Misoprostol vaginal delivery system (Mysodelle)

FERRING PHARMACEUTICALS

DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION

Misoprostol vaginal delivery system (Mysodelle): Reports of excessive uterine tachysystole (contractions) that may not respond to tocolytic treatment

Dear Healthcare Professional,

Ferring Pharmaceuticals in agreement with the European Medicine Agency and the Medicines and Healthcare Products Regulatory Agency (MHRA) would like to inform you of reports of excessive uterine tachysystole with misoprostol and actions to be taken.

Summary

- **Misoprostol can cause excessive uterine tachysystole that may not respond to tocolytic treatment.**
- **Misoprostol should be removed:**
    - **at onset of labour: rhythmic, firm contractions of adequate quality and that cause cervical change, and/or at the latest when cervical dilation is 4 cm**
    - **if prolonged or excessive uterine contractions occur**
    - **if there is a clinical concern for the mother and/or baby.**

Background on the safety concern

Misoprostol (Mysodelle) is used for induction of labour in women with an unfavourable cervix, from 36 weeks gestation, in whom induction is clinically indicated.

Cases of uterine tachysystole which did not subside with the use of tocolysis have been reported in clinical studies and following marketing of the medicine. A review of these cases concluded that excessive uterine tachysystole that may not respond to tocolytic treatment can be caused by the use of misoprostol, even when the medicine is used according to the product information. The product information has been updated to reflect this finding, and with actions to take to ensure that this risk is adequately handled.

The vaginal delivery system should be removed immediately in the following situations:

- Onset of labour: rhythmic, firm contractions of adequate quality and that cause cervical change, and/or at the latest when cervical dilation is 4 cm, or
- If uterine contractions are prolonged or excessive, namely:
    - Tachysystole: more than 5 contractions in a 10 minute window, averaged over a 30 minute window

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- Prolonged contractions: single contractions lasting 2 minutes or more
- Hypertonic contractions: contractions are too frequent and a high resting tone in the uterus.

- If there is a clinical concern for the mother and/or baby
- When 24 hours have elapsed since insertion

Being prepared to administer tocolytic therapy is recommended and should this be needed, it can be administered without delay after removal of Mysodelle.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme.

Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

It is easiest and quickest to report ADRs online via the Yellow Card website - https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store.

Alternatively, prepaid Yellow Cards for reporting are available by: writing to FREEPOST YELLOW CARD (no other address details necessary), by emailing yellowcard@mhra.gov.uk, at the back of the British National Formulary (BNF), by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789 o or by downloading and printing a form.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

Yours faithfully

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Other company contact point

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Prescribing Information: Mysodelle® (misoprostol) 200 micrograms vaginal delivery system.

Please consult the full Summary of Product Characteristics before prescribing.

Name of Product: Mysodelle® 200 micrograms vaginal delivery system.
Composition: Each vaginal delivery system contains 200 micrograms misoprostol (Prostaglandin E1).
Indication: Mysodelle® is indicated for induction of labour in women with an unfavourable cervix, from 36 weeks gestation, in whom induction is clinically indicated.
Dosage and administration: Mysodelle® 200 micrograms is a controlled release formulation. One vaginal delivery system is administered high into the posterior vaginal fornix. Mysodelle® should only be administered by trained obstetric personnel in a hospital setting where facilities for continuous fetal and uterine monitoring are available. The condition of the cervix should be assessed carefully before Mysodelle® is used. After insertion, uterine activity and fetal condition must be carefully monitored. The maximum recommended dose is one Mysodelle® vaginal delivery system (200 micrograms). Remove Mysodelle at onset of labour (3 or more contractions in 10 minutes), if tachysystole occurs (> 5 contractions in 10 minutes averaged over a 30 minute window) or if 24 hours have elapsed since insertion.
Contraindications: Hypersensitivity to the active substance or to any of the excipients; When labour has started; Suspicion or evidence of fetal compromise prior to induction; When oxytocic drugs and/ or other labour induction agents are being given; Suspicion or evidence of uterine scar resulting from previous uterine or cervical surgery; Uterine abnormality (e.g. bicornate uterus); Placenta praevia or unexplained vaginal bleeding after 24 weeks gestation with this pregnancy; Fetal malpresentation; Signs or symptoms of chorioamnionitis, unless adequate prior treatment has been instituted; Before week 36 of gestation.
Special Warnings and Precautions: Mysodelle® can cause excessive uterine stimulation that may not respond to tocolytic treatment. If tocolytic therapy is needed, it can be administered immediately after removal of Mysodelle. If uterine contractions are prolonged or excessive, or there is a clinical concern for the mother or baby, remove the vaginal delivery system; Mysodelle® should be removed before oxytocin administration is initiated; In women with pre-eclampsia, evidence or suspicion of fetal compromise should be ruled out; Mysodelle® has not been studied in women whose membranes have been ruptured for more than 48 hours prior to the insertion of Mysodelle®; For women with positive Group B Streptococcus status requiring prophylactic antibiotics, careful consideration should be given regarding timing of antibiotic therapy in order to achieve adequate protection for the neonates; No studies in multiple pregnancies have been performed; Mysodelle® has not been studied in women with more than 3 previous vaginal deliveries after 24 weeks gestation; Mysodelle® should be used with caution in patients with modified bishop score (mBS) >4; A second dose of Mysodelle® is not recommended; An increased risk of post-partum disseminated intravascular coagulation has been described in patients whose labour has been induced by any physiological or pharmacological method; Butylated hydroxyanisole (antioxidant in the cross-linked hydrogel polymer) can cause skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.
Side effects: Very common: foetal heart rate disorder, abnormal labour affecting foetus, meconium in amniotic fluid, uterine contractions abnormal (tachysystole). Common: neonatal respiratory depression, transient tachypnoea of the newborn, foetal acidosis, postpartum haemorrhage, uterine hypertonus, Apgar score low. Uncommon: hypoxic-ischaemic encephalopathy, nausea, vomiting, rash, antepartum haemorrhage, premature separation of placenta, pruritus genital, blood pressure increased, uterine rupture.
Special precautions for storage: Store in a freezer (-10 to -25°C). No thawing is required prior to use.
Presentation: Packs containing 5 vaginal delivery systems. Each vaginal delivery system is contained within an individual foil sachet.
Marketing Authorisation Number: PL 03194/0112. **Marketing Authorisation Holder:** Ferring Pharmaceuticals Ltd. Drayton Hall, Church Road, West Drayton, UB7 7PS, UK.
Legal category: POM. **Basic NHS price:** £465 per 5 x 200 micrograms vaginal delivery system
Date of preparation: December 2017; **PI Job Code: MYSO/1455/2014/UK(2)**
Mysodelle ® is a registered trademark.

Adverse events should be reported. Reporting forms and information can be found at
www.mhra.gov.uk/yellowcard.
Adverse events should also be reported to Ferring Pharmaceuticals Ltd.
Tel: 0844 931 0050. Email: **medical@ferring.com**