US approves "new class" of diabetes drug, under review in Canada

The United States' recent approval of a new drug to treat type 2 diabetes has paved the way for its introduction in Canada.

The US Food and Drug Administration (FDA) approved canagliflozin, a drug developed by Mitsubishi Tanabe Pharma Corporation and marketed by Johnson & Johnson under the brand name Invokana, on Mar. 29.

The company has also filed a new drug submission with Health Canada, says Jennifer McCormack, a spokesperson for Johnson & Johnson Canada.

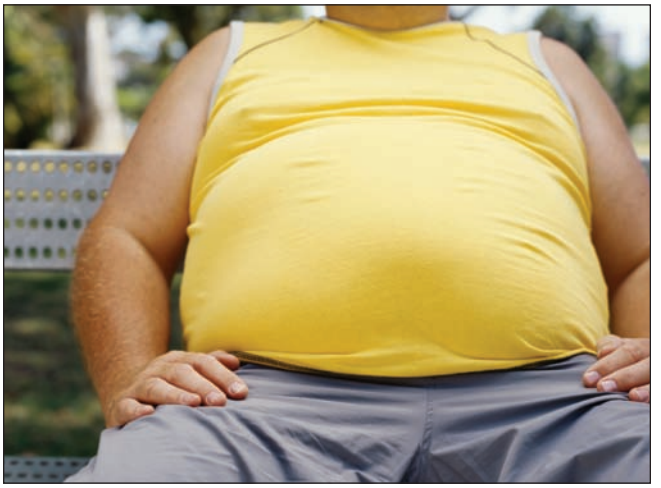
"This procedure is still ongoing so we can't speculate on the expected outcome or timelines at this point," says McCormack.

The once-a-day oral pill has been labelled a "new class" of diabetes medication because it works in the kidneys to inhibit sodium-glucose cotransporter 2 (SGLT2). After glucose is filtered from the blood into the kidneys, canagliflozin suppresses SGLT2 transporters from carrying the glucose back into the blood. Instead, the glucose is diverted and released into the urine. This effectively pushes excess blood glucose out of the body via the kidneys and urinary tract.

Each class of diabetes drug has a different mode of action in controlling blood glucose levels. Insulin sensitizers, for example, increase the sensitivity of insulin receptors to the body's own insulin; insulin secretagogues stimulate the pancreas to produce more insulin; biguanides reduce glucose production in the liver; and alphaglucosidase inhibitors lower blood glucose after meals by slowing down the absorption of glucose from complex carbohydrates.

Coined a "glucuretic" by Johnson & Johnson, canagliflozin complements other common glucose-lowering medications like metformin and insulin while boosting weight loss and lowering blood pressure, says the company.

Health Canada spokesperson Blossom Leung confirmed that canagliflozin has not received market authorization here and would not comment further about whether it would be approved.



Canagliflozin, a once-a-day oral pill, has been labeled a "new class" of diabetes medication because it works in the kidneys to inhibit sodium-glucose cotransporter 2 (SGLT2).

Doctors are often unable to help patients achieve optimum control of their diabetes, even with all of the existing diabetes drugs available, says Dr. Alexander Sorisky, chair of the division of endocrinology and metabolism and a professor at the University of Ottawa, Ontario. "So, new medications with a novel mechanism of action can be of potential help," says Sorisky, who is also a senior scientist and director of the chronic disease program of the Ottawa Hospital Research Institute.

However, Sorisky warns that regulators should consider the new drug carefully. "My preliminary opinion of canagliflozin is not overly enthusiastic. I am concerned about the way it acts to let glucose escape from the blood into the urine, as opposed to, for example, a medication that tries to help insulin work better or a medication that tries to improve glucose metabolism," he says.

Canagliflozin is the first SGLT2 suppressor the FDA has approved. In January 2012, the FDA rejected drug developers Bristol-Myers Squibb and AstraZeneca's bid for approval of its form of SGLT2 suppressor, dapagliflozin (Forxiga). The US regulatory agency cited an increased risk of breast and bladder cancer. Despite the FDA's rejection, the European Union approved that drug in November 2012.

Johnson & Johnson's clinical trials, the longest of which lasted 78 weeks, found the most common adverse effect of canagliflozin is the increased frequency of genital fungal infections resulting from the increase of glucose in the urine. In a 26-week trial, vaginal yeast infections occurred at a rate of 10% and urinary tract infections at a rate of 5%.

Sorisky also wants to know about the long-term effects of the drug. "Before a new diabetes medication is widely used, it is important to know if it is able to reduce clear-cut clinical endpoints, like cardiovascular disease, not just whether it can lower blood glucose," he says.

The FDA is requiring Johnson & Johnson to conduct five post-marketing studies on canagliflozin: a cardiovascular outcomes trial; an enhanced pharmacovigilance program to monitor for malignancies, serious cases of pancreatitis, severe hypersensitivity reactions, photosensitivity reactions, liver abnormalities and adverse pregnancy outcomes; a bone safety study; and two pediatric studies to document potential problems and long-term effects of the drug. — Hanna Lange-Chenier, *CMAJ*

***CMAJ* 2013. DOI:10.1503/cmaj.109-4483**