FDA Drug Safety Communication: FDA warns that SGLT2 inhibitors for diabetes may result in a serious condition of too much acid in the blood

[05-15-2015]

Safety Announcement

The U.S. Food and Drug Administration (FDA) is warning that the type 2 diabetes medicines canagliflozin, dapagliflozin, and empagliflozin may lead to ketoacidosis, a serious condition where the body produces high levels of blood acids called ketones that may require hospitalization. We are continuing to investigate this safety issue and will determine whether changes are needed in the prescribing information for this class of drugs, called sodium-glucose cotransporter-2 (SGLT2) inhibitors.

Patients should pay close attention for any signs of ketoacidosis and seek medical attention immediately if they experience symptoms such as difficulty breathing, nausea, vomiting, abdominal pain, confusion, and unusual fatigue or sleepiness. Do not stop or change your diabetes medicines without first talking to your prescriber. Health care professionals should evaluate for the presence of acidosis, including ketoacidosis, in patients experiencing these signs or symptoms; discontinue SGLT2 inhibitors if acidosis is confirmed; and take appropriate measures to correct the acidosis and monitor sugar levels.

SGLT2 inhibitors are a class of prescription medicines that are FDA-approved for use with diet and exercise to lower blood sugar in adults with type 2 diabetes. When untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease. SGLT2 inhibitors lower blood sugar by causing the kidneys to remove sugar from the body through the urine. These medicines are available as single-ingredient products and also in combination with other diabetes medicines such as metformin (see Table 1 below). The safety and efficacy of SGLT2 inhibitors have not been established in patients with type 1 diabetes, and FDA has not approved them for use in these

patients.

A search of the FDA Adverse Event Reporting System (FAERS) database identified 20 cases of acidosis reported as diabetic ketoacidosis (DKA), ketoacidosis, or ketosis in patients treated with SGLT2 inhibitors from March 2013 to June 6, 2014 (see Data Summary). All patients required emergency room visits or hospitalization to treat the ketoacidosis. Since June 2014, we have continued to receive additional FAERS reports for DKA and ketoacidosis in patients treated with SGLT2 inhibitors.

DKA, a subset of ketoacidosis or ketosis in diabetic patients, is a type of acidosis that usually develops when insulin levels are too low or during prolonged fasting. DKA most commonly occurs in patients with type 1 diabetes and is usually accompanied by high blood sugar levels. The FAERS cases were not typical for DKA because most of the patients had type 2 diabetes and their blood sugar levels, when reported, were only slightly increased compared to typical cases of DKA. Factors identified in some reports as having potentially triggered the ketoacidosis included major illness, reduced food and fluid intake, and reduced insulin dose.

We urge health care professionals and patients to report side effects involving SGLT2 inhibitors to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

Table 1. List of SGLT2 inhibitors

Brand name	Active ingredient(s)
Invokana	canagliflozin
Invokamet	canagliflozin and metformin
Farxiga	dapagliflozin
Xigduo XR	dapagliflozin and metformin extended-release
Jardiance	empagliflozin
Glyxambi	empagliflozin and linagliptin

Facts about Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors

More Info for Patients

More Info for Health Care Professionals

Data Summary

Drug Safety Communication (PDF - 50KB)

Related Information

- Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors

Contact FDA

For More Info
855-543-DRUG (3784)
and press 1
druginfo@fda.hhs.gov

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Complete and submit the report Online. Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

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