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(來函請敍明此檔案號碼) DH DO DIMC/7-30/1
(IN REPLY PLEASE QUOTE THIS FILE REF.)

31 Dec 2024

Dear Healthcare Professionals,

Potential risk of psychiatric withdrawal events with domperidone for stimulation of lactation

Your attention is drawn to the Singapore Health Sciences Authority's (HSA) announcement of a safety alert on the potential risk of psychiatric withdrawal events with domperidone for stimulation of lactation.

Domperidone is a selective dopamine receptor antagonist approved locally for the treatment of delayed gastric emptying, gastro-oesophageal reflux, oesophagitis, and nausea and vomiting. The approved recommended dose for adults is 30 mg/day, which can be increased to a maximum of 40 mg/day. The maximum treatment duration generally ranges from one to four weeks depending on the indication but may be extended upon re-assessment of the patient's need for continued treatment.

Domperidone has also been used off-label to promote lactation when deemed medically necessary by doctors. The prescribed dose and duration of treatment is based on the assessment of the individual patient's situation. Domperidone-containing products have been registered in Singapore since 1989 and there are currently nine products registered.

A small number of cases of psychiatric adverse events following sudden discontinuation or tapering of domperidone for stimulation of lactation have been reported overseas. These included nine cases identified by Health Canada and six cases by the US Food and Drug Administration (FDA). These cases reported various adverse events such as agitation, anxiety, confusion, depression and insomnia. In most of these cases, the patients had been taking daily doses greater than 30mg and for longer than four weeks prior to the sudden discontinuation or tapering attempt.

It should be noted that the number of cases is small, and the onset of psychiatric symptoms could be independently associated with the cessation of breastfeeding or the emotional distress resulting from

lactation difficulties, rather than being directly linked to domperidone discontinuation. These limit the assessment of a causal relationship between domperidone withdrawal and the reported psychiatric events. Nevertheless, there is a biological plausibility for the association. One postulated mechanism involves the abrupt decrease in plasma prolactin levels, which follows prolonged hyperprolactinaemia induced by long-term domperidone treatment. This could produce a sudden rise in dopaminergic activity and precipitate dopamine-mediated psychiatric events. Another hypothesis is that the higher doses of domperidone used for stimulation of lactation may result in significant penetration of the blood-brain-barrier, which is not generally associated with on-label doses.

As at 31 October 2024, HSA has not received any local adverse event report of psychiatric withdrawal events following domperidone use in stimulation of lactation from healthcare professionals. However, there was one medically unverified report from a consumer who reported that she experienced psychiatric events (including anxiety and depression) upon discontinuation of domperidone prescribed after delivery to help with breastfeeding. The dose and duration of domperidone prescribed was not provided and it was noted that she had a medical history of depression before pregnancy.

Healthcare professionals may wish to consider the above information in their management of patients prescribed with domperidone for stimulation of lactation.

Please refer to the following website in HSA for details:
https://www.hsa.gov.sg/announcements/safety-alert/potential-risk-of-psychiatric-withdrawal-events-with-domperidone-for-stimulation-of-lactation

In Hong Kong, there are 42 registered pharmaceutical products containing domperidone. All products are prescription-only medicines. So far, with regard to domperidone, the Department of Health (DH) has received one case of adverse drug reaction, but this case was not related to psychiatric withdrawal events. In light of the above HSA's announcement, the DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. 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 Clinical Trials and Pharmacovigilance 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,

pp (Terence MAN)
for Assistant Director (Drug)