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 and uterine haemorrhage.

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

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 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 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 0.5 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

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
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. 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 E_2 (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 PGE_2 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

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

Revised in 09/2024