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DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG REGISTRATION AND IMPORT/EXPORT CONTROL DIVISION
3/F., Public Health Laboratory Centre,
382 Nam Cheong Street, Kowloon, Hong Kong

5 May 2016

Dear Healthcare Professionals,

BCR-ABL Tyrosine Kinase Inhibitors

[GLEEVEC (imatinib mesylate), TASIGNA (nilotinib), BOSULIF (bosutinib), SPRYCEL (dasatinib), ICLUSIG (ponatinib hydrochloride)] - Risk of Hepatitis B Reactivation

Your attention is drawn to the Health Canada's announcement regarding a recent review of data from clinical trials and postmarketing experience showing that hepatitis B virus (HBV) reactivation can occur in chronic HBV carriers, after they received BCR-ABL tyrosine kinase inhibitors (TKIs). The Canadian Product Monographs will be updated to reflect this new safety information.

Some of these cases included acute hepatic failure or fulminant hepatitis leading to liver transplantation or death. These case reports indicate that HBV reactivation may occur at any time during BCR-ABL TKI treatment. Some of these patients had a documented history of hepatitis B. An increase in viral load or positive serology after initiating treatment with a BCR-ABL TKI occurred with HBV reactivation. For other cases, the serologic status at baseline was not known. HBV reactivation is considered to be a class-effect of BCR-ABL TKIs, although the mechanism and the frequency of HBV reactivation during exposure is not known at this time.

BCR-ABL TKIs are used for the treatment of specific types of blood cancers, including Philadelphia chromosome-positive (Ph+) chronic myelogenous leukemia (CML) and Ph+ acute lymphoblastic leukemia (ALL), and less commonly, other types of cancers. A recent review of clinical trials and reports received in the post-marketing period as well as published medical literature indicate that cases of HBV reactivation have occurred in patients who are carriers for the virus after receiving BCR-ABL TKIs. In some of the cases, HBV reactivation caused acute liver failure or fulminant hepatitis requiring liver transplantation or death. HBV reactivation occurred at different points during therapy, with cases reported worldwide between three weeks and more than 8 years after starting treatment. Although no mechanism for HBV reactivation has been identified to date, based on a review of the available evidence, HBV reactivation is considered to be a class effect of BCR-ABL TKIs.

Patients should be tested for HBV infection status before initiating treatment with BCR-ABL TKIs. Healthcare professionals should consult experts in liver disease and in the treatment of HBV promptly before starting treatment with BCR-ABL TKIs in patients with positive HBV serology (including those with active disease) and in patients who test positive for HBV infection during treatment.

Healthcare professionals should closely monitor patients who are carriers of HBV, who are currently on or require a BCR-ABL TKI treatment for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy.

Please refer to the following website in Health Canada for details:

http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2016/58222a-eng.php

In Hong Kong, there are 13 registered pharmaceutical products belong to the class of BCR-ABL TKIs (including 8 containing imatinib, 2 containing nilotinib and 3 containing dasatinib), while there is no registered product containing bosutinib and ponatinib. All of the products are prescription only medicines. Related news has been released by HSA and was posted on the Drug Office website on 31 March 2016. Letters to inform local healthcare professionals were issued on the same day. So far, the Department of Health (DH) has received four adverse drug reaction cases, three involved imatinib and one involved dasatinib. Amongst which, one case of suspected drug-induced liver injury was related to imatinib. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board; and DH will remain vigilant on the safety updates on the products from 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 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,

(Grant NG)

for Assistant Director (Drug)