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(來函請敍明此檔案號碼 DH DO PRIE/7-30/15
(IN REPLY PLEASE QUOTE THIS FILE REF.)

11 Nov 2020

Dear Healthcare Professionals,

**Concomitant use of Opsumit® (macitentan) Film-Coated Tablet 10mg with dual moderate CYP3A4/CYP2C9 inhibitors that could result in an increase in exposure to Opsumit®**

Your attention is drawn to the Singapore Health Sciences Authority's (HSA) announcement that a Dear Healthcare Professional Letter has been issued by Johnson & Johnson Pte Ltd to inform healthcare professionals of a potential drug-drug interaction (DDI) between Opsumit® (macitentan) and dual moderate CYP3A4/CYP2C9 inhibitors that could result in an increase in systemic exposure to Opsumit®.

A review has found CYP2C9 to be responsible for 26% of metabolism of macitentan as opposed to the previous understanding that it would provide a minor contribution. Co-administration of fluconazole (400 mg qd), a dual moderate CYP2C9 and CYP3A4 inhibitor, could result in a 3.8-fold increase in macitentan exposure due to the dual inhibition of the two most important metabolic pathways. Nonetheless, no safety concerns have been identified with the concurrent administration of dual CYP3A4/CYP2C9 inhibitors (e.g. fluconazole/amiodarone) and macitentan 10 mg and there is no change in the current recommended dose of macitentan 10 mg once daily. The package insert for Opsumit® will be updated accordingly to reflect the new DDI information. Healthcare professionals are advised to exercise caution when macitentan is administered concomitantly with moderate dual inhibitors of CYP3A4 and CYP2C9, or with both a moderate CYP3A4 inhibitor and a moderate CYP2C9 inhibitor.

Please refer to the following website in HSA for details:
https://www.hsa.gov.sg/announcements/dear-healthcare-professional-letter/concomitant-use-of-opsumit-(macitentan)-film-coated-tablet-10mg-with-dual-moderate-cyp3a4-cyp2c9-inhibitors-that-could-result-in-an-increase-in-exposure-to-opsumit

In Hong Kong, Opsumit Tablets 10mg (HK-64419) is a registered pharmaceutical product containing

macitentan. The product is registered by Johnson & Johnson (Hong Kong) Ltd, and is a prescription-only medicine. So far, the Department of Health (DH) has received 10 cases of adverse drug reaction related to macitentan, but these cases are not related to drug interaction. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities. 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)