Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Prostin E2 3mg Vaginal Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 3 mg dinoprostone.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Vaginal Tablet

White, biconvex, special shaped tablet, embossed with 'Upjohn 715' one side and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

The induction of labour when there are no gynaecological, obstetrical or medical conditions, either maternal or foetal, that preclude vaginal delivery.

4.2 Posology and method of administration

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.

Adults: One tablet to be inserted high into the posterior fornix. After insertion of the tablet, the patient should be under observation using external cardiotocography to monitor foetal heart rate and uterine activity.

If no contractions have occurred by 6 hours, a further tablet is inserted and monitoring continued as above.

Maximum dose 6 mg.

Once labour has started, the membranes may be ruptured and the foetal heart monitored using a scalp electrode. Uterine contractions should be monitored using external tocography.

If evidence of hypertonus develops, any remains of the tablet should be removed and an intravenous injection of a tocolytic agent given. Delivery by the appropriate route should be considered.

Elderly: Not applicable

Paediatric population: Not applicable

4.3 Contraindications

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

Prostin E2 Vaginal Tablets are not recommended in the following circumstances:

1. For 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 cephalopelvic disproportion may be present
- Cases in which foetal malpresentation is present
- Cases in which 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 ration favours surgical intervention.

2. In patients with a past history of, or existing, pelvic inflammatory disease, unless adequate prior treatment has been instituted.

3. In patients where there is clinical suspicion or definite evidence of placenta praevia or unexplained vaginal discharge and /or abnormal bleeding during this pregnancy.

4. 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 specialised obstetric units and should only be used where 24-hour resident medical cover is provided.

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 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.

Prostin E2 Vaginal Tablets and Prostin E2 Vaginal Gel are **not** bioequivalent.

Caution should be exercised in the administration of Prostin 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 pregnancy.

In labour induction, cephalopelvic relationships should be carefully evaluated before use of Prostin 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. Continuous electronic monitoring of uterine activity and foetal heart rate should be conducted during 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.

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 should be continuously monitored throughout labour. The possibility of uterine rupture should be borne in mind where high-tone uterine contractions are sustained in the absence of evidence of progression of labour.

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 (see section 4.8). Therefore, in those women the use of Prostin E2 Vaginal Tablets should be done 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 interactions

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

Dinoprostone is for use in pregnant women at or near term.

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 may decrease uterine blood flow and thereby could put the embryo or foetus at risk. Continuous electronic monitoring of uterine activity and foetal heart rate should be conducted during use of dinoprostone. (see section 4.4).

Breast-feeding

Prostaglandins are excreted in breast milk at very low concentrations. No measurable differences were observed in the milk of mothers delivering prematurely and at term.

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 E_1 during prolonged treatment. There is no evidence that short-term administration of prostaglandin E_2 can cause similar bone effects.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

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

Gastrointestinal disorders: Diarrhoea, nausea, vomiting

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)
Uterine contractile abnormalities (increase frequency, tone or duration), uterine rupture, abruptio placenta, pulmonary amniotic fluid embolism, rapid cervical dilatation

*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 vagina

General disorders and administration site conditions: Fever

Vascular disorders: Hypertension

Respiratory, thoracic and mediastinal disorders: Asthma, bronchospasm

Investigations: Foetal distress/altered foetal heart rate (FHR)

Post-marketing surveillance:

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 Special Warnings and Special Precautions for Use). The frequency of this adverse event, however, appears to be rare (<1 per 1,000 labours).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Overdosage may be expressed by uterine hypercontractility and uterine hypertonus. Because of the transient nature of PGE_2-induced myometrial hyperstimulation, non-specific, conservative management was found to be effective in the vast majority of the cases: i.e. maternal position change and administration of oxygen to the mother. B-adrenergic drugs may be used as a treatment of hyperstimulation following administration of PGE_2 for cervical ripening.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dinoprostone is a prostaglandin of the E series with actions on smooth muscle; the endogenous substance is termed prostaglandin E_2 (PGE_2). It induces contraction of 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 absorption of PGE_2 stimulates endogenous PGE_2 and PGF_{2a} production, similar to that which is seen in spontaneous labour.

5.2 Pharmacokinetic properties

General characteristics of active substance
Absorption is rapid. Dinoprostone is rapidly distributed and metabolised in the body, considerable metabolism occurring in the intestine prior to absorption. Urinary excretion represents the major route of elimination.

Characteristics in patients
No special characteristics (see "Special warnings and special precautions for use" for further information).

5.3 Preclinical safety data

Prostaglandin E_2 decreases mean arterial blood pressure, increases cardiac output and decreases peripheral resistances when administered intravenously to trained unanaesthetized dogs. The effect appears to be primarily due to peripheral vasodilation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose anhydrous
Microcrystalline cellulose
Maize starch
Magnesium stearate
Colloidal anhydrous silica

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store in a refrigerator at 2-8°C. Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Soft-tempered aluminium foil and low density polyethylene, heat sealed as Foil/PE/Tablet/PE/Foil, in strips of 4 tablets. Each carton contains 4 tablets (1 strip) or 8 tablets (2 strips).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pfizer Healthcare Ireland
9 Riverwalk
National Digital Park
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0822/133/004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 May 1985

Date of last renewal: 28 May 2005

10 DATE OF REVISION OF THE TEXT

July 2021