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(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

Domperidone for nausea and vomiting: lack of efficacy in children; reminder of contraindications in adults and adolescents

Your attention is drawn to the Medicines and Healthcare products Regulatory Agency's (MHRA) announcement that domperidone is no longer licensed for use in children younger than 12 years or those weighing less than 35 kg. Results from a placebo-controlled study in children younger than 12 years with acute gastroenteritis did not show any difference in efficacy at relieving nausea and vomiting compared with placebo.

A European review of the safety of domperidone in 2014 introduced new restrictions following continued reports of cardiac side effects. At the time, there were limited data to support paediatric use in the relief of the symptoms of nausea and vomiting, and studies were requested to provide further data to support efficacy.

A multicentre, double-blind, randomised, placebo-controlled, parallel-group, prospective study evaluated the safety and efficacy of domperidone in 292 children with acute gastroenteritis aged between 6 months and 12 years (median age 7 years). In addition to oral rehydration treatment (ORT), patients were randomised to receive domperidone oral suspension at 0.25 mg/kg (up to a maximum of 30 mg domperidone per day), or placebo, 3 times a day, for up to 7 days. This study did not show domperidone suspension plus ORT to be significantly more effective than placebo plus ORT at reducing vomiting episodes during the first 48 hours after the first treatment administration. The study did not reveal any new safety concern.

A European review assessed this new evidence that domperidone is not as effective in this population as previously considered. Consequently, the product information for United Kingdom domperidone medicines has been updated to remove the indication in children younger than 12 years of age.

Domperidone is also used outside of its authorised indications in children in the United Kingdom for gastrokinetic effects in conditions other than nausea and vomiting. If a specialist physician considers, based on their professional judgement and available evidence of the medical condition, that domperidone use in any condition is justified in a child younger than 12 years, the patient or parent/caregiver should be fully informed of the potential benefits and risks of the different options.

The European safety review in 2014 confirmed risk of serious cardiac adverse drug reactions related to domperidone, including QTc prolongation, torsade de pointes, serious ventricular arrhythmia, and sudden cardiac death. The review concluded that additional risk minimising measures were necessary to improve the balance between benefits and risks and to reduce the risk of serious cardiac adverse events. Recent regulatory studies in several European countries, including the United Kingdom, show a proportion of physicians are not aware of the changes in indication and the contraindications introduced in 2014. All healthcare professionals are thus reminded to follow the precautions for safe use of domperidone-containing products.

Healthcare professionals are advised:

- Domperidone is now authorised for the relief of symptoms of nausea and vomiting only in adults and adolescents 12 years of age or older and weighing 35 kg or more.
- Consider alternative treatments to domperidone in children younger than 12 years of age who need relief of symptoms of nausea and vomiting
- European regulatory studies show that some physicians, including in the United Kingdom, are not aware of the important precautions for use of domperidone introduced in 2014. For reminder of contraindications and recommendations for dose and treatment duration, please refer to the MHRA website.

Please refer to the following website in MHRA for details:
https://www.gov.uk/drug-safety-update/domperidone-for-nausea-and-vomiting-lack-of-efficacy-in-children-reminder-of-contraindications-in-adults-and-adolescents

In Hong Kong, there are 42 registered pharmaceutical products containing domperidone, and all products are prescription-only medicines. So far, the Department of Health (DH) has not received any case of adverse drug reaction related to domperidone.

News related to risk of serious cardiac adverse drug reactions related to domperidone was previously issued by various overseas drug regulatory authorities, and was posted on the Drug Office website since 8 Mar 2012, with the latest update posted on 7 Jun 2017. Letters to inform local healthcare professionals were issued by DH on 8 Mar 2012 and 10 Mar 2014. In Feb 2012 and May 2014, the Registration Committee of the Pharmacy and Poisons Board discussed the matter and

decided to update the sales pack or package insert of domperidone-containing products to include the appropriate safety information related to cardiovascular risk and to tighten the control over the sale of oral domperidone products.

In light of the above MHRA's announcement regarding removal of the indication in children younger than 12 years of age, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Undesirable Medical Advertisements and Adverse Drug Reaction Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Joseph LEE)
for Assistant Director (Drug)