Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

Glandin-E2 Vaginal Tablet 3mg

2. Qualitative and quantitative composition

Each vaginal tablet contains:

Dinoprostone……3mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Vaginal Tablet

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

One Tablet (3 mg) to be inserted into the posterior fornix. A second tablet may be inserted after 6- 8 hours if labour is not established. Maximum dose 6 mg (2 tablets).

Method of administration

Vaginally. The tablets should be inserted high into the posterior fornix**.**

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 Tablet 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

This product is only available to hospitals and clinics with specialized obstetric units and should only be used where 24-hour resident medical cover is provided.

Use caution in handling this 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.

Caution should be exercised in the administration of Glandin E2 Vaginal Tablets 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 Tablets. 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.

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 (see section 4.8). Therefore, in these women, the use of dinoprostone should be undertaken with caution. Measures should be applied to detect as soon as possible an evolving fibrinolysis in the immediate post-partum phase.

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 E2Vaginal Tablet 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

Cardiac disorders: Cardiac arrest

Vascular disorders: Hypertension

Gastrointestinal disorders: Diarrhoea, nausea, vomiting

General disorders and administration site conditions: Fever

Immune system disorders: Hypersensitivity reactions such as anaphylactoid reactions and anaphylactic reactions including anaphylactic shock.

Musculoskeletal and connective tissue disorders: Back pain

Pregnancy, puerperium and perinatal conditions: Foetal death, stillbirth, neonatal death* (Frequency not known- cannot be estimated from the available data)

Maternal-related conditions*:* Uterine hypertonus, uterine rupture, abruptio placentae, pulmonary amniotic fluid embolism, rapid cervical dilatation

Foetal conditions: Uterine hypercontractility with/without foetal bradycardia, foetal distress/altered foetal heart rate (FHR)

Neonatal conditions: Neonatal distress, neonatal death, stillbirths, low Apgar score

*Foetal death, stillbirth, and neonatal death have been reported after application of dinoprostone, especially following the occurrence of serious

events such as uterine rupture (see sections 4.2, 4.3, and 4.4).

Reproductive system and breast disorders: Warm feeling in the vagina, irritation, pain

Respiratory, thoracic, and mediastinal disorders: Asthma, bronchospasm

Skin and subcutaneous tissue disorders: Rash

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, either with dinoprostone or oxytocin (see section 4.4). 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

Overdosage may be expressed by uterine hypercontractility and uterine hypertonus. 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. Because of the transient nature of prostaglandin E2 (PGE2)-induced myometrial hyperstimulation, non-specific, conservative management was found to be effective in the vast majority of cases: i.e., maternal position change and administration of oxygen to the mother. If conservative management is not effective, ß- adrenergic drugs may be used as a treatment of hyperstimulation following administration of PGE2 for cervical ripening, in appropriate patients.

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 E_2. 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 PGE_2 stimulates endogenous PGE_2 and $PGF_{2\alpha}$ production, similar to that which is seen in spontaneous labour.

5.2 Pharmacokinetic properties

General characteristics of the active substance

Following insertion of the tablet, PGE_2 absorption (as measured by the presence of PGE_2 metabolites) increases to reach a peak at about 40 minutes. PGE_2 is rapidly metabolised to 13, 14-dihydro, 15-keto PGE_2, which is converted to 13, 14-dihydro, 15-keto PGA_2 which binds covalently to albumen.

There has been found to be inter-patient variability regarding systemic absorption of PGE_2. This can be attributed to different conditions of the vaginal mucosa between patients.

When given vaginally, PGE_2 is rapidly absorbed. Plasma levels of 15-keto PGE_2 equivalents peak at 1.5 hours after administration of a 5 mg dose. *In vitro* work indicates that PGE_2 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 PGE_2 dose to metabolites.

There has been found to be inter-patient variability regarding systemic absorption of PGE_2. 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 sternebrae 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 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 dog and monkey.

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

Colloidal Silicone Dioxide (Aerosil # 200)

Maize Starch

Microcrystalline Cellulose (Avicel PH 112)

Lactose anhydrous

Magnesium Stearate

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

Glandin-E2 Vaginal Tablet is supplied in 1's & 4's Aluminum Strip, which is further packed in a bleach board single carton.

6.6 Special precautions for disposal and other handling

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 Tablet 3mg: H2010/15776/252

9. **Date of first authorization/renewal of the authorization**

   Date of first authorization: 1ST APRIL 2010

   Date of renewal of authorization: ---

10. **Date of revision of text:**

    25 July 2025