Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

FDA ADVISORY
No. 2019-169

02 JUL 2019

TO: **ALL HEALTHCARE PROFESSIONALS AND MARKET AUTHORIZATION HOLDERS**

SUBJECT: **Safety Information: SGLT2 inhibitors and risk of necrotizing fasciitis of the perineum (Fournier's gangrene)**

Introduction

The US FDA has released safety announcement on rare occurrences of a serious infection of the genitals with sodium-glucose cotransporter-2 (SGLT2) inhibitors. The serious rare infection, called necrotizing fasciitis of the perineum, is also referred to as Fourneir's gangrene.

Scientific Discussion

SGLT2 inhibitors are approved for use as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. They lower plasma glucose concentrations by increasing renal excretion of glucose.

Three SGLT2 inhibitors have been registered in the Philippines since 2014, either as single ingredient or fixed-dose combinations. These are:

SGLT2 inhibitors	Brand	Market Authorization Holders
Canagliflozin	Invokana	Johnson & Johnson (Phils.) Inc.
Dapagliflozin	Forxiga	AstraZeneca Pharmaceuticals (Phils.), Inc.
Dapagliflozin + Metformin	Xigduo XR	AstraZeneca Pharmaceuticals (Phils.), Inc.
Dapagliflozin + Saxagliptin	Qtern	AstraZeneca Pharmaceuticals (Phils.), Inc.
Empagliflozin	Jardiance	Boehringer Ingelheim (Philippines), Inc.
Empagliflozin + Metformin	Jardiance Duo	Boehringer Ingelheim (Philippines), Inc.
Empagliflozin + Linagliptin	Glyxambi	Boehringer Ingelheim (Philippines), Inc.

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. Men are more often affected than women. Identified predisposing factors include diabetes mellitus, obesity, and other conditions leading to immunosuppression.

To date, FDA Philippines has not received any adverse drug reactions reports of fournier's gangrene with SGLT2 inhibitors.

Safety Advisory

Healthcare professionals are advised to assess patients for Fournier's gangrene if they present symptoms of pain, tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise. If suspected, consider discontinuation of SGLT2 inhibitor, provide appropriate alternative therapy for glycemic control and start treatment immediately with broad-spectrum antibiotics and surgical debridement if necessary.

Advise all patients to seek medical attention immediately if they experience any symptoms above.

Healthcare professionals are also encouraged to report any serious adverse reactions, including Fournier's gangrene, related to SGLT2 inhibitors to the FDA.

Information for Market Authorization Holders

The Market Authorization Holders of SGLT2 inhibitors as listed above shall update their respective package inserts to appear the information on risk of necrotizing fasciitis of the perineum (Fournier's gangrene). This information shall be discussed under Warnings and Precautions. MAHs who have not yet submitted their revised package inserts in relation to the above safety concern shall submit variation application within 3 months after this issuance.

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