

DATA SHEET

PROSTIN[®] E2 (PGE2)

Dinoprostone 1 mg and 2 mg vaginal gel

Presentation

PROSTIN E2 vaginal gel is a translucent, thixotropic gel formulation containing either 1 mg or 2 mg dinoprostone in each 3.0 g (2.5 ml).

Uses

Actions

Prostaglandin E2 stimulates uterine and gastrointestinal smooth muscle. Although the exact mechanism of action is not fully understood, it is theorised that the pharmacologic actions of prostaglandin E2 are related to its ability to regulate intracellular levels of cyclic 3, 5-adenosine monophosphate (cAMP) and cellular membrane calcium ion transport. In many tissues prostaglandin E2 stimulates the synthesis of cAMP by activating adenylate cyclase. Contractions produced by the gravid uterus by prostaglandin E2 are similar to those occurring in the term uterus during spontaneous labour. Prostaglandin E2 also produces cervical dilation and softening.

Pharmacokinetics

Prostaglandin E2 is widely distributed in the body, and is rapidly metabolized in the liver, lungs, kidneys, spleen, and other tissues, primarily by oxidation of the side chains to at least nine inactive metabolites. The drug and its metabolites are excreted primarily in the urine, but small amounts are excreted in the faeces.

Indications

PROSTIN E2 is indicated for the induction of labour in term or near term women who have favourable induction features; and who have singleton pregnancy with a vertex position.

Dosage and Administration

An initial dose of 1 mg should be inserted into the posterior fornix. After 6 hours a second dose of either 1 mg or 2 mg may be administered depending on need; i.e. an absence of response to the initial 1 mg doses indicates the 2 mg dose should be given, while a 1mg dose should be suggested to augment an already present response to the initial dose.

Contraindications

Dinoprostone should not be used in patients with a hypersensitivity to dinoprostone or any other component of the product.

Dinoprostone should not be used in patients in whom oxytocic drugs are generally contraindicated such as:

- Multiple gestation
- Grand multiparity (6 or more previous term pregnancies)
- Engagement of the head not taken place
- Previous uterine surgery (e.g. caesarean section, hysterotomy)
- Cephalopelvic disproportion
- Foetal heart rate pattern suggests incipient foetal compromise
- Obstetric conditions where either maternal or foetal benefit/risk ratio favours surgical intervention
- Unexplained vaginal discharge and/or abnormal uterine bleeding during current pregnancy
- Nonvertex position.

Precautions

Dinoprostone products should be used with caution in patients with impaired cardiovascular, hepatic or renal function, asthma, glaucoma or raised intraocular pressure, or ruptured chorioamniotic membranes.

PROSTIN E2 Vaginal Gel is an intravaginal product. It is not to be used intra-cervically. The intracervical placement of dinoprostone gel may result in inadvertent disruption and subsequent embolization of antigenic tissue. This may cause, in rare circumstances, the development of Anaphylactoid Syndrome of Pregnancy (Amniotic Fluid Embolism).

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 labor induction (see Adverse Effects). Therefore, in these women, 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. The product is available only to hospitals and clinics with specialised obstetric units.

Continuous electronic monitoring of uterine activity and foetal heart rate should be conducted during use of this product. Patients who develop uterine hypertonias or hypercontractility, or in whom unusual foetal heart patterns develop, should be managed in a manner that addresses the welfare of the foetus and mother. As with any oxytocic agent, the risk of uterine rupture should be considered.

Prostaglandin E2 produced an increase in skeletal anomalies in rats and rabbits and has been shown to be embryotoxic in rats and rabbits.

Any dose that produces sustained increased uterine tone could put the embryo or fetus at risk.

Prostaglandins are excreted in breast milk at very low concentrations. No measurable differences in prostaglandins E₂ and F₂ were observed in the milk of mothers delivering prematurely and at term.

Interactions

The response to oxytocin may be accentuated in the presence of exogenous prostaglandin therapy. Concurrent use with other oxytocic agents is not recommended. The sequential use of oxytocin following PROSTIN E₂ is recommended, with a dosing interval of at least 6 hours.

Adverse Effects

Maternal adverse events

Uterine contractile abnormalities (increase frequency, tone, or duration), uterine rupture, nausea, vomiting, diarrhoea, fever, back pain, warm feeling in vagina, hypersensitivity reactions (e.g., anaphylactic reaction, anaphylactic shock and anaphylactoid reaction).

In post-marketing surveillance, an increased risk of post-partum disseminated intravascular coagulation has been described in patients whose labor was induced by pharmacological means, including dinoprostone (see Precautions). The frequency of this adverse event, however, appears to be rare (<1 per 1,000 labors)

Foetal adverse events

Foetal distress/altered foetal heart rate (FHR) and still birth.

Overdosage

Overdosage may be expressed by uterine hypercontractility and uterine hypertonus. Because of the transient nature of PGE₂-induced myometrial hyperstimulation, nonspecific, 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 PROSTIN E₂ Vaginal gel for cervical ripening.

Pharmaceutical Precautions

Store between 2-8°C.

Medicine Classification

Prescription Medicine.

Package Quantities

PROSTIN E2 gel is available in syringes of 1 mg or 2 mg.

Further Information

PROSTIN is a registered trademark

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