

F. No. 12-74/13-DC
Government of India
Directorate General of Health Services
Central Drugs Standard Control Organization
(New Drugs Division)

FDA Bhawan, Kotla Road
New Delhi

Dated: 25-03-2019

To
All State/UT Drugs Controllers,

Subject: - Safety Warning for SGLT2 inhibitors - regarding

Sir,

Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors lower blood sugar by causing the kidneys to remove sugar from the body through the urine. SGLT2 inhibitor class includes drugs such as Canagliflozin, Dapagliflozin, Empagliflozin etc.

This office has received safety updates of the said drugs along with safety communications by Health Canada and US-FDA from M/s Johnson & Johnson Private Limited and M/s Boehringer Ingelheim India Pvt. Ltd.

Health Canada has published Summary Safety Review of SGLT2 inhibitors by assessing the potential risk of inflammation of the pancreas (acute and chronic pancreatitis) on 20.07.2018 wherein it has been concluded that there may be a link between the use of SGLT2 inhibitors and acute pancreatitis. Health Canada is working with the manufacturers to update the product safety information on SGLT2 inhibitors to inform about this risk and will continue to monitor safety information involving SGLT2 inhibitors to identify and assess potential harms.

USFDA has given safety announcement on 29.08.2018 wherein the U.S. Food and Drug Administration (FDA) is warning that cases of a rare but serious infection of the genitals and area around the genitals have been reported with this class of type 2 diabetes medicines i.e., Sodium-Glucose Cotransporter-2 (SGLT2) inhibitors. This serious rare infection, called necrotizing fasciitis of the perineum, is also referred to as Fournier's gangrene. They require a new warning about this risk to be added to the prescribing information of all SGLT2 inhibitors and to the patient.

In light of concerns raised with regard to safety of SGLT2 inhibitors, the matter has been examined by CDSCO in consultation with the Subject Expert Committee (SEC-Endocrinology & Metabolism) in its meeting held on 27.09.2018 wherein presentation was made by the firm before the committee about the safety signals from Health Canada regarding Pancreatitis and from USFDA regarding Fournier's gangrene with the use of SGLT-2 inhibitors.

On the basis of these reports the SEC had recommended that

- 1) Data should be obtained from NCC-PvPI regarding any signals on the SGLT2 inhibitors emphasizing the above two conditions in Indian patients.
- 2) CDSCO should closely monitor for any further new information /development with SGLT2 inhibitors.

In view of the above, IPC, NCC-PvPI was requested to provide the information about the details ADRs, if any or any signals on SGLT-2 inhibitors emphasizing the acute pancreatitis & Fournier's gangrene in Indian patients received under PvPI. Accordingly, PvPI has replied with the details of Individual Case Safety Reports (ICSRs) reported to them.

The issue along with ICSR received from PvPI was deliberated again in the SEC meeting held on 22.01.2019.

The committee took cognizance of ICSR received from IPC, NCC-PvPI & deliberated on the issue in light of global reporting on the subject.

After detailed deliberation, the committee has opined that NCC PvPI should be requested to furnish further details on 08 ICSR reported for genital infections with the use of SGLT2 inhibitors in terms of severity, type, duration & outcome of these infections. In the mean time the committee has recommended that CDSCO should request all the State Drugs Controllers to direct the manufacturers of SGLT2 inhibitors to include warning in this regard in the package insert as taken by other regulatory authorities like USFDA.

Accordingly, you are requested to direct the manufacturers of SGLT2 inhibitor class drugs such as Canagliflozin, Dapagliflozin, Empagliflozin, etc. under your jurisdiction to include the following warning in the package insert and promotional literature of these drugs.

Warning - Cases of a rare but serious infection of the genitals and area around the genitals have been reported with this class of type 2 diabetes medicines i.e., Sodium-Glucose Cotransporter-2 (SGLT2) inhibitors. This serious rare infection, called necrotizing fasciitis of the perineum, is also referred to as Fournier's gangrene.

Action taken in this regard may be intimated to this office.

Yours faithfully,



(Dr. S. Eswara Reddy)
Drugs Controller General (India)

Copy for information and necessary follow up to:

- All Zonal/Sub Zonal offices of CDSCO.