Prescribing Information

PROSTIN F2 ALPHA STERILE SOLUTION
(dinoprost tromethamine)

For intra-amniotic administration only.

Presentation

One ampoule containing a colourless, sterile, aqueous solution of dinoprost tromethamine equivalent to 5 mg per ml dinoprost (prostaglandin $F_{2\alpha}$). Also contains benzyl alcohol and water for injection.

Therapeutic indications

Oxytocic agent. Prostin F2 Alpha Sterile Solution is indicated for use by the intra-amniotic route in the therapeutic termination of pregnancy in the second trimester.

Dosage and administration

The initial dose of Prostin F_2 Alpha Sterile Solution is 40 mg (8 ml) administered into the amniotic cavity. Preceding administration, an amniocentesis should be performed, withdrawing at least 1 ml of amniotic fluid with an appropriately-sized needle, to confirm the presence of the needle in the amniotic sac. Prostin F2 Alpha Sterile Solution should be administered only if the fluid is clear. The first ml should be injected very slowly (1 to 2 minutes) to determine possible sensitivity prior to completing the total 40 mg dose. If this procedure is followed, the chances of anaphylaxis occurring may be reduced; this should also reduce the chances of the inadvertent intravascular injection of a bolus of drug that might cause hypertension, bronchospasm or severe vomiting. If within 24 hours of the initial dose the abortion process has not been established or completed (and in the presence of intact membranes), a further administration of 10 - 40 mg (2-8 ml) can be made, following the same procedure. The dose must be adapted to produce satisfactory uterine activity without hyperstimulation.

Continuous administration of the drug for more than two days is not recommended.

Contra-indications

1. Hypersensitivity to PROSTIN F2 ALPHA or other prostaglandins.
2. Where there is a risk of uterine rupture, e.g. patients with a scarred uterus, evidence of a potential for obstructed labour;
3. In the presence of (or suspected) untreated pelvic inflammatory disease;
4. Patients with clinically significant cardiac, pulmonary, renal or hepatic disease.

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.

Caution should be exercised in the administration of Prostin F2 Alpha 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) Cardiovascular disease
(v) Hypertension.

As with any oxytocic agent, Prostin F2 Alpha should be used with caution in patients with compromised (scarred) uteri.

As in spontaneous abortion, where the process is sometimes incomplete, PROSTIN F2 ALPHA induced abortion may sometimes be incomplete. In such cases, other measures should be taken to assure complete abortion.

Evidence from some animal studies has suggested that certain prostaglandins may have some teratogenic potential. Therefore, any failed pregnancy termination with PROSTIN F2 ALPHA should be completed by some other means.

The possibility of uterine rupture should be borne in mind where high-tone uterine contractions are sustained in the absence of evidence of progression of labour.

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 $F_{2\alpha}$ can cause similar bone effects.

Interactions with other medicaments and other forms of interaction:

Prostaglandins potentiate the effect of oxytocin, therefore concomitant use with other oxytocic agents is not recommended. If used in sequence, the patient's uterine activity should be carefully monitored.

Effects on ability to drive and to use machines:

Not applicable.

Adverse effects:

A number of adverse reactions associated with the use of PROSTIN F2 ALPHA for abortion have been reported from the 7,862 patients studied in the NDA trials, from post marketing surveillance studies and from voluntary reports from physicians using the drug. The most commonly reported events were vomiting (in about one-half of the patients), nausea (in about one-fourth of the patients) and diarrhea (in about one-fifth of the patients). Certain rare (less than 1/1000) but serious events-that should be especially noted are: hypersensitivity to the drug; uterine rupture; and cardiac arrest. These have been reported rarely in patients receiving prostaglandin $F_{2\alpha}$.

In clinical trials and post-marketing studies, the following adverse effects, reported in decreasing order of severity, have been reported. Not all of these events were thought to be related to prostaglandin $F_{2\alpha}$:

1. Events occurring in approximately one to five percent of cases:
   Blood loss;
   Uterine infections;
   Fever.
2. Events occurring in approximately 5/10,000 cases:
   Disseminated intravascular coagulation;
   Hypovolemic shock;
   Exacerbation of asthma/bronchospasm;
   Hypertension or hypotension;
   Perforation of the cervix;
   Headache;
   Dyspnoea;
   Urinary tract infections;
   Syncope or dizziness;
   Chills
   Uterine pain;
   Unspecified pain;
   Coughing;
   Tachycardia;
   Drowsiness.
3. Events occurring less frequently than approximately 5/10,000 cases:
   Pulmonary/amniotic fluid embolism;
   Perforated uterus post-instrumentation;
   Pelvic thrombophlebitis;

Hypokalaemia;
Congestive heart failure;
Second degree heart block;
Ventricular arrhythmia;
Aggravation of diabetes;
Chest pain;
Backache;
Skin eruption;
Paralytic ileus;
Weakness;
Bradycardia;
Urinary incontinence;
Dysuria;
Haematuria;
Unspecified muscle spasm;
Urinary atony or hypertonicity;
Hiccoughs;
Malaise;
Diplopia;
Polydipsia;
Hyperventilation;
Burning sensation in eye or breast;
Pupil constriction;
Paraesthesia;
Pruritus;
Petechiae;
Breast engorgement;
Sweating;
Nosebleed;
Dehydration;
Excitement;
Cyanosis.

In addition, other adverse reactions that have been seen with the use of PROSTIN F2 ALPHA for term labour induction have included:

Uterine hypercontractility with foetal bradycardia;
Uterine hypercontractility without foetal bradycardia
Low Apgar scores in the newborn.

Use in pregnancy and lactation:

Prostin F2 Alpha Sterile Solution is only used during pregnancy for the therapeutic termination of pregnancy in the second trimester. 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 in spontaneous abortion, where the process is sometimes incomplete), appropriate measures to ensure complete evacuation of the pregnant uterus should be instituted in all instances.

Prostaglandins are excreted in breast milk, but given the indication for use, this is unlikely to be a hazard.

Overdosage:

Uterine hypertonus or unduly severe uterine contractions have rarely been encountered, but can result from overdosage. Treatment is symptomatic. If there is evidence of excessive uterine activity, the rate of infusion should be decreased or discontinued. In cases of massive overdosage resulting in extreme uterine hypertonus, appropriate obstetric procedures are indicated to evacuate the uterus and support the mother's condition.

Incompatibilities:

None known.

Pharmaceutical precautions

Prostin F2 Alpha Sterile Solution has a shelf-life of 48 months when stored below 30°C.

Manufacturer

Pfizer Manufacturing Belgium NV/SA

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

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved on January 2010.