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United Drug Distributors
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9 Riverwalk
National Digital Park
Citywest Business Campus
Dublin 24, Ireland

16th June 2021

DINOPROSTONE

PROPESS 10 MG VAGINAL DELIVERY SYSTEM (PA1009/029/001)

PROSTIN E2 1MG VAGINAL GEL (PA0822/178/001)

PROSTIN E2 2MG VAGINAL GEL (PA0822/178/002)

PROSTIN E2 1MG/ML CONCENTRATE FOR SOLUTION FOR INFUSION (PA0822/133/003)

PROSTIN E2 3MG VAGINAL TABLETS (PA 0822/133/004) (NOT MARKETED)

Strengthening of wordings on dose recommendations, warnings and recommendations regarding the risks of uterine hyperstimulation, uterine rupture and foetal/neonatal death and inclusion of wordings on restriction of usage to qualified health care professionals and to hospitals and clinics as recommended by PRAC, CMDh and Health Products Regulatory Authority (HPRA)

Dear Healthcare Professional,

Ferring Ireland Limited and Pfizer Healthcare Ireland in agreement with the Health Products Regulatory Authority (HPRA) would like to inform you of the following upcoming updates to the dinoprostone product information for the above listed products. The purpose of these updates is to strengthen existing warnings and contraindications to further minimize the risk of serious complications due to uterine hyperstimulation and rupture. This is a joint communication being distributed by Ferring Ireland Limited and Pfizer Healthcare Ireland who both market dinoprostone products in Ireland under the tradenames PROPESS and PROSTIN respectively.

SUMMARY OF UPDATES

- Strengthening of wordings to emphasise restriction of usage to qualified health care professionals and to hospitals and clinics with specialized obstetric units with facilities for continuous monitoring

- Strengthening of warning and recommended risk mitigation measures regarding the risks of uterine hyperstimulation and uterine rupture and their serious complications, including foetal and neonatal death

- Strengthening of the warning and recommendations regarding adherence to the maximum dose (both PROPESS and PROSTIN) and adherence to the correct dosing interval (PROSTIN only).

- Strengthening of the contraindications (PROPESS only) and warnings and precautions for use, including the recommendation against the concurrent use of oxytocic agents and for the appropriate dosing interval for sequential use of dinoprostone and oxytocin (at least 30 minutes following removal of PROPESS and at least 6 hours following administration of PROSTIN).

BACKGROUND ON THE SAFETY CONCERN AND THE RECOMMENDATIONS

PROPESS 10 MG VAGINAL DELIVERY SYSTEM (PA1009/029/001) is indicated for the initiation of cervical ripening in patients at term.

PROSTIN E2 1MG VAGINAL GEL (PA0822/178/001) and PROSTIN E2 2MG VAGINAL GEL (PA0822/178/002) are indicated for the induction of labour in the absence of foetal and maternal contraindications.

PROSTIN E2 1MG/ML CONCENTRATE FOR SOLUTION FOR INFUSION (PA0822/133/003) is indicated for the induction of labour by the intravenous route.

PROSTIN E2 3MG VAGINAL TABLETS (PA 0822/133/004) (NOT MARKETED) is indicated in the induction of labour when there are no gynaecological, obstetrical or medical conditions, either maternal or foetal, that preclude vaginal delivery.

In a review of post-marketing data, a number of cases of uterine hyperstimulation and uterine rupture that lead to serious complications of foetal and neonatal death were reported in the context of medication errors and off-label use. Medication errors identified were the use of higher doses than recommended and in the case of PROSTIN, use of a higher frequency of dosing interval. Off-label use reported included use in contraindicated patients (previous caesarean section or a history of a scarred uterus) and concurrent use of oxytocin.

With regard to uterine hyperstimulation, uterine rupture and associated complications of foetal and neonatal death the product information will be updated as follows:

Update of section 4.2 (Posology and method of administration) of the SmPC to include wording to restrict usage to qualified health care professionals and hospitals and clinics with specialised obstetric units with facilities for continuous monitoring and a strengthening of the warning regarding the maximum recommended dose/dosing interval.

Update of sections 4.3 (Contraindications) and 4.4 (Special warnings and precautions for use) of the SmPC to further strengthen the contraindications and warnings and precautions for use.

Update of section 4.8 (Undesirable effects) of the SmPC to add ‘foetal death, stillbirth and neonatal death’ as an adverse reaction with frequency not known.

The Package Leaflet (PL) will also be updated accordingly.

Use of dinoprostone in accordance with the recommended labelling will further mitigate against these serious complications and ensure that the benefits of administering dinoprostone to pregnant women continue to outweigh the risks.

This communication is being disseminated at this time at the request of HPRA. On approval of the product information updates by the HPRA, the updated SmPCs and PIs/PILs, as appropriate, will be posted on www.hpra.ie and www.medicines.ie.

CALL FOR REPORTING

Suspected adverse reactions and **any medication error** should be reported to the Health Products Regulatory Authority (HPRA) via the HPRA Website: www.hpra.ie.

COMPANY CONTACT POINTS

FERRING

Suspected PROPESS adverse reactions may also be reported to Ferring using email:

EnquiriesIrelandMailbox@Ferring.com

For further information, please contact Medical Information at Ferring Ireland Limited, United Drug Distributors, Magna Drive, Magna Business Park, Citywest Road, Dublin 24, Ireland. Phone 086 048 3100 during business hours or +44 (0) 800 111 4126.

PFIZER

Suspected PROSTIN adverse reactions may also be reported to Pfizer Medical Information on +44 (0) 800 633 363.

For further information, please contact Medical Information at the following Address: Pfizer Healthcare Ireland, 9 Riverwalk, National Digital Park, Citywest Business Campus, Dublin 24, Ireland. Phone: 1-800 633 363, Fax: 01 467 6501 or Email: eumedinfo@pfizer.com.

Yours sincerely,

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