PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

PREPIDIL® GEL 0,5 mg

COMPOSITION

Each unit dose of 3 g contains 0,5 mg dinoprostone.

CATEGORY AND CLASS

A 19 Oxytocics

PHARMACOLOGICAL ACTION

Dinoprostone (PGE_2), administered endocervically, facilitates preinduction cervical softening (cervical maturation) in patients with unfavourable induction features. The specific mechanism of action is not fully defined. However, experimental data in humans demonstrates that PGE_2 increases the volume of blood flow in the cervix similar to that observed in early stages of spontaneous labour. This data strongly suggests that endocervical administration of PGE_2 affects cervical haemodynamics, thus leading to cervical maturation.

In both laboratory animals and man, large doses of PGE_2 can lower blood pressure, probably as a consequence of its effect on smooth muscle of the vascular system, and

transient elevations of the body temperature have been observed. PGE_2 is also capable of stimulating the smooth muscle of the gastro-intestinal tract.

INDICATIONS

Cervical ripening in term or near term pregnant women who have a single baby (or foetus) with a vertex presentation.

CONTRAINDICATIONS

Endocervically administered PREPIDIL Gel is not recommended for the following:

1. Patients in whom oxytocic drugs are generally contra-indicated or where prolonged contractions of the uterus are considered inappropriate, such as:
   - Cases with a history of caesarean section or major uterine surgery.
   - Cases in which major degree of cephalopelvic disproportion may be present.
   - Cases in which there is a history of difficult labour and/or traumatic delivery.
   - Grand multiparae with six or more previous term pregnancies.
   - Engagement of the head has not taken place.
   - Obstetric conditions where either maternal or foetal benefit risk ratio favours surgical intervention.
2. Patients with ruptured membranes.
3. Patients with known hypersensitivity to prostaglandin.
4. Patients with unexplained vaginal bleeding/discharge and/or unexplained uterine bleeding during the pregnancy.
5. Patients with non-vertex presentations.
6. Foetal heart rate pattern suggesting incipient foetal compromise.

WARNINGS AND SPECIAL PRECAUTIONS

Since it has been found that PREPIDIL Gel may potentiate the effect of oxytocin, it is recommended that, if these drugs are used in sequence, the patient's uterine activity be carefully monitored.

Special Precautions:

1. Prior to and during use, uterine activity, foetal status, and the character of the cervix (dilation and effacement) should be carefully monitored to detect possible evidence of undesired responses, e.g. hypertonus, sustained uterine contractility or foetal distress. In cases where there is a known history of hypertonic uterine contractility or tetanic uterine contractions, it is recommended that uterine contractions and the state of the foetus be continuously monitored. The possibility of uterine rupture should be born in mind where high-tone myometrial contractions are sustained.
2. Foeto-pelvic relationships should be carefully evaluated before the use of PREPIDIL Gel 0,5 mg.
3. Caution should be exercised in the administration of PREPIDIL Gel 0,5 mg in patients with:
   a) Asthma or a history of asthma, as acute bronchospasm can be precipitated.
   b) Glaucoma or raised intraocular pressure.
   c) Compromised cardiovascular, hepatic or renal function.
   d) Ruptured chorioamniotic membranes.
4. 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 E_1 during prolonged

treatment. There is no evidence that short term administration of prostaglandin E_2 can cause similar bone effects.

5. Caution should be taken so as not to administer the PREPIDIL Gel 0,5 mg above the level of the internal os. Placement of PREPIDIL Gel 0,5 mg into the extra amniotic space has been associated with uterine hyperstimulation.
6. Caution should also be exercised in the administration of oxytocic agents, including PREPIDIL Gel 0,5 mg, for the induction of labour in patients with Multiple Gestation.

Women aged 35 years or older, those with complications during pregnancy and those with a gestational age over 40 weeks have been shown to have an increased risk of post-partum disseminated intravascular coagulation. In addition, these factors may further increase the risk associated with labour induction. Therefore, in these women, use of PREPIDIL Gel 0,5 mg should be undertaken with caution. Measures should be applied to detect as soon as possible an evolving fibrinolysis in the immediate post-partum phase.

INTERACTIONS

The response to oxytocin may be accentuated in the presence of exogenous prostaglandin therapy including PREPIDIL Gel. Concurrent use with other oxytocic agents is not recommended. The sequential use of oxytocin following administration of PREPIDIL Gel 0,5 mg is recommended, with a dosing interval of at least 6 hours.

HUMAN REPRODUCTION

Pregnancy

Prostaglandin E_2 produced an increase in skeletal anomalies in rats and rabbits. Dinoprostone has been shown to be embryotoxic in rats and rabbits. Any dose that produces sustained increased uterine tone could put the embryo or foetus at risk.

Lactation:

Prostaglandins are excreted in breast milk at very low concentrations.

DOSAGE AND DIRECTIONS FOR USE:

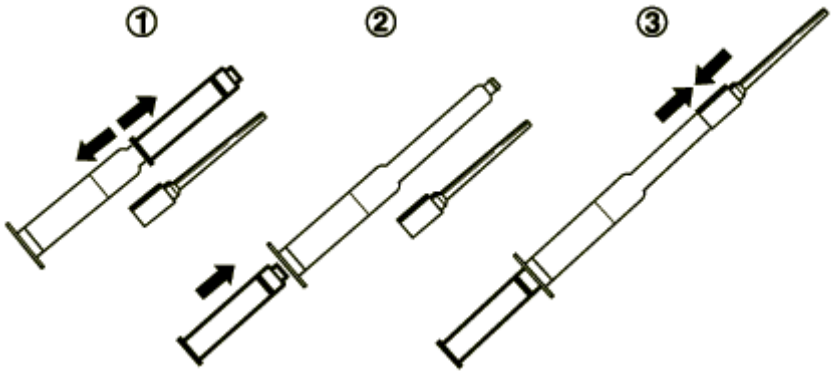
PREPIDIL Gel 0,5 mg is supplied as a translucent sterile gel preparation of 0,5 mg PGE_2 per 3 g, in syringes with an accompanying catheter for **endocervical application**. See attached diagram for assembly instructions.

Utilizing the catheter provided, the entire contents of the syringe should be administered by gentle expulsion into the cervical canal just below the level of the internal cervical os. After placement of the gel, the patient should be instructed to remain in the dorsal position for 10 - 15 minutes to minimise gel leakage.

METHOD OF ASSEMBLY OF SYRINGE AND CATHETER

INSTRUCTIONS

Remove sterile catheter and sterile syringe from package.



1. Remove protective end cap (to serve as plunger extension/rod).
2. Insert protective end cap into plunger stopper assembly in barrel of syringe.
3. Firmly attach catheter hub to syringe tip (catheter has to click into place).
4. Administer syringe contents endocervically.

SIDE-EFFECTS

Very Common: ≥ 1/10 (≥ 10%)

Common: ≥ 1/100 and < 1/10 (≥ 1% and < 10%)

Very rare: < 1/10 000 (< 0,01%)

SYSTEM ORGAN CLASS	FREQUENCY	UNDESIRABLE EFFECTS
Immune system disorders	Very rare	Hypersensitivity reactions
Gastrointestinal disorders	Common	Diarrhoea, nausea, vomiting
Musculoskeletal and connective tissue disorders	Common	Back pain
Pregnancy, puerperium and perinatal conditions	Common	Uterine contractile abnormalities (increase frequency, tone, or duration)
	Very rare	Uterine rupture
Reproductive system and breast disorders	Common	Warm feeling in vagina
General disorders and administration site conditions	Common	Fever
Pregnancy, puerperium and perinatal conditions	Very rare	Still birth Depressed neonates at birth (Apgar scores < 7)
Investigations	Very common	Foetal distress/altered foetal heart rate (FHR)

Post-marketing experience

Blood and lymphatic system disorders: An increased risk of post-partum disseminated intravascular coagulation has been described in patients whose labour was induced by pharmacological means, including PREPIDIL Gel 0,5 mg. The frequency of this adverse event, however, appears to be rare (<1 per 1,000 labours).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Treatment of overdosage must be symptomatic, since clinical studies with prostaglandin antagonists have not progressed to the point where recommendations may be made.

IDENTIFICATION

A translucent gel.

PRESENTATION

PREPIDIL Gel 0,5 mg is supplied as a translucent sterile gel as follows:

0,5 mg PGE_2 per 3 g in syringe with accompanying catheter for endocervical application.

STORAGE INSTRUCTIONS

Store in a refrigerator at 4 °C.

Keep out of reach of children.

REGISTRATION NUMBER

U/19/259

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Pfizer Laboratories (Pty) Ltd

85 Bute Lane

Sandton, 2196

South Africa

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION

Date of registration: 23 August 1988

Date of last SAHPRA approval: 15 August 2008

BOTSWANA: S2

Reg. No.: B9312115

NAMIBIA: S2

Reg. No.: 90/19/001346