衞生署藥物辦公室
藥物註冊及進出口管制部

香港九龍南昌街 382 號公共衞生檢測中心三樓

2319 8458

電話號碼 Tel. No.:
詢問處 Enquiries (852) 2319 8458
傳真號碼 Faxline No. (852) 2803 4962
本署檔號 OUR REF.: DH DO PRIE/7-30/15

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

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(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

FDA warns about rare occurrences of a serious infection of the genital area with SGLT2 inhibitors for diabetes

Your attention is drawn to the US Food and Drug Administration's (FDA) announcement that cases of a rare but serious infection of the genitals and area around the genitals have been reported with the class of type 2 diabetes medicines called sodium-glucose cotransporter-2 (SGLT2) inhibitors. This serious rare infection, called necrotizing fasciitis of the perineum, is also referred to as Fournier's gangrene. FDA is requiring a new warning about this risk to be added to the prescribing information of all SGLT2 inhibitors and to the patient medication guide.

Fournier's gangrene is an extremely rare but life-threatening bacterial infection of the tissue under the skin that surrounds muscles, nerves, fat, and blood vessels of the perineum. The bacteria usually get into the body through a cut or break in the skin, where they quickly spread and destroy the tissue they infect. Having diabetes is a risk factor for developing Fournier's gangrene, however, this condition is still rare among diabetic patients. Overall published literature about the occurrence of Fournier's gangrene for men and women is very limited. Publications report that Fournier's gangrene occurs in 1.6 out of 100,000 males annually in the US, and most frequently occurs in males 50-79 years (3.3 out of 100,000). In the FDA's case series, however, FDA observed events in both women and men.

In the five years from Mar 2013 to May 2018, FDA identified 12 cases of Fournier's gangrene in patients taking an SGLT2 inhibitor. This number includes only reports submitted to FDA and found in the medical literature, so there may be additional cases about which FDA is unaware. In 2017, an estimated 1.7 million patients received a dispensed prescription for an SGLT2 inhibitor from US outpatient retail pharmacies.

Although most cases of Fournier's gangrene have previously been reported in men, the FDA's 12 cases included 7 men and 5 women. Fournier's gangrene developed within several months of the patients starting an SGLT2 inhibitor and the drug was stopped in most cases. All 12 patients were hospitalized and required surgery. Some patients required multiple disfiguring surgeries, some developed complications, and one patient died. In comparison, only six cases of Fournier's gangrene (all in men) were identified in review of other antidiabetic drug classes over a period of more than 30 years.

Patients should seek medical attention immediately if they experience any symptoms of tenderness, redness, or swelling of the genitals or the area from the genitals back to the rectum, and have a fever above 100.4 F or a general feeling of being unwell. These symptoms can worsen quickly, so it is important to seek treatment right away. Healthcare professionals should assess patients for Fournier's gangrene if they present with the symptoms described above. If suspected, start treatment immediately with broad-spectrum antibiotics and surgical debridement if necessary. Discontinue the SGLT2 inhibitor, closely monitor blood glucose levels, and provide appropriate alternative therapy for glycemic control.

Please refer to the following website in FDA for details:
https://www.fda.gov/Drugs/DrugSafety/ucm617360.htm

In Hong Kong, there are 17 registered pharmaceutical products containing SGLT2 inhibitors, including canagliflozin (2 products), dapagliflozin (5 products) and empagliflozin (10 products). All products are prescription-only medicines. So far, the Department of Health (DH) has received 2 cases of adverse drug reaction related to canagliflozin, 3 cases related to dapagliflozin and 1 case related to empagliflozin, but these cases are not related to Fournier's gangrene. In light of the above 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)