FDA removes *Boxed Warning* about risk of leg and foot amputations for the diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR)
Based on our review of new clinical trial data

This information is an update to the FDA Drug Safety Communication: FDA confirms increased risk of leg and foot amputations with the diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR) issued on May 16, 2017.

8-26-2020 FDA Drug Safety Communication

Based on a U.S. Food and Drug Administration (FDA) review of new data from three clinical trials, we have removed the *Boxed Warning* about amputation risk from the diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR) prescribing information.

We required the *Boxed Warning* in 2017 based on our assessment that the risk of amputations was very serious in relation to the potential benefit of canagliflozin, which was initially approved to be used with diet and exercise to lower blood sugar in adults with type 2 diabetes. Subsequent FDA reviews of new clinical trial data demonstrated additional heart- and kidney-related benefits, which led to additional approved uses. Specifically, in 2018, canagliflozin was approved to reduce the risk of major heart-related events such as heart attack, stroke, or death in patients with type 2 diabetes who have known heart disease; and, in 2019, it was approved to reduce the risk of end-stage kidney disease, worsening of kidney function, heart-related death, and being hospitalized for heart failure in certain patients with type 2 diabetes and diabetic kidney disease.

Collectively, these newly identified effects of canagliflozin on heart and kidney disease show significantly enhanced benefit of this medicine. Safety information from recent clinical trials also suggests that the risk of amputation, while still increased with canagliflozin, is lower than previously described, particularly when appropriately monitored. Based upon these considerations, we have concluded that the *Boxed Warning* should be removed. The amputation risk with canagliflozin remains and is still described in the *Warnings and Precautions* section of the prescribing information.

Health care professionals and patients should continue to recognize the importance of preventative foot care and monitor for new pain, tenderness, sores, ulcers, and infections in the legs and feet. Risk factors that may predispose patients to the need for amputation should be considered when choosing antidiabetic medicines.

Canagliflozin belongs to a class of medicines called sodium-glucose cotransporter-2 (SGLT2) inhibitors. It lowers blood sugar by causing the kidneys to remove sugar from the body through the urine. Untreated, type 2 diabetes can lead to serious problems, including blindness, nerve and kidney damage, and heart disease.

We urge health care professionals and patients to report side effects involving canagliflozin and other medicines to the FDA MedWatch program, using the information in the "Contact FDA"

box at the bottom of the page.

Related Information

Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors

National Institute of Diabetes and Digestive and Kidney Diseases: Diabetes

The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective

Think It Through: Managing the Benefits and Risks of Medicines