Dear Healthcare Professionals,

**Baricitinib (Olumiant▼): increased risk of diverticulitis, particularly in patients with risk factors**

Your attention is drawn to the Medicines and Healthcare products Regulatory Agency’s (MHRA) announcement that a European review has assessed cases of diverticulitis associated with baricitinib reported in clinical trials and in clinical (post-marketing) use worldwide. The risk of diverticulitis has been added to the product information for baricitinib with an uncommon frequency and healthcare professionals are asked to use caution in patients at risk of this condition.

Baricitinib (Olumiant▼) is a Janus kinase (JAK) inhibitor drug. Diverticulitis is also a potential side effect of tofacitinib (Xeljanz▼), another JAK inhibitor. Prescribers of tofacitinib should exercise the same caution in patients with risk factors for diverticulitis.

In clinical trials of baricitinib to treat rheumatoid arthritis, there were 21 cases of diverticulitis (including 3 [14%] with a complication of gastrointestinal perforation) in 3770 patients across 13,380 patient-years of observation (incidence rate 0.16 per 100 patient-years [95% CI 0.10–0.24]). Of the 21 patients, 7 (33%) had diverticulosis or diverticulitis noted in their medical history. For concomitant medicines, 13 (62%) of the 21 patients were on chronic corticosteroid treatment, 9 patients were chronically treated with NSAIDs, and 4 patients with acetylsalicylic acid (aspirin) medications. Cases of diverticulitis and diverticulosis were also reported in clinical trials of baricitinib for other conditions not authorised in the United Kingdom. Overall, the observed frequency of diverticulitis in baricitinib use in clinical trials was 0.43% (uncommon).

For post-marketing use of baricitinib outside of clinical trials, 35 spontaneous cases of diverticulitis have been reported worldwide up to 31 Dec 2019. Of these, 25 (71%) cases specifically included a medical history of diverticulitis and/or chronic use of NSAIDs, corticosteroids or opioids, which are known

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important risk factors for diverticulitis. However, 10 cases had no pre-existing conditions or use of concomitant medications as confounding factors. Gastrointestinal perforation as a complication of diverticulitis was reported in 5 (14%) cases. None of the cases were fatal.

The time to onset of clinical trial and post-marketing cases ranged from 6 days to 6 years. The majority of cases occurred after more than 90 days of treatment.

Advice for healthcare professionals:
- Cases of diverticulitis and gastrointestinal perforation have been reported in patients taking baricitinib.
- Most, but not all, cases of diverticulitis occurred in patients who were concomitantly taking medicines associated with an increased risk of diverticulitis.
- Use caution in patients with pre-existing diverticular disease and in patients on long-term concomitant medications associated with an increased risk of diverticulitis such as non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and opioids.
- Advise patients on baricitinib to seek immediate medical care if they experience severe abdominal pain especially accompanied with fever, nausea and vomiting or other symptoms of diverticulitis.
- Ensure prompt evaluation of any patients on baricitinib who present with new-onset abdominal signs and symptoms to identify early diverticulitis or gastrointestinal perforation.

Please refer to the following website in MHRA for details:

In Hong Kong, Olumiant Tablets 2mg (HK-65663) and Olumiant Tablets 4mg (HK-65664) are pharmaceutical products registered by Eli Lilly Asia, Inc. Xeljanz Tablets 5mg (HK-63303) and Xeljanz XR Extended Release Tablets 11mg (HK-66141) are pharmaceutical products registered by Pfizer Corporation Hong Kong Limited. All products are prescription-only medicines. So far, the Department of Health (DH) has not received any case of adverse drug reaction related to baricitinib. The DH has received 7 cases of adverse drug reaction related to tofacitinib, but these cases are not related to diverticulitis and gastrointestinal perforation.

The current package insert of the local Xeljanz products contain safety information on the risk of diverticulitis and gastrointestinal perforation. In light of the above MHRA’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.

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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)