

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

PROPESS® 10 mg Vaginal delivery system

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vaginal delivery system consists of a non-biodegradable polymeric drug delivery device containing 10 mg dinoprostone (prostaglandin E₂) dispersed throughout its matrix and releases approximately 0,3 mg/hour prostaglandin E₂ (PGE₂) over a 24 hour period.

PROPESS® is sugar free.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Vaginal delivery system

PROPESS® is presented as a 0.8 mm thin, flat, semi-transparent polymeric vaginal delivery system which is rectangular in shape (29 mm by 9.5 mm) with rounded corners contained within a knitted polyester retrieval system.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

PROPESS® is indicated for the initiation and/or continuation of cervical ripening in patients, at term (from 37 completed weeks of gestation).

4.2 Posology and method of administration

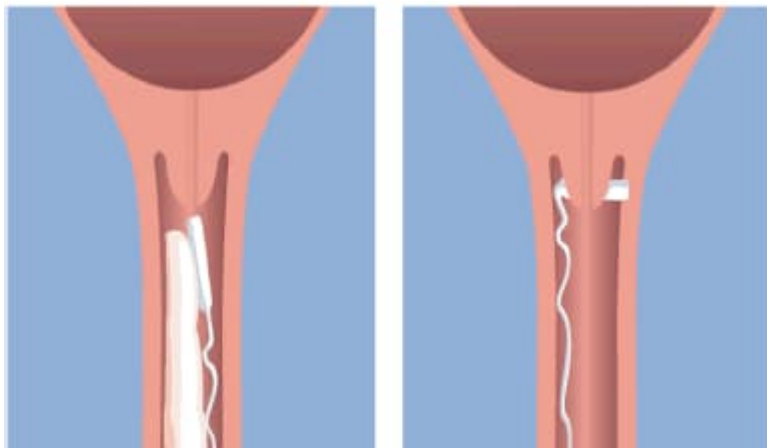
PROPESS® should only be administered by appropriately qualified healthcare personnel in hospitals and

clinics with specialised obstetric units with facilities for continuous foetal and uterine monitoring.

After insertion, uterine activity and foetal condition must be carefully and regularly monitored.

Posology

One vaginal delivery system is administered high into the posterior vaginal fornix.



The vaginal delivery system should be removed after 24 hours irrespective of whether cervical ripening has been achieved.

A dosing interval of at least 30 minutes is recommended for the sequential use of uterotonic medicines following the removal of the vaginal delivery system. Only one application of PROPESS® is recommended.

Paediatric population

The safety and efficacy of PROPESS® in pregnant women aged less than 18 years has not been established. No data are available.

Method of administration

Administration

PROPESS® should be removed from the freezer just prior to the insertion. No thawing is required prior to use.

There is a “tear mark” on the side of the foil sachet. Open the package along the tear mark across the top of the sachet. Do not use scissors or other sharp objects which may cut the retrieval system.

The vaginal delivery system should be inserted high into the posterior vaginal fornix using only small amounts of water-soluble lubricants to aid insertion. After the vaginal delivery system has been inserted, the withdrawal tape may be cut with scissors always ensuring there is sufficient tape outside the vagina to allow removal.

No attempt should be made to tuck the end of the tape into the vagina as this may make retrieval more difficult.

The patient should be recumbent for 20 – 30 min. after insertion. As PGE₂ will be released continuously over a period of 24 hours, it is important to monitor uterine contractions and foetal condition at frequent regular intervals.

Removal

The vaginal delivery system can be removed quickly and easily by gentle traction on the retrieval tape. Remove the vaginal delivery system to terminate drug administration when cervical ripening is judged to be complete or for any of the reasons listed below.

1. Onset of labour, for the purpose of induction of labour with PROPESS®, the onset of labour is defined as the presence of regular, painful uterine contractions occurring every 3 minutes irrespective of any cervical change. There are two important points to note:
 - i. Once regular, painful contractions have been established with PROPESS®, they will not reduce in frequency or intensity as long as PROPESS® remains in situ because PGE₂ is still being administered.
 - ii. Patients, particularly multigravidae, may develop regular, painful contractions without any apparent

cervical change. Effacement and dilation of the cervix may not occur until uterine activity is established.

Because of this, once regular, painful uterine activity is established with PROPESS® in situ, the vaginal delivery system should be removed irrespective of cervical state to avoid the risk of uterine hyperstimulation.

2. Spontaneous rupture of the membranes or amniotomy.
3. Any suggestion of uterine hyperstimulation or hypertonic uterine contractions.
4. Evidence of foetal distress.
5. Evidence of maternal systemic PGE2 adverse effects such as nausea, vomiting, hypotension or tachycardia.
6. At least 30 minutes prior to starting an intravenous infusion of other uterotonic medicines, as there is a much greater risk of hyperstimulation if the dinoprostone source is not removed before administration of uterotonic medicines.

The opening on one side of the retrieval device is present only to allow the manufacturer to enclose the vaginal delivery system into the retrieval device during manufacture. The vaginal delivery system should NEVER be removed from the retrieval device.

Upon removal of the product from the vagina, the vaginal delivery system will have swollen 2 – 3 times its original size and be pliable. The whole product should be disposed of as clinical waste.

4.3. Contraindications

PROPESS® should not be used or left in place:

1. When labour has started.
2. When uterotonic medicines and /or other labour induction agents are being given.
3. When strong, prolonged uterine contraction would be inappropriate such as in patients:
 - a. who have had previous major uterine surgery e.g. caesarean section, myomectomy etc. (see section 4.4 and 4.8)

- b. who have had previous major uterine cervix surgery (e.g. other than biopsies and cervical abrasion) or rupture of the uterine cervix.
 - c. with cephalopelvic disproportion.
 - d. with foetal malpresentation
 - e. with suspicion or evidence of foetal distress
4. When there is current pelvic inflammatory disease, unless adequate prior treatment has been instituted.
5. When there is hypersensitivity to PGE₂ or to any of the excipients listed in section 6.1.
6. When there is placenta praevia or unexplained vaginal bleeding during the current pregnancy.

4.4 Special warnings and precautions for use

The condition of the cervix should be assessed carefully before PROPESS® is used. After insertion, uterine activity and foetal condition must be monitored carefully and regularly by appropriately qualified healthcare personnel. PROPESS® must only be used in hospitals and clinics with specialised obstetric units with facilities for continuous foetal and uterine monitoring.

If there is any suggestion of maternal or foetal complications or if adverse effects occur, the vaginal delivery system should be removed from the vagina.

Uterine rupture has been reported in association with the use of PROPESS®, mainly in patients with contraindicated conditions (see section 4.3). Therefore, PROPESS® should not be administered to patients with a history of previous caesarean section or uterine surgery given the potential risk for uterine rupture and associated obstetrical complications.

If uterine contractions are prolonged or excessive, there is the possibility of uterine hypertonus or rupture and the vaginal delivery system should be removed immediately.

A second dose of PROPESS® is not recommended, as the effects of a second dose have not been studied.

PROPESS® should be used with caution in patients with a previous history of uterine hypertonus, glaucoma or asthma.

The experience of PROPESS® in patients with ruptured membranes is limited. Therefore, PROPESS® should be used with caution in those patients. Since the release of dinoprostone from the delivery system can be affected by the presence of amniotic fluid, special attention should be given to uterine activity and foetal condition.

Women aged 35 and over, women with complications during pregnancy, such as gestational diabetes, arterial hypertension and hypothyroidism, and women at gestational age above 40 weeks have a higher post-partum risk for developing disseminated intravascular coagulation (DIC). These factors may additionally enhance the risk of disseminated intravascular coagulation in women with pharmacologically induced labour (see section 4.8). Therefore, uterotonic medicines such as dinoprostone should be used with caution in these women. In the immediate post-partum phase the medical practitioner should look out carefully for early signs of a developing DIC (e.g. fibrinolysis).

The medical practitioner should be alert that use of dinoprostone may result in inadvertent abruption of placenta and subsequent embolisation of antigenic tissue causing in rare circumstances the development of Anaphylactoid Syndrome of Pregnancy (Amniotic Fluid Embolism).

PROPESS® is not recommended when there is a multiple pregnancy. No studies in multiple pregnancy have been performed.

PROPESS® should be used with caution when the woman has had more than three full term deliveries. No studies in woman with more than three full term deliveries have been performed.

The use of PROPESS® in patients with diseases which could affect the metabolism or excretion of PGE₂,

e.g. lung, liver or renal disease, has not been specifically studied. The use of PROPESS® in such patients is not recommended.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed specifically with PROPESS®.

Prostaglandins potentiate the uterotonic effect of uterotonic medicines. Concurrent use of PROPESS® in patients receiving uterotonic medicines is not recommended.

Medication with non-steroidal anti-inflammatory medicines, including aspirin, should be stopped before administration of dinoprostone.

4.6 Fertility, pregnancy and lactation

Pregnancy

PROPESS® is indicated for the initiation and/or continuation of cervical ripening in patients, at term (from 37 completed weeks of gestation) (see section 4.1).

PROPESS® should not be used during pregnancy prior to 37 completed weeks of gestation.

Breastfeeding

No studies have been performed to investigate the amount of dinoprostone in colostrum or breast milk following the use of PROPESS®.

Dinoprostone may be excreted in colostrum and breast milk, but the level and duration is expected to be very limited and should not hinder breastfeeding. No effects on the breastfed new-borns have been observed in the clinical studies conducted with PROPESS®.

Fertility

Not relevant

4.7 Effects on ability to drive and use machines

The effect of PROPESS® on the ability to drive and use machines is unknown.

4.8 Undesirable effects

Summary of safety profile:

The table below displays the main ADRs distributed by system organ classes (SOC) and frequency. Further, the ADRs seen during post-marketing experience are mentioned with unknown frequency.

Adverse reactions observed in clinical studies are presented according to their incidence, post authorisation reported adverse reactions are presented in the column frequency unknown.

System Organ Class	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1000 and < 1/100)	Not known: (cannot be estimated from the available data)
Blood and lymphatic system disorders			Disseminated intravascular coagulation
Immune system disorders			Anaphylactic reaction, hypersensitivity
Nervous system disorders		Headache	
Cardiac disorders	Foetal heart rate disorder ^{1*}		
Vascular disorders		Hypotension	
Respiratory, thoracic and mediastinal disorders		Neonatal respiratory distress related conditions	
Gastrointestinal disorders			Abdominal pain, nausea, vomiting, diarrhoea

Hepato-biliary disorders		Neonatal hyper-bilirubinaemia	
Skin and subcutaneous tissue disorders		Pruritus	
Pregnancy, puerperium and perinatal conditions	Abnormal labour affecting foetus ^{2*} , uterine contractions abnormal, uterine tachysystole, uterine hyperstimulation, uterine hypertonus, meconium in amniotic fluid	Postpartum haemorrhage, premature separation of placenta, apgar score low, arrested labour, chorioamnionitis, uterine atony	Anaphylactoid syndrome of pregnancy, foetal distress syndrome ^{3*} foetal death, stillbirth, neonatal death ^{4*}
Reproductive system and breast disorders		Vulvovaginal burning sensation	Genital oedema
General disorders and administration site conditions		Febrile disorders	
Injury, poisoning and procedural complications			Uterine rupture

^{1*} “Foetal heart rate disorder” was in clinical studies reported as “foetal heart rate abnormalities”, “foetal bradycardia”, “foetal tachycardia”, “unexplained absence of normal variability”, “foetal heart rate decreased”, “foetal heart rate deceleration”, “early or late decelerations”, “variable decelerations”, “prolonged decelerations”.

^{2*} “Abnormal labour affecting foetus” as expression for hyperstimulation syndrome was in clinical studies reported as “uterine tachysystole” combined with “late decelerations”, “foetal bradycardia”, or

“prolonged decelerations”

^{3*} “Foetal distress syndrome” was also reported as “foetal acidosis”, “pathological CTG”, “foetal heart rate abnormalities”, “intrauterine hypoxia” or “threatening asphyxia”. The term itself is unspecific, has a low positive predictive value and is often associated with an infant who is in good condition at birth.

^{4*} Foetal death, stillbirth, and neonatal death have been reported after application of dinoprostone, as contained in PROPESS®, especially following the occurrence of serious events such as uterine rupture (see sections 4.2, 4.3 and 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Overdosage may lead to hyperstimulation of the uterine muscle with or without foetal distress. If foetal distress occurs, remove PROPESS® immediately and manage in accordance with local protocol.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: uterotonics, prostaglandins, ATC code: G02AD02

Prostaglandin E₂ (PGE₂) is a naturally occurring compound found in low concentrations in most tissues of the body. It functions as a local hormone.

Prostaglandin E₂ plays an important role in the complex set of biochemical and structural alterations involved in cervical ripening. Cervical ripening involves a transformation of the uterine cervix which must

be transformed from a rigid structure to a soft, dilated configuration to allow passage of the foetus through the birth canal. This process involves activation of the enzyme collagenase which is responsible for the breakdown of the collagen.

Local administration of PGE₂ to the cervix results in cervical ripening which then induces the subsequent events which complete labour

5.2 Pharmacokinetic properties

PGE₂ is rapidly metabolised primarily in the tissue of synthesis. Any which escapes local inactivation is rapidly cleared from the circulation with a half-life generally estimated as 1 – 3 minutes. No correlation could be established between PGE₂ release and plasma concentrations of its metabolite, PGE_m. The relative contributions of endogenously and exogenously released PGE₂ to the plasma levels of the metabolite PGE_m could not be determined.

The reservoir of 10 mg dinoprostone serves to maintain a controlled and constant release. The release rate is approximately 0,3 mg per hour over 24 hours in woman with intact membranes whereas release is higher and more variable in woman with premature rupture of membranes, PROPESS® releases PGE₂ to the cervical tissue continuously at a rate which allows cervical ripening to progress until complete, and with the facility to remove the PGE₂ source when the clinician decides that cervical ripening is complete or labour started, at which point no further PGE₂ is required.

5.3 Preclinical Safety Data

Preclinical studies have demonstrated that dinoprostone is a locally acting substance which is rapidly inactivated and thus it has no significant systemic toxicity.

The hydrogel and polyester polymers are inert compounds with good local tolerability.

Reproduction toxicity, genotoxic or carcinogenic effects of the polymers have not been investigated but systemic exposure is negligible.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Crosslinked macrogol (hydrogel);

Polyester yarn

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store unopened in a deep-freezer (between -10 °C and -25 °C).

Store in the original container in order to protect from moisture.

No thawing is required prior to use.

The product is not stable when stored at room temperature.

6.5 Nature and contents of container

PROPESS® vaginal delivery system is presented in individual sealed aluminium/polyethylene laminated sachets in packs containing 5 vaginal delivery systems.

6.6 Special precautions for disposal and other handling

PROPESS® should be inserted immediately after removal from the freezer.

Any unused product or waste material should be disposed of as clinical waste. Contact Ferring (Pty) Ltd or your pharmacist.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ferring (Pty) Ltd.
Propess[®] Vaginal delivery system (33/19/0059)
Dinoprostone 10 mg per unit

Professional Information
SAHPRA Approved 21 May 2025

Ferring (Pty) Ltd.

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Irene Ext 30, 0157

SOUTH AFRICA

8. REGISTRATION NUMBER(S)

A33/19/0059

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 8 February 1999

10. DATE OF REVISION OF THE TEXT

21 May 2025

MANUFACTURER:

Ferring Controlled Therapeutics Ltd,
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NAMIBIA REGISTRATION NUMBER(S):

Namibia NS2 Reg No/Nr.: 04/19/0854
