

## **Canagliflozin May Cause Increased Risk of Leg and Foot Amputations**

On May 16<sup>th</sup>, 2017, the FDA announced new warnings be added to the canagliflozin drug label after data from two clinical trials showed an increased risk of leg and foot amputations. Canagliflozin (Invokana, Invokamet) is a sodium-glucose cotransporter-2 (SGLT2) inhibitor used to help control blood sugar in adults with type 2 diabetes. The CANVAS and CANVAS-R studies evaluating canagliflozin versus placebo revealed that leg and foot amputations occurred twice as frequently in patients receiving canagliflozin. Amputation of the toes and the midfoot were more common, however some patients experienced amputations of the leg and both limbs. Because of this data, the FDA mandated that a black box warning be added to the label.

Amputations of the leg and foot are more common among adults with type II diabetes than adults without diabetes. Diabetes can cause complications such as poor circulation and nerve damage, which can exacerbate sores or ulcers on the feet. When untreated, these sores can quickly become infected or necrotic due to lack of sensation in the feet caused by peripheral neuropathy. Adults with diabetes should practice good foot hygiene, including daily foot checks, wearing appropriate-fitting shoes and clean socks, and keeping toenails trimmed, to reduce the risk of foot and leg amputations. Healthcare professionals should advise patients taking canagliflozin to inform their physicians immediately regarding any new sores or ulcers on the feet. Canagliflozin should be used with caution in patients with peripheral vascular disease, neuropathy, or a history of frequent foot ulcers or previous amputation.

### **References:**

- Information for Healthcare Professionals. Canagliflozin (Invokana). FDA. Available at: <https://www.fda.gov/Drugs/DrugSafety/ucm500965.htm>
- Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondur N, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med*. 2017; 377 (7): 644-657.
- Canagliflozin [package insert]. Titusville, NJ: Janssen Pharmaceuticals; 2013.

Erin Barthelmess, PharmD Candidate