PRODUCT INFORMATION
PROSTIN® F₂ alpha injection 5 mg/1 mL

NAME OF THE MEDICINE
Non-proprietary name: Dinoprost trometamol

DESCRIPTION
PROSTIN F₂ alpha (dinoprost) is the synthetic or partially synthetic, naturally-occurring prostaglandin, F₂ alpha present in this product in the form of its crystalline trometamol (THAM) salt. Its structural formula is

![Structural formula of dinoprost trometamol](image)

The molecular weight of dinoprost is 354.47 and that of its trometamol salt, depicted above, is 475.6.

In the form of its trometamol (THAM) salt, it is a white or slightly off-white crystalline powder that is readily soluble in water at room temperature in concentrations up to at least 200 mg/mL.

It is supplied as:
Sterile Aqueous Solution dinoprost, 5 mg/1 mL. (present as 6.71 mg/mL of dinoprost trometamol salt) containing 0.9% benzyl alcohol as preservative.

PHARMACOLOGY
Although the exact mode of action in pregnancy termination in humans is not fully defined, when PROSTIN F₂ alpha is administered by the intrauterine 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 F₂ alpha has been shown to be luteolytic in several animal species, it is unlikely that this is the mechanism involved when the drug is utilised in therapeutic termination of pregnancy in the human as described in this leaflet.
PROSTIN F₂ alpha 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 F₂ alpha.

In some animals and in man, large doses of PROSTIN F₂ alpha can bring about an increase in blood pressure, probably due to its effect on vascular smooth muscle. At the doses recommended for the therapeutic termination of pregnancy, this effect has not been clinically significant.

INDICATIONS

Therapeutic termination of pregnancy (PROSTIN F₂ alpha Sterile Solution 5 mg/1 mL).

1. PROSTIN F₂ alpha is indicated for the therapeutic termination of pregnancy during the first or second trimester.

2. PROSTIN F₂ alpha may be used for evacuation of the uterus in cases of foetal death in utero, missed abortion, as a non-surgical treatment for the evacuation of hydatidiform moles and as an alternative measure to complete therapeutic termination of pregnancy when intra-amniotic saline injections have failed.

NOTE: At the present time, this product should only be used in hospitals or in locations with facilities for emergency obstetric and gynaecological care.

CONTRAINDICATIONS

The use of PROSTIN F₂ alpha is contraindicated in the following circumstances:

1. In patients with a history of hypersensitivity to prostaglandins.

2. Patients with known pelvic infections should receive adequate treatment prior to attempt 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. In patients with a history of caesarean section or prior major uterine surgery.

PRECAUTIONS

There has been some evidence in animals of teratogenic activity, therefore, if termination of pregnancy 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.

It has been found that prostaglandins potentiate the effect of oxytocin and it is therefore recommended that use of these drugs simultaneously or in sequence be carefully monitored.
Caution should be exercised in the administration of PROSTIN F\textsubscript{2} alpha for therapeutic termination of pregnancy in patients with a history of asthma, glaucoma or raised intraocular pressure.

The possibility of uterine rupture should be borne in mind where high tone myometrial contractions are sustained.

Alcohol and beta stimulants neutralise the effects of PROSTIN F\textsubscript{2} alpha and if the patient has taken either of these, this should be considered.

In the therapeutic termination of pregnancy, physicians are reminded that a live born foetus may occur particularly as gestational age approaches the end of the second trimester.

ADVERSE EFFECTS

Most common side effects are nausea, vomiting and diarrhoea.

Certain rare (less than 1/1000) but serious events should be especially noted: hypersensitivity to the drug, uterine rupture and cardiac arrest.

Clinical experience to date indicates that Prostin F\textsubscript{2} alpha administered by the intrauterine (extra-amniotic or intra-amniotic) routes is more effective and better tolerated than by the intravenous route.

Other adverse events reported in decreasing order of severity were:

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
   - Uterine pain
   - Hypovolaemic shock
   - Unspecified pain
   - Bronchospasm
   - Coughing
   - Hypertension or
   - Hypotension

   - Tachycardia
   - Perforation of the cervix
   - Drowsiness
   - Headache
   - Syncope or dizziness
   - Dyspnoea
   - Chills
   - Urinary tract infections

3. Events occurring less frequently than approximately 5/10,000 cases:
   - Pulmonary embolism
   - Hiccough
   - Perforated uterus-post instrumentation
   - Malaise
   - Pelvic thrombophlebitis
   - Diplopia
   - Hypokalaemia

   - Paraesthesias
   - Backache
   - Pruritus
   - Skin eruption
   - Petechiae
   - Paralytic ileus
   - Breast engorgement
Polydipsia
Congestive heart failure
Hyperventilation
Second degree heart block
Burning sensation – eye
Ventricular arrhythmia
Burning sensation – breast
Aggravation of diabetes
Pupil constriction
Chest pain
Convulsions
Weakness
Sweating
Bradycardia
Nosebleed
Urinary incontinence
Dehydration
Dysuria
Excitement
Haematuria
Cyanosis
Unspecified muscle spasm
Uterine atony or hypertonicity

DIRECTIONS FOR THE PREPARATION OF DILUTE SOLUTIONS FROM THE 5 mg/1 mL STERILE SOLUTION

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

For Extra-Amniotic Use (250 μg/mL solution).

Withdraw 1.0 mL from the ampoule, using an aseptic technique and add 19.0 mL of sterile normal saline to make 20 mL of a solution containing 250 μg/mL. Shake to ensure uniformity. Use the dilute solution within 48 hours of preparation.

For Intra-Amniotic Use

The 5 mg/1 mL solution is used as it comes from the ampoule, without dilution.

The intravenous administration is not approved in Australia.

DOSAGE AND ADMINISTRATION

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

For Extra-Amniotic Route

A solution containing 250 μg/mL PROSTIN F₂ alpha should be prepared. Insert a 12 to 14 French gauge Foley catheter with self-retaining 30 mL balloon through the cervix into the space between the foetal membranes and the uterine wall (extra-ovular or extra-amniotic), so that the balloon passes just beyond the internal os. Fill the balloon with 30 mL sterile water (a fine polyethylene catheter has also been used). The PROSTIN F₂ alpha solution should then be instilled through the catheter.

After filling the catheter system deadspace with a predetermined quantity of dilute solution, the initial dose should be 1 mL. Subsequent instillations should be 3 mL, unless side effects ensue, when the dose may be reduced to 1 or 2 mL or the interval between doses prolonged. Two hours should usually elapse between each installation and never less than 1 hour.
For Intra-Amniotic Route

A transabdominal tap of the amniotic sac should be accomplished with an appropriate sized needle and at least 1 mL of amniotic fluid should be withdrawn, then 40 mg (8 mL) of PROSTIN F<sub>2</sub> alpha is slowly injected into the amniotic sac. It is suggested that the first millilitre be injected very slowly to determine possible sensitivity prior to completing the total 40 mg dose. (Do not inject medication in the case of a bloody tap).

If within 24 hours of the initial dose the abortion process has not been established or completed (and in the presence of intact membranes), an additional 10-40 mg (2-8 mL) of PROSTIN F<sub>2</sub> alpha may be administered.

Concomitant Medication

Other drugs which have been employed during PROSTIN F<sub>2</sub> alpha administration for the symptomatic relief of side effects include:

a. For suprapubic pain: meperidine (pethidine).

b. For nausea and vomiting: prochlorperazine, metoclopramide.

c. For diarrhoea: atropine, tincture opii, diphenoxylate.

These medications should be employed in their usual dosages.

PRESENTATION AND STORAGE CONDITIONS

 PROSTIN F<sub>2</sub> alpha is available as:

Sterile Solution, each millilitre contains 5 mg PROSTIN® F<sub>2</sub> alpha (dinoprost), as trometamol salt, supplied as:

5 mg/1 mL, 20 mg/4 mL (not marketed) and 40 mg/8 mL (not marketed) ampoules.

PROSTIN F<sub>2</sub> alpha is stable for five years from date of manufacture if stored below 25°C.

NAME AND ADDRESS OF THE SPONSOR

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POISON SCHEDULE

S4 (Prescription Only Medicine)
DATE OF TGA APPROVAL

Approved by TGA on 27 February 2006

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