

## Prescribing Information

# Prostin™ E2 Sterile solution (dinoprostone, 10 mg per ml)

For intrauterine (extra-amniotic) administration.

### Presentation

0.5 ml ampoule of colorless sterile solution containing 10 mg/ml dinoprostone, prostaglandin E2, in alcohol.

### Pharmacology

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

### Pharmacokinetics

Dinoprostone is rapidly metabolized in the body. When given extra-amniotically, prostaglandin E2 levels in amniotic fluid rise rapidly with peak levels achieved between 1.5 and 2 hours after administration.

### Indications

PROSTIN E2 is indicated for therapeutic termination of pregnancy and missed abortion, as a non-surgical treatment by vaginal application, as follows:

1. PROSTIN E2 is indicated as a therapeutic abortifacient during the first or second trimester of pregnancy.
2. PROSTIN E2 can be used for evacuation of the uterus in cases of missed abortion.
3. PROSTIN E2 can be used as an alternative measure to complete therapeutic termination of pregnancy when intra-amniotic saline injections have failed.

Clinical experience to date indicates that PROSTIN E2 administered by the extra-amniotic route is more effective and better tolerated than by the intravenous route.

### Directions for the preparation of dilute solutions from the 10 mg/ml sterile solution

*For extra-amniotic use for therapeutic termination of pregnancy (100 micrograms per ml)*

Withdraw 0.5 ml from the ampoule, using an aseptic technique, and add to 50 ml of diluent (bacteriostatic saline). Shake to ensure uniformity. After dilution, affix a label and store in the refrigerator at 4°C if not used immediately.

Use diluted solution within 48 hours of preparation.

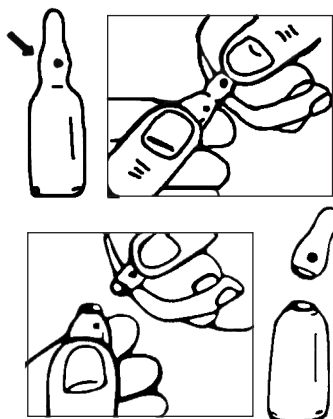
### Dosage

In all cases the dose should be adapted to the patient's response.

A solution containing 100 micrograms per ml PROSTIN E2 should be prepared using the diluent provided as described earlier in this leaflet. This should be instilled into the extra-ovular space via a 12-14 French gauge Foley catheter with self-retaining balloon (a fine polythene catheter may also be used). After filling the catheter system dead space with a predetermined quantity of dilute drug solution, the initial instillation should be 1 ml. Subsequent instillations will vary between 1 and 2 ml (usually 2 ml) in accordance with uterine response. Two hours should usually elapse between each instillation and never less than 1 hour. Continuous administration of the drug for more than two days is not recommended.

### IMPORTANT

No ampoule file is needed to open the ampoules. The neck of the ampoule is prescored at the point of constriction. A colored dot on the ampoule head helps to orientate the ampoule. Take the ampoule and face the colored dot. The ampoule opens easily by placing the thumb on the colored dot and gently pressing downwards as shown.



### Contraindications

The use of PROSTIN E2 is contraindicated:

1. In patients with a history of hypersensitivity to prostaglandins.
2. Patients with known pelvic infections should receive adequate treatment prior to attempting to induce termination of pregnancy.

3. The extra-amniotic route of administration should not be employed in the presence of cervicitis or vaginal infections.
4. Patients already receiving intravenous oxytocic drugs.

### Warnings

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, the appropriate treatment for complete evacuation of the pregnant uterus should be instituted in all instances.

The product should only be used where 24 hours medical cover is provided.

### Precautions

Caution should be exercised in the administration of PROSTIN E2 for therapeutic termination of pregnancy in patients with

- (i) glaucoma or raised intraocular pressure,
- (ii) asthma or history of asthma,
- (iii) epilepsy or a history of epilepsy,
- (iv) active cardiac, pulmonary, renal or hepatic disease or
- (v) hypertension.

As with any oxytocic agent, PROSTIN E2 should be used with caution in patients with compromised (scarred) uteri.

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 PROSTIN E2 can cause similar bone effects.

### Drug interactions

Oxytocin or other oxytocics

(concurrent or sequential use with dinoprostone may potentiate the effects of oxytocin, possibly resulting in uterine hypertonus, which may cause uterine rupture or cervical laceration, especially in the absence of adequate cervical dilatation; although combinations are sometimes used to therapeutic advantage, oxytocin administration should be begun 6 to 12 hours after administration of dinoprostone vaginal suppository or cervical gel and 12 to 24 hours after administration of the vaginal gel and the patient should be continuously monitored)

### Side effects

Clinical studies at recommended doses have not revealed any life-threatening adverse reactions. Where seen, adverse effects have generally been dose dependent, transient, and reversible on discontinuation of therapy. Nausea and/or vomiting and diarrhoea are frequently observed with the lower dose required by the extra-amniotic route.

Some transient vasovagal symptoms have been reported, including flushing, shivering, headache, and dizziness.

Certain rare events that should be especially noted are: hypersensitivity to the drug; uterine rupture and cardiac arrest. Other adverse events, in decreasing order of severity, reported with use of dinoprostone are: pulmonary/amniotic fluid embolism; uterine hypercontractility or hypertonus; hypertension - systemic (maternal); bronchospasm/asthma; rapid cervical dilation; fever; back ache; rash.

A temporary pyrexia and elevated WBC are not usual, but both have reverted after termination of therapy.

As with other intrauterine techniques, the risk of local infection when employing the extra-amniotic route must be borne in mind and appropriate therapy initiated if necessary.

### Storage

The product should be stored in a refrigerator at 4°C. Do not freeze. Dilute solutions for IV or EA use should be used within 24 or 48 hours respectively.

### Further information

PROSTIN E2 (dinoprostone) is the synthetic or partially synthetic naturally occurring prostaglandin E2.

#### Actions

Although the exact mode of action in pregnancy termination in humans is not fully defined, when PROSTIN E2 is administered by the intravenous or extra-amniotic route it initiates rhythmical uterine contractions which, if continued for a sufficient time, are capable of expelling the contents of the uterus.

Sensitivity of the pregnant uterus to prostaglandins is lower during early and mid-pregnancy than at term.

While PROSTIN E2 has been shown to be luteolytic in several animal species, it is unlikely that this is the principal mechanism involved when the drug is utilised in the therapeutic termination of pregnancy in the human as described in this leaflet.

PROSTIN E2 is also capable of inducing contractions of the smooth muscle of the intestinal tract. This action may be the cause of the vomiting and diarrhoea which are associated with the use of PROSTIN E2 but this has yet to be shown conclusively.

In some animals and in man, large doses of PROSTIN E2 can bring about a decrease in blood pressure probably due to its effect on vascular smooth muscle. At the doses recommended for therapeutic termination of pregnancy, this effect has not been clinically significant.

### Manufacturer

Pfizer Manufacturing Belgium NV/SA.

### License Holder

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