SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Prostin E2 Sterile Solution 1 mg/ml.

2 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).

For the full list of excipients, see section 6.1.

3. 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.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oxytocic agent. Prostin E2 Sterile Solution 1 mg/ml is indicated for the induction of labour by the intravenous route.

4.2 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.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
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.

4.4 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). 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.

4.5 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.

4.6 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.

4.7 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.

4.8 Undesirable effects

The table below lists the adverse reactions identified through clinical trial experience and post-marketing surveillance by system organ class and frequency. Adverse reactions identified from post-marketing experience are included in italics. The frequency grouping is defined using the following convention: 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); and Not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1. Adverse Reactions

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
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

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)
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.

4.9 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Prostaglandins, ATC-code: G02AD02

Dinoprostone is a prostaglandin of the E series with actions on smooth muscle. It induces contraction of uterine muscle at any stage of pregnancy.

5.2 Pharmacokinetic properties

Dinoprostone is rapidly metabolised in the body. Intravenous administration results in very rapid distribution and metabolism, with only 3% of unchanged drug remaining in the blood after 15 minutes. At least nine PGE_2 metabolites have been identified in human blood and urine.

5.3 Preclinical safety data

There are no preclinical data of relevance which are additional to that already included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol, anhydrous.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 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 48 hours.

6.5 Nature and contents of container

Ph. Eur. Type I glass ampoule, containing 0.75 ml sterile solution, packed in a carton.

6.6 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.

7 MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich
Kent
CT13 9NJ
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00057/1028

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 June 1986

Date of latest renewal: 28 October 2004

10 DATE OF REVISION OF THE TEXT

21/06/2024