Indian Health Service
National Pharmacy and Therapeutics Committee
Pharmacovigilance Drug Safety Alert

August 26, 2020

FDA Removes Boxed Warning About Risk of Leg and Foot Amputations for Canagliflozin (Invokana®)

Background: Canagliflozin belongs to a class of medicines called sodium-glucose cotransporter-2 (SGLT2) inhibitors. It is used in patients with Type 2 Diabetes to lower blood glucose.

2013	FDA approves canagliflozin for the treatment of Type 2 Diabetes.
2017	A Boxed Warning that canagliflozin may increase the risk of leg and foot amputation is added to the package insert**.**
2018	Canagliflozin is approved by the FDA 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.
2019	Canagliflozin is approved by the FDA 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.
2020	FDA removes Boxed Warning about risk of leg and foot amputations for canagliflozin: • Recent clinical trials show that there continues to be an increased risk of leg and foot amputation with canagliflozin; however, the risk is lower than previously described, especially when treatment is appropriately monitored. • Recently observed cardiovascular and renal protection effects increases the benefit of canagliflozin therapy in patients with type 2 diabetes.

Recommendation: Although the Boxed Warning will be removed, there is still an increased risk of leg and foot amputations. **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.

Report all significant or unusual Adverse Drug Events (ADEs) to the FDA MedWatch program as described in the Indian Health Manual. Instructions for submitting an ADE can be found on the IHS Pharmacovigilance website. Please ensure “IHS” or “Indian Health Service” is entered in the Reporter Information section of the form (section G).

For more information, the full FDA Drug Safety Alert and other resources can be found on the FDA website