衞生署藥物辦公室
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DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG REGISTRATION AND IMPORT/EXPORT CONTROL DIVISION
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382 Nam Cheong Street, Kowloon, Hong Kong

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(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

Diabetes medicine canagliflozin: EMA reviews the drug following data on toe amputations in ongoing study

Your attention is drawn to the European Medicines Agency's (EMA) announcement regarding EMA has started a review of the diabetes medicine canagliflozin after an increase in amputations, mostly affecting toes, was observed in an ongoing clinical trial called CANVAS.

Canagliflozin is an SGLT2 inhibitor. It works by blocking a protein in the kidneys called sodium glucose co-transporter 2 (SGLT2). SGLT2 absorbs glucose back into the bloodstream as the blood is filtered in the kidneys. By blocking the action of SGLT2, canagliflozin causes more glucose to be removed via the urine, thereby reducing glucose in the blood. The other SGLT2 inhibitors are dapagliflozin and empagliflozin.

Cases of lower limb amputation occurred in both the canagliflozin and placebo groups in the trial and the possibility that canagliflozin increases lower limb amputations is currently not confirmed. EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has requested more information from the company to assess whether canagliflozin causes an increase in lower limb amputations and whether any changes are needed in the way this medicine is used in the EU.

Patients with diabetes (especially those with poorly controlled diabetes and pre-existing problems with the heart and blood vessels) are at increased risk of infection and ulceration which can result in lower limb amputations. No increase in such amputations was seen in 12 other completed clinical trials with canagliflozin. A small, non-statistically significant increase in the number of amputations occurred in another ongoing study called CANVAS-R. Both CANVAS and CANVAS-R involve patients at high risk of problems with the heart and blood vessels. Details of the studies can be found at the EMA website.

The PRAC will also ask for data on other SGLT2 inhibitors. Based on this, the PRAC may decide to extend the scope of the review to cover these medicines.

While the review on canagliflozin is ongoing, healthcare professionals in the EU will receive a letter reminding them about the importance of routine foot care to avoid cuts or sores of the feet and to treat them promptly should they occur to prevent infection and ulceration. Patients at increased risk of amputation (such as those who have had a previous amputation) should be carefully monitored. As a precautionary measure, doctors may consider stopping treatment with canagliflozin in patients who develop significant foot complications.

Please refer to the EMA's website for details:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Canagliflozin/human_referral_prac_000059.jsp&mid=WC0b01ac05805c516f

In Hong Kong, there are two registered pharmaceutical products containing canagliflozin, namely Invokana Tablets 100mg (HK-63499) and Invokana Tablets 300mg (HK-63500) which are registered by Johnson & Johnson (HK) Ltd, and are prescription only medicines. According to our record, there is no application for clinical trial certificates for CANVAS and CANVAS-R in Hong Kong. So far, the Department of Health (DH) has received one case of adverse drug reaction in connection with canagliflozin, but it was not related to amputation. DH will remain vigilant on the conclusion of the review and any safety updates 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)