PRODUCT INFORMATION
Prostin® F₂ alpha

NAME OF THE MEDICINE
Non-proprietary name: Dinoprost trometamol.

DESCRIPTION
Dinoprost is the synthetic or partially synthetic, naturally-occurring prostaglandin, F₂ alpha present in this product in the form of its crystalline trometamol salt. Its structural formula is:

![Structural formula of dinoprost](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 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, clear, colourless solution. Each millilitre of Prostin F₂ alpha Solution for Injection contains 5 mg dinoprost (present as 6.71 mg/mL of dinoprost trometamol salt). Prostin F₂ alpha also contains 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 is indicated for the therapeutic termination of pregnancy during the first or second trimester.

- Prostin F₂ alpha may be used for evacuation of the uterus in cases of fetal 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:

- patients with a history of hypersensitivity to prostaglandins or any components of Prostin F₂ alpha

- patients with known pelvic infections should receive adequate treatment prior to attempt to induce termination of pregnancy

- extra-amniotic route of administration in the presence of cervicitis or vaginal infections

- patients with active cardiac, pulmonary, renal or hepatic disease

- 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. Concomitant use with other oxytocic agents is not recommended. As with any oxytocic agent, Prostin F₂ alpha should be used with caution in patients with compromised (scarred) uteri.

Caution should be exercised in the administration of Prostin F₂ alpha for therapeutic termination of pregnancy in patients with a history of asthma, glaucoma hypertension, raised intraocular pressure, cardiovascular disease or history of epilepsy.
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 F₂ 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 fetus may occur particularly as gestational age approaches the end of the second trimester.

Similar to 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.

**Use in Pregnancy**

Physicians are reminded that Prostin F₂ alpha contains benzyl alcohol which can cross the placenta. Benzyl alcohol is associated with severe adverse effects, including fatal “gasp ing syndrome”. The minimum amount of benzyl alcohol at which toxicity may occur is unknown. The risk of benzyl alcohol toxicity depends on the quantity administered and the capacity of the liver and kidney to detoxify the chemical.

**ADVERSE EFFECTS**

*Most common side effect:* 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 F₂ 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:*

*Events occurring in approximately one to five percent of cases:*

- Blood loss
- Uterine infections
- Fever.

*Events occurring in approximately 5/10,000 cases:*

<table>
<thead>
<tr>
<th>Disseminated intravascular Coagulation</th>
<th>Tachycardia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine pain</td>
<td>Perforation of the cervix</td>
</tr>
<tr>
<td>Hypovolaemic shock</td>
<td>Drowsiness</td>
</tr>
<tr>
<td>Unspecified pain</td>
<td>Headache</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>Syncope or dizziness</td>
</tr>
<tr>
<td>Coughing</td>
<td>Dyspnoea</td>
</tr>
<tr>
<td>Hypertension or Hypotension</td>
<td>Chills</td>
</tr>
<tr>
<td>Urinary tract infections.</td>
<td></td>
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</tbody>
</table>
Events occurring less frequently than approximately 5/10,000 cases:

<table>
<thead>
<tr>
<th>Event</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary embolism</td>
<td>Paraesthesia</td>
</tr>
<tr>
<td>Hiccough</td>
<td>Backache</td>
</tr>
<tr>
<td>Perforated uterus-post instrumentation</td>
<td>Pruritus</td>
</tr>
<tr>
<td>Malaise</td>
<td>Skin eruption</td>
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<tr>
<td>Pelvic thrombophlebitis</td>
<td>Petechiae</td>
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<tr>
<td>Diplopia</td>
<td>Paralytic ileus</td>
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<tr>
<td>Hypokalaemia</td>
<td>Breast engorgement</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>Weakness</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Sweating</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>Second degree heart block</td>
<td>Nosebleed</td>
</tr>
<tr>
<td>Burning sensation – eye</td>
<td>Urinary incontinence</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Burning sensation – breast</td>
<td>Dysuria</td>
</tr>
<tr>
<td>Aggravation of diabetes</td>
<td>Excitement</td>
</tr>
<tr>
<td>Pupil constriction</td>
<td>Haematuria</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Cyanosis</td>
</tr>
<tr>
<td>Convulsions</td>
<td>Unspecified muscle spasm</td>
</tr>
<tr>
<td>Uterine atony or hypertonicity.</td>
<td></td>
</tr>
</tbody>
</table>

**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 fetal 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 F₂ 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 F₂ alpha may be administered.

**Directions for the Preparation of Dilute Solutions from the 5 mg/mL Sterile Solution**

The neck of the ampoule is pre-scored at the point of constriction. (An ampoule file is not 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).**

Aseptically withdraw 1.0 mL from the ampoule 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 (5 mg/mL)**

Withdraw 1.0 mL from the ampoule. Dilution of the solution before use is not required. Intravenous administration is not approved in Australia.

**Concomitant Medication**

Other drugs which have been employed during Prostin F₂ alpha administration for the symptomatic relief of side effects include:

- for suprapubic pain: meperidine (pethidine).
- for nausea and vomiting: prochlorperazine, metoclopramide.
- for diarrhoea: atropine, tincture opii, diphenoxylate.

These medications should be employed in their usual dosages.

**PRESENTATION AND STORAGE CONDITIONS**

**Presentation**

Prostin F₂ alpha is available as a sterile Solution for Injections, each millilitre contains 5 mg dinoprost, as trometamol salt. It is available as 5 mg/1 mL, 20 mg/4 mL and 40 mg/8 mL ampoules.

*All presentations are no longer supplied.*

**Storage conditions**

Store below 25°C.
NAME AND ADDRESS OF THE SPONSOR

Pfizer Australia Pty Ltd
ABN 50 008 422 348
38-42 Wharf Road
West Ryde NSW 2114.

POISON SCHEDULE OF THE MEDICINE

S4, Prescription Only Medicine.

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)


DATE OF MOST RECENT AMENDMENT

5 August 2016.

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