

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Prostin[®] E2 10 mg/ml

2 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).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection

The solution is a clear, colourless, alcoholic sterile solution, for intravenous administration after appropriate dilution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Therapeutic termination of pregnancy, missed abortion.

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.

Adults: Ampoule contents must be diluted before use and full instructions on method of dilution and dosage are given on the package insert which should be consulted prior to initiation of therapy. The following is a guide to dosage:

Dilute with normal saline or 5% dextrose according to the package insert to produce a 5 micrograms/ml solution. The 5 micrograms/ml solution is infused at 2.5 micrograms/minute for 30 minutes and then maintained or increased to 5 micrograms/minute. The rate should be maintained for at least 4 hours before increasing further.

Elderly: Not applicable.

Children: Not applicable.

4.3 Contraindications

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

Prostin[®] E2 10 mg/ml should not be used where the patient is sensitive to prostaglandins.

Prostin[®] E2 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.

4.4 Special warnings and precautions for use

<p>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.</p>
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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. 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.

It is advised that Prostin® E2 10 mg/ml 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 10 mg/ml 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 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 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 0.5 ml ampoule of Prostin E2 Sterile Solution 10 mg/ml contains 400 mg anhydrous ethanol (see section 2), 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.

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 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.

4.7 Effects on ability to drive and use machines

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

4.8 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).

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). 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form <https://sideeffects.health.gov.il/>

4.9 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 E₂ (PGE₂-)-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 PGE₂ or appropriate measures should be considered.

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 PGE₂ metabolites have been identified in human blood and urine.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber 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

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store in a refrigerator at 2° - 8°C.

6.5 Nature and contents of container

Prostin E2 10 mg/ml WC 080821

Type I glass ampoule, containing 0.5 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.

7. License holder

Pfizer PFE Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725

Revised in 08/2021 according to MoH guidelines