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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.)

25 Apr 2025

Dear Healthcare Professionals,

Cyclin-dependent kinase inhibitors (abemaciclib, palbociclib and ribociclib) and HMG-CoA reductase inhibitors (atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin and simvastatin) (Statins): Assessing the potential risk of rhabdomyolysis due to drug interaction

Your attention is drawn to the Health Canada's announcement that it reviewed the potential risk of rhabdomyolysis and the drug interaction between cyclin-dependent kinase inhibitors (CDKIs) and HMG-CoA reductase inhibitors, more commonly known as statins. The safety review was triggered by the European Medicines Agency (EMA)'s investigation of the risk with palbociclib and statins.

Rhabdomyolysis is a rare and potentially life-threatening condition in which muscles break down and their contents are released into the blood stream. This can lead to organ damage, such as kidney failure. Rhabdomyolysis is a known risk associated with statins. Some drugs may increase the body's exposure to statins, thereby increasing the patient's risk of statin-related rhabdomyolysis. Though the risk of rhabdomyolysis is known and well labelled for statins, this review investigated the potential risk of rhabdomyolysis due to the drug interaction between CDKIs and statins.

Cyclin-dependent kinase inhibitors are a class of prescription drugs authorized for sale in Canada for the treatment of a specific, but common, type of breast cancer. Statins are prescription drugs authorized for sale in Canada, to be used along with diet, to lower cholesterol and triglyceride (fat) levels in the blood, and to reduce the risk of heart attack or stroke in patients with risk factors for heart problems.

Health Canada reviewed the available information provided by the manufacturers, as well as from searches of the Canada Vigilance database and the scientific literature. Health Canada reviewed 13 cases (1 Canadian and 12 international) of rhabdomyolysis in patients taking both a CDKI (palbociclib

or ribociclib) and statin (rosuvastatin or simvastatin). All 13 cases were found to be possibly linked to the drug interaction between CDKIs and statins. There were no deaths reported among the cases. In all 13 cases, patients had been on statin therapy prior to starting CDKI therapy. In 8 of those cases, statin therapy was ongoing without reported rhabdomyolysis for over 1 year prior to the start of CDKI therapy. In 6 of these 8 cases, rhabdomyolysis occurred within 30 days of the addition of a CDKI, which suggests the possibility that CDKI introduction increased the body's exposure to statins, leading to rhabdomyolysis.

While a drug interaction between CDKIs and statins is not currently labelled for either class of product, information contained in the Canadian product monograph (CPM) concerning how they work in the body supports the possibility of a drug interaction. Health Canada also reviewed a study that investigated the potential interaction between palbociclib and atorvastatin using computer simulation. This study suggested that 125 mg/day of palbociclib could moderately increase the exposure of 40 mg/day atorvastatin in healthy volunteers, thereby potentially increasing the risk of rhabdomyolysis.

Although observed rhabdomyolysis cases were limited to the combined administration of palbociclib or ribociclib, and rosuvastatin or simvastatin, the totality of evidence supports the precautionary conclusion that rhabdomyolysis is a potential risk due to a drug interaction between CDKIs and statins.

Health Canada's review of the available information found a possible link between rhabdomyolysis and the drug interaction between CDKIs and statins. Health Canada will work with the manufacturers to update the CPM for all CDKIs to include the risk of rhabdomyolysis due to the drug interaction with statins. Health Canada will also inform healthcare professionals about this update through a Health Product InfoWatch communication.

Please refer to the following website in Health Canada for details:
https://dhpp.hpfb-dgpsa.ca/review-documents/resource/SSR1742565339867

In Hong Kong, there are registered pharmaceutical products containing abemaciclib (3 products), palbociclib (6 products) and ribociclib (1 product). All products are prescription-only medicines. So far, the Department of Health (DH) has received adverse drug reaction with regard to abemaciclib (26 cases), palbociclib (147 cases) and ribociclib (28 cases), but these cases were not related to drug interaction. In light of the above Health Canada's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

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,

(Vincent CHIANG)
for Assistant Director (Drug)