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DEPARTMENT OF HEALTH
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(來函請敍明此檔案號碼)
(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

Xeljanz, Xeljanz XR (tofacitinib): Drug Safety Communication - Due to an Increased Risk of Blood Clots and Death with Higher Dose

Your attention is drawn to the United States Food and Drug Administration's (FDA) announcement that it has approved new warnings about an increased risk of blood clots and of death with the 10 mg twice daily dose of Xeljanz, Xeljanz XR (tofacitinib), which is used in patients with ulcerative colitis. In addition, the approved use of tofacitinib for ulcerative colitis will be limited to certain patients who are not treated effectively or who experience severe side effects with certain other medicines. The FDA approved these changes, including adding the most prominent Boxed Warning, after reviewing interim data from an ongoing safety clinical trial of tofacitinib in patients with rheumatoid arthritis (RA) that examined a lower and this higher dose of the medicine.

Tofacitinib works by decreasing the activity of the immune system; an overactive immune system contributes to RA, psoriatic arthritis (PsA), and ulcerative colitis. Tofacitinib was first approved in 2012 to treat adult patients with RA who did not respond well to the medicine methotrexate. When FDA first approved tofacitinib in 2012, FDA required a post-marketing clinical trial in patients with RA on background methotrexate, to evaluate the risk of heart-related events, cancer, and infections. The trial is studying two different doses of tofacitinib (5 mg twice daily, which is the currently approved dose for RA, and a higher, 10 mg twice daily dosage) in comparison to a tumour necrosis factor (TNF) blocker. In RA, the body attacks its own joints, causing pain, swelling, and loss of function. An interim analysis of the trial's results found an increased occurrence of blood clots and of death in patients treated with tofacitinib 10 mg twice daily compared to patients treated with tofacitinib 5 mg twice daily or a TNF blocker. In 2017, the FDA approved the medicine to treat patients with a second condition that causes joint pain and swelling, PsA, who did not respond well to methotrexate or other similar medicines. In 2018, the FDA approved tofacitinib to treat ulcerative colitis, which is a chronic, inflammatory disease affecting the colon.

Advice to Patients

Patients should tell your health care professionals if you have a history of blood clots or heart problems, and talk to them about any questions or concerns. Stop taking tofacitinib and seek emergency medical attention right away if you experience any unusual symptoms, including those that may signal a blood clot such as:

- Sudden shortness of breath
- Chest pain that worsens with breathing
- Swelling of a leg or arm
- Leg pain or tenderness, or red or discolored skin in the painful or swollen leg or arm

Do not stop taking tofacitinib without first talking to your health care professional, as doing so can worsen your condition.

Healthcare Professionals

Healthcare professionals should discontinue tofacitinib and promptly evaluate patients with symptoms of thrombosis. Counsel patients about the risks and advise them to seek medical attention immediately if they experience any unusual symptoms, including those of thrombosis listed above. Reserve tofacitinib to treat ulcerative colitis for patients who have failed or do not tolerate tumor necrosis factor (TNF) blockers. Avoid tofacitinib in patients who may have a higher risk of thrombosis. When treating ulcerative colitis, use tofacitinib at the lowest effective dose and limit the use of the 10 mg twice daily dosage to the shortest duration needed.

Please refer to the following website in FDA for details:

https://www.fda.gov/safety/medwatch-safety-alerts-human-medical-products/xeljanz-xeljanz-xr-tofacitinib-drug-safety-communication-due-increased-risk-blood-clots-and-death

In Hong Kong, Xeljanz Tablets 5mg (HK-63303) and Xeljanz XR Extended Release Tablets 11mg (HK-66141) are registered pharmaceutical products containing tofacitinib. Both products are registered by Pfizer Corporation Hong Kong Limited, and are prescription-only medicines. So far, the Department of Health (DH) has received 3 cases of adverse drug reaction related to tofacitinib, but these cases are not related to blood clots. Related news was previously issued by the FDA, Health Canada, European Medicines Agency, Therapeutic Goods Administration, and Medicines and Healthcare products Regulatory Agency, and was posted on the Drug Office website on 26 Feb 2019, 16 Mar 2019, 21 Mar 2019 and 18 May 2019 respectively. In light of the recent FDA'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 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,

(Joseph LEE)
for Assistant Director (Drug)