoprostone gel may result in advertent disruption and subsequent embolization of antigenic tissue causing in rare circumstances the development of Anaphylactoid Syndrome of Pregnancy (Amniotic Fluid Embolism).

Effects on ability to drive and use machines:
Not applicable.

Other undesirable effects:
The most commonly reported events are vomiting, nausea and diarrhoea. Certain rare events that should be especially noted are: hypersensitivity reaction (e.g. anaphylactic reaction, anaphylactic shock, anaphylactoid reaction); uterine rupture and cardiac arrest.

Other adverse effects, reported with use of dinoprostone are:
- Pulmonary/amniotic fluid embolism;
- Abruptio placenta;
- Uterine hypercontractility or hypertonus;
- Foetal distress / altered foetal heart rate (FHR);
- Hypertension - systemic (maternal);
- Bronchospasm / asthma;
- Rapid cervical dilation;
- Fever;
- Backache;
- Rash;
- Vaginal symptoms - warmth, irritation, pain;
- Neonatal distress / low Apgar scores in the newborn;
- Coma;
- Foetal death, stillbirth, neonatal death*.

*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).

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).

Fertility, pregnancy and lactation:
Prostin E2 Vaginal Gel is only used during pregnancy, to induce labour.

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

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

Use the total contents of the syringe for one patient only. Discard after use. Use caution in handling the 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. Continuous electronic 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.

Prostin E2 Vaginal Gel and Prostin E2 Vaginal Tablets are not bioequivalent.

Caution should be exercised in the administration of prostaglandin E2 in patients with:

i asthma or a history of asthma;
ii epilepsy or a history of epilepsy;
iii glaucoma or raised intra-ocular pressure;
iv compromised cardiovascular, hepatic or renal function;
v hypertension;
vi 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 prostaglandin E2. 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. 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.

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 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 E1 during prolonged treatment. There is no evidence that short-term administration of prostaglandin E2 can cause similar bone effects.

Women aged 35 years or older, those with complications during the 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 those women the use of Prostin E2 Vaginal Gel should be done with caution. Measures should be applied to detect as soon as possible an evolving fibrinolysis in the immediate post-partum phase.

Overdose:
Uterine hypertonus or unduly severe uterine contractions have rarely been encountered, but might be anticipated to result from overdosage. Where there is evidence of foetal distress or uterine hypertonus,

then prompt delivery is indicated. Treatment of overdosage must be, at this time, symptomatic, since clinical studies with prostaglandin antagonists have not progressed to the point where recommendations may be made.

Pharmaceutical precautions
Store in a refrigerator 2°C-8°C. Keep out of the sight and reach of children. The contents of one syringe to be used for one patient. Do not use after/use by expiry date on the carton and syringe label. Discard after use.

Package quantities
Prostin E2 Vaginal Gel is available in single packs of 1 mg or 2 mg.

Further information
Unlike other oxytocics, prostaglandin E2 exhibits the capacity of the prostaglandins to influence uterine activity at any stage of gestation. Other Prostin E2 dosage forms are available for induction of labour (oral, vaginal and IV routes), foetal death in utero (IV route), therapeutic termination of pregnancy (IV and extra-amniotic routes), missed abortion and hydatidiform mole (IV route).

Marketing Authorisation Numbers

Ireland:
PA 822/178/1 Prostin E2 1 mg Vaginal Gel
PA 822/178/2 Prostin E2 2 mg Vaginal Gel

Malta:
MA 505/02202 Prostin E2 1 mg Vaginal Gel
MA 505/02203 Prostin E2 2 mg Vaginal Gel

Marketing Authorisation Holder

Ireland:
Pfizer Healthcare Ireland Unlimited Company
The Watermarque Building
Ringsend Road
Dublin 4
D04 K7N3
Ireland.

Malta:
Pfizer Hellas S.A.
243 Messoghion Ave.
Neo Psychiko 15451,
Greece

METHOD OF ASSEMBLY OF THE SYRINGE
1. Remove from packaging.
2. Remove the syringe cap from the syringe.
3. Insert syringe cap into barrel of syringe.

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Package Leaflet: Information for the user

Prostin® E2 1 mg and 2 mg Vaginal Gels
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Pfizer Logo

Read all of this leaflet carefully before you start using 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 Vaginal Gel is and what it is used for

Prostin E2 Vaginal Gel 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 will only be given to you in a hospital or clinic which has an obstetric and maternity unit.

2. What you need to know before you are given Prostin E2 Vaginal Gel

Most women can be treated with Prostin E2 Vaginal Gel. 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 Vaginal Gel 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 Vaginal Gel

- 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 hypersensitivity include wheezing, breathlessness, swelling of the hands, face, itchy rash or redness of the skin.

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

- you have heart, lung, kidney or liver disease
- you have had a Caesarean section or any major surgery to your womb
- the size of your baby's head means there may be a problem with the delivery
- 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 have a past history or existing 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 and the cause of the bleeding is not known
- your baby is not lying with his or her head down or the baby's head is not engaged
- you are expecting more than one baby e.g. twins, triplets
- the risks involved in proceeding with a normal delivery are higher than the benefits to either you or your baby and your doctor feels surgery is more suitable

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
- if any of the following apply to you:
    - you are 35 years or older
    - you have had complications during this pregnancy
    - you are over 40 weeks gestation
    - if so, you may have 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 Vaginal Gel 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 Vaginal Gel

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

Prostin E2 Vaginal Gel 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 Vaginal Gel. If you need this medicine, your doctor or midwife will make sure they are not given to you close together and will watch over the contractions very carefully.

Pregnancy, breast-feeding and fertility

Prostin E2 Vaginal gel 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.

Driving and using machines

No effect on your ability to drive or use machinery is expected after being given Prostin E2 Vaginal gel.

3. How Prostin E2 Vaginal Gel is given to you

Prostin E2 Vaginal Gel will be given to you by a trained professional in a hospital or clinic where facilities for monitoring you and your baby are available. Before you are given this medicine, you will be examined by your doctor or midwife. They need to know the position of your baby's head and how dilated (wide) your cervix (neck of the womb) is.

You will be given a numbered score after you have been examined. This is known as the Bishop score. The lower your Bishop score, the less ready you are to go into labour without any help. In this case, a higher dose of Prostin E2 Vaginal Gel is given.

Prostin E2 Vaginal Gel will be inserted into the posterior fornix (an area high up in your vagina) while you are lying down. You will then be asked to stay lying down for at least 30 minutes.

The usual dose is 1 mg. If this is your first pregnancy and you have a low Bishop score, you will be given 2 mg.

Your doctor or midwife may decide to give you a second dose of gel if you do not start having contractions or if you are only having weak contractions. Because this treatment can take a long time to have an effect in some women, your doctor or midwife will not give you a second dose until they are sure that it is needed. You should not have a second dose for at least six hours and many doctors and midwives will wait much longer than this. This means that you could even have your second dose the following day. You should not be given more than 4 mg in total.

Your doctor or midwife should be keeping a very close eye on you during your treatment. 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.

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 Vaginal Gel could cause you to have an asthmatic attack. **You must tell your doctor or midwife if you suffer from asthma or if you have difficulty 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 or anaphylactic reactions including anaphylactic shock (symptoms may include wheezing, breathlessness, swelling of the hands, face, neck or throat, itchy rash or redness of the skin, sudden drop in blood pressure, abdominal pain and collapse).

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

Common: may affect up to 1 in 10 people

- vomiting (being sick)
- nausea (feeling sick)

- diarrhoea

These have seldom been bad enough for the woman to stop the treatment.

Not known: frequency cannot be estimated from the available data
Women having prostaglandin E2 vaginally have experienced the following problems. These problems have also been seen in women not taking prostaglandins and include:

- 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
- placenta becoming detached
- abnormally strong, frequent or long contractions of the womb, slowing or quickening of the baby's heart rate and distress in the baby
- itching, soreness or rash of the vaginal area
- high blood pressure in the mother
- very quick opening of the cervix
- running a high temperature
- backache
- rash
- 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).
- fever
- alteration of conscious level (coma)
- severe bleeding disorder
- Foetal death, stillbirth and death of the newborn baby (neonatal death); especially following serious events such as tearing of the womb.

Studies have shown proliferation (thickening) of bone in newborn 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 Vaginal Gel.

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 Gel. 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.

Prostin Gel may be placed into the cervix. In this case, a rare event may occur where some fluid from the baby is released into the mother's bloodstream due to reasons not known (in some cases, the connection of the placenta to the wall of the uterine may have been damaged) and trigger a serious and potentially fatal reaction like a severe allergic reaction causing shortness of breath, fast pulse and low blood pressure (anaphylactoid reaction of pregnancy). In some cases, excessive bleeding may occur where normal clotting of your blood is lessened. Some of these symptoms may be indistinguishable from what you may experience at the time of labour. You may wish to discuss this with your doctor prior to use of Prostin Gel.

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, pharmacist or midwife. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see below details). By reporting side effects you can help provide more information on the safety of this medicine.

Ireland:
HPRA Pharmacovigilance. Website: www.hpra.ie.

Malta:
ADR Reporting

Website: www.medicinesauthority.gov.mt/adrportal

5. How to store Prostin E2 Vaginal Gel

The medicine will be kept out of the sight and reach of children.

Prostin E2 Vaginal Gel will not be given to you after the expiry date stated on the carton after 'EXP'. The expiry date refers to the last day of that month.

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

6. Contents of the pack and other information

What Prostin E2 Vaginal Gel contains

The active substance is called dinoprostone. Each 3 g (2.5 ml) syringe contains 1 mg or 2 mg of the active substance.
The other ingredients are triacetin and silica, colloidal anhydrous.

What Prostin E2 Vaginal Gel looks like and contents of the pack

Prostin E2 Vaginal Gel is packed in syringes that contain 1 mg or 2 mg of dinoprostone in 3 grams of gel. Each pack contains one pre-filled syringe and the syringes are for single use only.

Marketing Authorisation Holder:

Ireland:
Pfizer Healthcare Ireland Unlimited Company
The Watermarque Building
Ringsend Road
Dublin 4
D04 K7N3
Ireland
Malta:
Pfizer Hellas S.A.
243 Messoghion Ave.
Neo Psychiko 15451,
Greece

Manufacturer:
Pfizer Manufacturing Belgium NV
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2870 Puurs-Sint-Amands
Belgium

Company contact address:
For further information on your medicine contact Medical Information at the following address:
Pfizer Healthcare Ireland Unlimited Company, The Watermarque Building, Ringsend Road, Dublin 4, D04 K7N3, Ireland
Telephone: 1-800 633 363

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