

Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

Glandin-E2 Vaginal Gel 2mg

2. Qualitative and quantitative composition

Each 3g (2.5ml) vaginal gel contains:

Dinoprostone.....2mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Vaginal Gel

Description: A clear, colorless, translucent viscous gel.

4. Clinical particulars

4.1 Therapeutic indications

Induction of labour in the absence of foetal and maternal contraindications.

4.2 Posology and method of administration

Posology

Usage is restricted to qualified health care professionals and to hospitals and clinics with specialised obstetric units with facilities for continuous monitoring.

The recommended dose should not be exceeded, and the dosing interval should not be shortened as this increases the risk of uterine hyperstimulation, uterine rupture, uterine haemorrhage, foetal and neonatal death.

Method of administration

Adults: In primigravida patients with unfavourable induction features (Bishop score of 4 or less), an initial dose of 2 mg should be administered vaginally. In other patients an initial dose of 1 mg should be administered vaginally.

In both groups of patients, a second dose of 1 mg or 2 mg may be administered after 6 hours as follows:

- 1mg should be used where uterine activity is insufficient for satisfactory progress of labour.
- 2mg may be used where the response to the initial dose has been minimal.

Maximum dose 4 mg in unfavourable primigravida patients or 3 mg in other patients. The gel should be inserted high into the posterior fornix, avoiding

administration into the cervical canal. The patient should be instructed to remain recumbent for at least 30 minutes.

After insertion of the gel, the patient should be under observation using continual external cardiotocography to monitor foetal heart rate and uterine activity.

Elderly: Not applicable.

Paediatric population: Not applicable.

4.3 Contraindications

Hypersensitivity to Dinoprostone, other prostaglandins, or to any of the excipients listed in section 6.1.

- Glandin E2 Vaginal Gel is not recommended in the following circumstances:

For patients in whom oxytocic drugs are generally contraindicated or where prolonged contractions of the uterus are considered inappropriate, such as:

- Cases with a history of Caesarean section or major uterine surgery
 - Cases where there is cephalopelvic disproportion
 - Cases in which foetal malpresentation is present
 - Cases where there is clinical suspicion or definite evidence of pre-existing foetal distress.
 - Cases in which there is a history of difficult labour and/or traumatic delivery
 - Multiple gestation
 - Engagement of the head has not taken place
 - Obstetric conditions where either maternal or foetal benefit/risk ratio favours surgical intervention.
- In patients with a past history of, or existing, pelvic inflammatory disease, unless adequate prior treatment has been instituted.
 - In patients where there is clinical suspicion or definite evidence of placenta praevia or unexplained vaginal discharge and /or abnormal bleeding during this pregnancy.
 - Patients with active cardiac, pulmonary, renal, or hepatic disease.

4.4 Special warnings and precautions for use

Use the total contents of the syringe for one patient only. Discard after use. Use caution in handling the product to prevent contact with skin. Wash hands thoroughly with soap and water after administration.

As with any oxytocic agent, the risk of uterine rupture should be considered. Concomitant medication, maternal and foetal status should be taken into

consideration in order to minimise the risk of uterine hyperstimulation, uterine rupture, uterine haemorrhage, foetal and neonatal death. Continuous electronic monitoring of uterine activity and foetal heart rate should be conducted during the use of dinoprostone. Patients who develop uterine hypertonus or hypercontractility, or in whom unusual foetal heart rate patterns develop, should be managed in a manner that addresses the welfare of the foetus and mother.

Glandin E2 Vaginal Gel and Glandin E2 Vaginal Tablets are not bioequivalent.

Caution should be exercised in the administration of Glandin E2 Vaginal Gel for the induction of labour in patients with:

- (i) asthma or a history of asthma
- (ii) epilepsy or a history of epilepsy
- (iii) glaucoma or raised intra-ocular pressure
- (iv) compromised cardiovascular, hepatic, or renal function
- (v) hypertension
- (vi) ruptured chorioamniotic membranes.

Dinoprostone should be used with caution in patients with multiple pregnancies.

In labour induction, cephalopelvic relationships should be carefully evaluated before the use of Glandin E2 Vaginal Gel. During use, uterine activity, foetal status, and the progression of cervical dilation should be carefully monitored to detect possible evidence of undesired responses, e.g., hypertonus, sustained uterine contractions, or foetal distress. Patients who develop uterine hypertonus or hypercontractility, or in whom unusual foetal heart rate patterns develop, should be managed in a manner that addresses the welfare of the foetus and mother.

In cases where there is a known history of hypertonic uterine contractility or tetanic uterine contractions, it is recommended that uterine activity and the state of the foetus (where applicable) should be continuously monitored throughout labour. The possibility of uterine rupture should be borne in mind where high-tone uterine contractions are sustained.

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 received prostaglandin E1 during prolonged treatment. There is no evidence that short-term administration of prostaglandin E2 can cause similar bone effects.

Women aged 35 years or older, those with complications during the 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 those women, the use of

Glandin E2 Vaginal Gel should be done with caution. Measures should be applied to detect as soon as possible an evolving fibrinolysis in the immediate post-partum phase.

The Clinician should be alert that the intracervical placement of dinoprostone gel may result in inadvertent disruption and subsequent embolization of antigenic tissue, causing, in rare circumstances, the development of Anaphylactoid Syndrome of Pregnancy (Amniotic Fluid Embolism).

4.5 Interaction with other medicinal products and other forms of interaction

The response to oxytocin may be accentuated in the presence of exogenous prostaglandin therapy. Concurrent use with other oxytocic agents is not recommended. A dosing interval of at least 6 hours is recommended in case of oxytocin use is considered necessary following dinoprostone administration.

4.6 Fertility, pregnancy, and lactation

Pregnancy

Glandin E2 Vaginal Gel is only used during pregnancy to induce labour.

Breast-feeding

Prostaglandins are excreted in breast milk. This is not expected to be a hazard given the circumstances in which the product is used.

4.7 Effects on the ability to drive and use machines

Not Applicable.

4.8 Undesirable effects

The most commonly reported events are vomiting, nausea, and diarrhoea. Certain rare events that should be especially noted are: hypersensitivity reactions (e.g., anaphylactic reaction, anaphylactic shock, anaphylactoid reaction); uterine rupture and cardiac arrest. Other adverse events reported with use of dinoprostone are:

- Pulmonary/amniotic fluid embolism
- Abruptio placenta
- Uterine hypercontractility or hypertonus
- Foetal distress / altered foetal heart rate (FHR)
- Hypertension – systemic (maternal) • Bronchospasm/asthma
- Rapid cervical dilation
- Fever
- Backache
- Rash
- Vaginal symptoms – warmth, irritation, pain
- Neonatal distress/low Apgar scores in the newborn

- Coma.
- Foetal death, stillbirth, neonatal death* (Frequency not known-cannot be estimated from the available data).

*Foetal death, stillbirth, and neonatal death have been reported after application of dinoprostone, especially following the occurrence of serious events such as uterine rupture. An increased risk of post-partum disseminated intravascular coagulation has been described in patients whose labour was induced by pharmacological means, either with dinoprostone or oxytocin. The frequency of this adverse event, however, appears to be rare (< 1 per 1,000 labours).

Reporting of suspected adverse reactions

Healthcare professionals are requested to report any suspected adverse reactions via the pharmacy and the Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS) <https://pv.pharmacyboardkenya.org>

4.9 Overdose

Uterine hypertonus or unduly severe uterine contractions have rarely been encountered, but might be anticipated to result from overdosage. Where there is evidence of foetal distress or uterine hypertonus, then prompt delivery is indicated.

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

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Prostaglandins, ATC-code: G02AD02

Dinoprostone is a prostaglandin of the E series with actions on smooth muscle; the endogenous substance is termed prostaglandin E₂. It induces contraction of the uterine muscle at any stage of pregnancy and is reported to act predominantly as a vasodilator on blood vessels and as a bronchodilator on bronchial muscle. It is postulated that vaginal absorption of PGE₂ stimulates endogenous PGE₂ and PGF_{2α} production, similar to that which is seen in spontaneous labour.

5.2 Pharmacokinetic properties

General characteristics of the active substance

When given vaginally, PGE₂ is rapidly absorbed. Plasma levels of 15-keto PGE₂ equivalents peak at 1.5 hours after administration of a 5 mg dose. *In*

vitro work indicates that PGE₂ is 73% bound to human plasma albumin. It is rapidly metabolised in the lungs, kidneys, spleen, and liver, with a single pass of the circulatory system converting 90% of an injected PGE₂ dose to metabolites.

There has been found to be inter-patient variability regarding systemic absorption of PGE₂. This can be attributed to different conditions of the vaginal mucosa between patients.

Characteristics in patients

No special characteristics.

5.3 Preclinical safety data

In mice and rats, the oral LD₅₀ values were >500 mg/kg and 141-513 mg/kg, respectively.

Three-month oral administration to rats resulted in significantly heavier stomach weights for treated compared with untreated rats, which effect was reversible on treatment cessation. Treated rats had a dose-related acanthotic squamous glandular junction and thickened glandular gastric mucosal epithelium. No significant alterations were recognized in the routine evaluation of the sternbrae and the femur.

A fourteen-day oral toxicity study in dogs showed a maximum tolerated dose of 6-20 mg/kg/day. All treated dogs had microscopic evidence of increased fundic and pyloric mucus. The fundic and pyloric mucosa were thickened, having a cobblestone appearance, and had an increased gastric mucus in both the 20 mg/kg/day treated dogs and the 60 mg/kg/day male dog. These were the only gross and microscopic drug-related changes observed.

Satisfactory results were obtained in intravenous and intramuscular tolerability tests performed in dogs and monkeys.

Teratogenic effects were observed in rats injected subcutaneously with 0.5 mg/animal. No teratogenic effects were seen in the rabbit at dosage levels of up to 1.5 mg/kg/day.

No evidence of mutagenicity was obtained using the Ames Assay, the DNA Damage/Alkaline Elution Assay, and the micronucleus test.

6. Pharmaceutical particulars

6.1 List of excipients

Triacetine
Aerosil #200

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C-8°C).

6.5 Nature and contents of container

Plastic Applicator packed in Aluminum Foil in a Unit Carton

6.6 Special precautions for disposal and other handling

Use the total contents of the syringe for one patient only. Discard after use. Use caution in handling this product to prevent contact with skin. Wash hands thoroughly with soap and water after administration.

7. Marketing authorization holder

Nabiqasim Industries Pvt. Ltd.
17/24, Korangi Industrial
Area, Korangi, Karachi-
Pakistan

8. Marketing authorization number(s)

Glandin-E2 Vaginal Gel 2mg: H2010/15776/252

9. Date of first authorization/renewal of the authorization

Date of first authorization: 23rd January 2020

Date of renewal of authorization: N/A

10. Date of revision of text:

26th March 2026