



PROSTIN F2 ALPHA[®]

(Dinoprost Trometamol)

1. NAME OF THE MEDICINAL PRODUCT

PROSTIN F2 ALPHA[®]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PROSTIN F2 ALPHA[®] is available as Sterile solution, each mL contains 5 mg Prostin F2 ALPHA (dinoprost)

3. PHARMACEUTICAL FORM

Sterile solution for injection

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

1. Intraamniotic administration.

PROSTIN F2 ALPHA[®] Sterile Solution (dinoprost tromethamine) is indicated for aborting a pregnancy between the 16th and 20th weeks of gestation as calculated from the first day of the last normal menstrual period.

2. Intravenous administration.

PROSTIN F2 ALPHA[®] Sterile Solution is indicated for term induction of labor and for evacuation of a third trimester fetal death *in utero*.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

1. For abortion

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the amniotic sac should be accomplished with an appropriate sized needle and at least 1 ml of amniotic fluid should be withdrawn, then 40 mg (8 ml) of PROSTIN F2 ALPHA (as the tromethamine salt) is slowly injected into the amniotic sac. The first 5 mg (1.0 ml) of PROSTIN F2 ALPHA should be injected very slowly and only if the amniotic tap fluid is clear (not blood tinged). 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), an additional 10-40 mg (2-8 ml) of

PROSTIN F2 ALPHA (as the tromethamine salt) may be administered. Continuous administration of the drug for more than two days is not recommended.

2. For term labor induction and/or evacuation of a third trimester death *in utero*.

At 15 µg/ml solution is infused at a rate of 2.5 µg/minute for at least 30 minutes. This level may then be maintained if an appropriate uterine response has ensued or the dose may be increased by 2.5 µg/minute every hour until a satisfactory uterine response has been reached, but a level of 20 µg/minute should not be exceeded.

If hypertonus of the uterus develops with or without fetal bradycardia, the infusion should be discontinued and the situation reassessed before restarting the infusion at a lower rate.

If no response is seen within the first 12-14 hours of treatment, the medication should be discontinued.

4.3. CONTRAINDICATIONS

1. Hypersensitivity to PROSTIN F2 ALPHA.
2. Acute pelvic inflammatory disease.
3. Patients with active cardiac, pulmonary, renal or hepatic disease.
4. Where PROSTIN F2 ALPHA is being used for term labor induction, the following are also contraindications:
 - a) Patients with a history of previous Caesarian Section or major uterine surgery.
 - b) Patients with significant cephalopelvic disproportion.
 - c) Patients with a history of previous difficult labor and/or traumatic delivery.
 - d) Patients who are grand multipara (with six or more previous term pregnancies).
 - e) Patients with unexplained vaginal bleeding during the second or third trimester of this pregnancy.
 - f) Patients with pre-existing fetal distress.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Precautions

1. General Precautions
 - a) 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 have received prostaglandin E1 during prolonged treatment. There is no evidence that short term administration of PROSTIN F2 ALPHA Sterile Solution can cause similar bone effects.
 - b) In patients with a history of asthma, glaucoma, hypertension, cardiovascular disease or history of epilepsy, PROSTIN F2 ALPHA should be used with caution.
 - c) Concomitant use with other oxytocic agents is not recommended.
2. Precautions when PROSTIN F2 ALPHA is being used for abortion.

- a) As with any oxytocic agent, PROSTIN F2 ALPHA should be used with caution in patients with compromised (scarred) uteri.
 - b) 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.
 - c) 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.
3. Precautions when PROSTIN F2 ALPHA is being used for term labor induction and/or evacuation of a third trimester fetal death *in utero*.
- a) Feto-pelvic relationships should be carefully evaluated before using PROSTIN F2 ALPHA.
 - b) During use, uterine activity, fetal status (where appropriate) and the progression of cervical effacement and dilatation should be carefully monitored to detect evidence of undesired responses, e.g. hypertonus, sustained uterine contractility and fetal distress. In cases where there is a known history of hypertonic uterine contractility or tetanic uterine contractions, it is recommended that uterine activity and the status of the fetus be continuously monitored throughout the induced labor. The possibility of uterine rupture should always be considered when high-tone uterine contractions are sustained.

Warnings

The preservative benzyl alcohol has been associated with serious adverse events, including the “gasping syndrome”, and death in pediatric patients. Although normal therapeutic doses of this product ordinarily deliver amounts of benzyl alcohol that are substantially lower than those reported in association with the “gasping syndrome”, the minimum amount of benzyl alcohol at which toxicity may occur is not known. The risk of benzyl alcohol toxicity depends on the quantity administered and the **liver and kidneys’** capacity to detoxify the chemical.¹ Premature and low-birth weight infants may be more likely to develop toxicity.

The amount of benzyl alcohol is 09 mg/mL.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Concomitant use with other oxytocic agents is not recommended

4.6. FERTILITY, PREGNANCY AND LACTATION

Pregnancy

Benzyl alcohol can cross the placenta (See section 4.4. **Special warnings and precautions for use**).

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Information not available

4.8. UNDESIRABLE EFFECTS

Adverse Reactions

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 should be especially noted; hypersensitivity to the drug, uterine rupture, and cardiac arrest.

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
- Hypovolemic shock
- Bronchospasm
- Hypertension or hypotension
- Perforation of the cervix
- Headache
- Dyspnea
- 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 embolism
- Perforated uterus-post instrumentation
- Pelvic thrombophlebitis
- Hypokalemia
- Congestive heart failure
- Second degree heart block
- Ventricular arrhythmia
- Aggravation of diabetes
- Chest pain
- Backache
- Skin eruption
- Paralytic ileus
- Weakness
- Bradycardia
- Urinary incontinence
- Dysuria
- Hematuria
- Unspecified muscle spasm
- Urinary atony or hypertonicity
- Hiccough
- Malaise
- Diplopia
- Polydipsia
- Hyperventilation
- Burning sensation - eye
- Burning sensation - breast
- Pupil constriction

- Paresthesias
- 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 labor induction have included:

1. Uterine hypercontractility with fetal bradycardia;
2. Uterine hypercontractility without fetal bradycardia; and
3. Low Apgar scores in the newborn.

4.9. OVERDOSE

Information not available

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES

Information not available

5.2. PHARMACOKINETIC PROPERTIES

Information not available

5.3. PRECLINICAL SAFETY DATA

Information not available

6. PHARMACEUTICAL PARTICULARS

6.1. STORAGE

Store at controlled room temperature (15°C-30°C). Protected from light.

6.2. HOW SUPPLIED

PROSTIN F2 ALPHA[®] is available as Sterile solution, each mL contains 5 mg Prostin F2 ALPHA (dinoprost) supplied:

1, 4, 5 and 8 ml ampoules, for use with the following routes and indication:

- (i) Intravenous Labour Induction: 1 ml ampoule.
- (ii) Intravenous Termination of Pregnancy: 5 ml ampoule.
- (iii) Extra amniotic Termination of Pregnancy: 1 ml, ampoule to be added to a 19.0 ml vial of Sterile normal saline with 0.9% Benzyl Alcohol.
- (iv) Intraamniotic Termination of Pregnancy: 4, 5 and 8 ml ampoules.

7. REFERENCES

1. Module 2.5 Clinical Overview: Benzyl Alcohol Excipient Warning Update to Support Multiple Product CDSs OCTOBER 2015