misoprostol vaginal insert (MISODEL®)

Riskier than dinoprostone for inducing labour

- The vaginal insert containing misoprostol has more adverse effects related to uterine hyperactivity than the dinoprostone vaginal insert.

In many countries, including France, labour is artificially triggered in about 15% to 40% of pregnancies, for both medical and non-medical reasons (1,2). One major risk associated with labour induction is the need for emergency Caesarean section due to failure of induction or to fetal heart rate disorders.

When the cervix is "unfavourable", prostaglandins are used first to relax the cervix (a). Sometimes they manage to induce or stimulate uterine contractions, otherwise oxytocin is used (2).

In France, dinoprostone, a prostaglandin E2 analogue, is authorised for labour induction in various forms, including a 10 mg vaginal insert. Tablets of misoprostol, a physiological prostaglandin E1 analogue, are sometimes used off-label by various routes, despite ill-defined conditions of use and an off-label use (3,4). An E1 analogue, is sometimes used, a physiological prostaglandin 10-mg vaginal insert. Tablets of dinoprostone are sometimes used in labour induction in various forms, including a dinoprostone (E2 analogue, is authorised for labour induction in various countries. Does it have any advantages over dinoprostone vaginal inserts?

No reduction in Caesarean section rates. Clinical evaluation of the vaginal insert containing 200 microg of misoprostol is based on a randomised, double-blind, "non-inferiority" trial versus dinoprostone 10 mg vaginal inserts in 1358 women, two-thirds of whom had never previously given birth. Labour was induced after at least 37 weeks of gestation in almost every case. All women had an unfavourable cervix and an unscarred uterus (b)(4,6).

The rate of Caesarean delivery was about 27% in both groups (4,6). About 1% of women in each group failed to achieve vaginal delivery after the first attempt at induction. The median time between introduction of the insert and vaginal delivery was shorter with misoprostol than with dinoprostone (22 versus 33 hours, p<0.001). Fewer women in the misoprostol group received oxytocin prior to delivery (48% versus 74%, p<0.001) (4,6).

Additional risks associated with uterine hyperactivity. In this trial, serious adverse events during childbirth were more frequent with misoprostol than with dinoprostone (12% versus 7%) (4,6). There were no deaths.

Adverse events associated with excessive uterine activity were significantly more frequent with misoprostol than with dinoprostone (49% versus 25%). They included uterine tachysystole (13% versus 4%), sometimes requiring treatment (4% versus 1%), or uterine tachysystole associated with fetal heart rate disorders (10% versus 3%) (c)(4). The presence of meconium in the amniotic fluid was more frequent in the misoprostol group (18% versus 14%), as was the use of tocolytic agents (12% versus 4%) (4).

Certain adverse events of concern for the mother or newborn were also more frequent in the misoprostol group, including: uterine rupture (one case versus none); a 5-minute neonatal Apgar score below 7 out of 10 (14 versus 7 cases); fetal acidosis (8 versus 4 cases); and hypoxic-ischaemic neonatal encephalopathy (4 versus 0 cases) (4). In contrast, dinoprostone was associated with significantly more infections of the placenta and amniotic fluid (chorioamnionitis) (9% versus 6% with misoprostol) and more frequent use of injectable antibiotics during and after childbirth (9% versus 5%), probably due to prolonged labour (4,6).

Similar vaginal inserts, longer misoprostol half-life. The conditions of use and storage of the dinoprostone and misoprostol vaginal inserts are similar.

According to the respective summaries of product characteristics (SPC), misoprostol has a longer half-life than dinoprostone (40 minutes versus 1 to 3 minutes) (7,8). This is a disadvantage if, for example, the device has to be removed because of adverse effects (persistent drug exposure of the mother and fetus), or if oxytocin needs to be administered (risk of over-stimulating the uterus) (8). According to the SPC, a waiting period of at least 30 minutes must be respected between insert removal and oxytocin administration (8).

In practice. As compared with the dinoprostone vaginal insert, the misoprostol insert reduces time to delivery (about 22 versus 33 hours) as well as the incidence of infections (chorioamnionitis), but it does not avoid the need for Caesarean section. The misoprostol insert increases the risk of uterine tachysystole that requires treatment or is associated with fetal heart rate disorders. The dinoprostone vaginal insert is safer for both the mother and her newborn.

misoprostol vaginal insert

MISODEL®

- 200 microg of misoprostol per vaginal insert (approximately 7 microg/hour released over 24 hours)

prostaglandin E1 analogue

- Indication: "(...) induction of labour in women with an unfavourable cervix, from 36 weeks of gestation, in whom induction is clinically indicated".

[European decentralised procedure]