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(IN REPLY PLEASE QUOTE THIS FILE REF.)

19 Jun 2020

Dear Healthcare Professionals,

Xeljanz and Xeljanz XR (tofacitinib) and Jakavi (ruxolitinib) - Janus Kinase (JAK) inhibitors - Assessing the Potential Risk of Blood Clots in the Deep Veins (Venous Thromboembolic Events)

Your attention is drawn to the Health Canada's announcement that it reviewed the potential risk of venous thromboembolic events (VTE), including blood clots in the veins of the legs and arms (deep vein thrombosis) and blood clots in the lungs (pulmonary embolism), linked with the use of Janus Kinase (JAK) inhibitors. This review was triggered by early results from an ongoing safety study for Xeljanz (tofacitinib).

Given that there were already serious warnings for VTE in the product safety information for Olumiant (baricitinib), another JAK inhibitor, the safety review focused on the safety findings of the other JAK inhibitors marketed in Canada at the time of the review, Xeljanz and Xeljanz XR (tofacitinib) and Jakavi (ruxolitinib).

The safety review found that an ongoing safety study for Xeljanz showed an increased risk of blood clots in the lungs and death when the drug was taken at a high dose of 10 mg twice a day. This study is being conducted in patients 50 years of age or older with rheumatoid arthritis and at least one cardiovascular risk factor.

Health Canada's assessment focused on 51 cases (8 Canadian and 43 international) of VTE in people taking Xeljanz/Xeljanz XR. Of the 51 cases, 38 were found to be possibly linked to Xeljanz/Xeljanz XR, 3 were not likely to be linked and 10 cases did not have enough information to be assessed. Among the 51 cases, there were 2 deaths possibly linked to the use of Xeljanz/Xeljanz XR. The patients described in the case reports also had inflammatory diseases that may increase the risk of VTE.

Health Canada also assessed 8 Canadian cases of VTE in patients taking Jakavi. Of the 8 cases, 3 cases showed a possible link to Jakavi. Among the 8 cases, there was one death, but the report did not contain enough information to link the death to the use of Jakavi. The patients described in the case reports also had blood disorders that may increase the risk of VTE. The information available from the published literature did not provide case reports or information that linked VTE with the use of Xeljanz/Xeljanz XR and/or Jakavi.

Health Canada's review has concluded that there is a link between the risk of VTE and the use of Xeljanz. The review has concluded that Xeljanz/Xeljanz XR should be avoided in patients at increased risk of thrombosis and it should be discontinued in patients with signs of thrombosis. Xeljanz should be used at the lowest dose that works well and for the shortest duration in patients with ulcerative colitis. The product safety information for Xeljanz/Xeljanz XR has been updated to include this new safety information. Health Canada's review also found a possible link between Jakavi and VTE. Health Canada will be working with the manufacturer to update the product safety information for Jakavi to include the risk of VTE.

Please refer to the following website in Health Canada for details:
https://hpr-rps.hres.ca/reg-content/summary-safety-review-detail.php?lang=en&linkID=SSR00240

In Hong Kong, there are 2 registered pharmaceutical products containing tofacitinib, namely Xeljanz Tablets 5mg (HK-63303) and Xeljanz XR Extended Release Tablets 11mg (HK-66141) which are registered by Pfizer Corporation Hong Kong Limited; 4 products containing ruxolitinib, namely Jakavi Tab 20mg (HK-61972), Jakavi Tab 5mg (HK-61973), Jakavi Tab 15mg (HK-61974) and Jakavi Tablets 10mg (HK-66148) which are registered by Novartis Pharmaceuticals (HK) Limited; and 2 products containing baricitinib, namely Olumiant Tablets 2mg (HK-65663) and Olumiant Tablets 4mg (HK-65664) which are registered by Eli Lilly Asia, Inc. All products are prescription-only medicines.

So far, the Department of Health (DH) has received 6 cases of adverse drug reaction related to tofacitinib, of which 2 cases are related to deep vein thrombosis. The DH has received 17 cases of adverse drug reaction related to ruxolitinib, but these cases are not related to deep vein thrombosis or pulmonary embolism. The DH has not received any case of adverse drug reaction related to baricitinib.

Related news on the risk of blood clots of tofacitinib was previously issued by various overseas drug regulatory authorities, and was posted on the Drug Office website since 26 Feb 2019, with the latest update posted on 19 Mar 2020. Letters to inform local healthcare professionals were issued by the DH on 29 Jul 2019. In Dec 2019, the Registration Committee of the Pharmacy and Poisons Board discussed the matter, and decided that the sales pack or package insert of tofacitinib should include the relevant safety information.

Related news on the risk of blood clots of baricitinib was previously issued by the United Kingdom Medicines and Healthcare products Regulatory Agency, and was posted on the Drug Office website on 19 Mar 2020. The current local product inserts already contain safety information on the risk of venous thromboembolism.

In light of the risk of venous thromboembolic events associated with the use of ruxolitinib in the above Health Canada's announcement, 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)