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Health Canada has approved INVOKANA^{®*} (canagliflozin) for reduction of major adverse cardiovascular events (MACE), the first SGLT2 inhibitor in Canada to receive this indication¹

INVOKANA[®] has been shown to reduce the combined risk of cardiovascular death, nonfatal myocardial infarction and nonfatal stroke in patients with type 2 diabetes and established cardiovascular disease by 18 per cent compared to placebo²

TORONTO, ON (October 17, 2018) – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that Health Canada has approved INVOKANA[®] (canagliflozin) for reduction of the risk of major adverse cardiovascular events (MACE), which is composed of cardiovascular death, nonfatal myocardial infarction (heart attack) and nonfatal stroke, in adults with type 2 diabetes mellitus who have established cardiovascular disease.³

Health Canada's approval is based on the findings from the CANVAS Program, which is the longest completed cardiovascular outcome program of any sodium glucose cotransporter-2 (SGLT2) inhibitor to-date.⁴ The CANVAS Program evaluated the effect of INVOKANA[®] on cardiovascular risk in a broad population of more than

10,000 adults with type 2 diabetes who had established cardiovascular disease or were at risk (with two or more risk factors) for cardiovascular disease.

Overall, treatment with INVOKANA[®] significantly reduced the combined risk of cardiovascular death, nonfatal myocardial infarction and nonfatal stroke by 14 per cent.⁵ When assessed separately, the three components of MACE showed similar reductions – 13 per cent (95 per cent Confidence Interval (CI) 0.72 - 1.06) for cardiovascular death; 15 per cent (95 per cent CI 0.69 - 1.05) for nonfatal myocardial infarction; and 10 per cent (95 per cent CI 0.71 - 1.15) for nonfatal stroke.⁶ In patients with established cardiovascular disease, treatment with INVOKANA[®] reduced the combined risk of cardiovascular death, nonfatal myocardial infarction and nonfatal stroke by 18 per cent.⁷

“Since its approval in 2014, INVOKANA[®] has proven its ability to help type 2 diabetes patients achieve tangible clinical benefits, such as lower A1C levels and weight loss,” said Dr. Vincent Woo, CANVAS Program investigator and endocrinologist at the Diabetes Research Group, University of Manitoba. **

“Canadians living with diabetes have a higher risk for cardiovascular events, and addressing these risks is a key part of diabetes management. INVOKANA[®] now has demonstrated efficacy in reducing the risk of major adverse cardiovascular events among a broad population of patients.”

Of the over 3.5 million Canadians living with diabetes, at least 90 per cent have been diagnosed with type 2 diabetes.⁸ By 2028, it is estimated that the number of Canadians with diabetes will grow to more than 4.6 million.⁹ Canadians with diabetes are at risk of developing cardiovascular disease 15 years earlier than those without the condition, which can cause individuals to have complications including heart attack or stroke.¹⁰

Individuals living with diabetes are over three times more likely to be hospitalized due to cardiovascular disease,¹¹ and each year, 30 per cent of strokes and 40 per

cent of heart attacks are a result of diabetes.¹² It is important for patients to manage their diabetes with diet and exercise as well as treatment to help reduce their risk of these associated complications.¹³

About the CANVAS Program

The CANVAS Program is composed of two, nearly-identical, large cardiovascular outcome studies: CANVAS (CANagliflozin CardioVascular Assessment Study) and CANVAS-R (Study of the Effects of Canagliflozin on Renal Endpoints in Adult Subjects with T2DM).¹⁴ It is the longest completed cardiovascular outcome program of any SGLT2 inhibitor to-date.

The CANVAS Program evaluated the effect of INVOKANA[®] on cardiovascular risk in 10,142 adults with type 2 diabetes who had established cardiovascular disease or were at risk (with two or more risk factors) for cardiovascular disease. It was conducted in 30 countries, including Canada with 16 Canadian trial site locations and 19 Canadian investigators.

In the CANVAS Program, a vast majority (90 per cent) of patients had a history of hypertension and 66 per cent of patients had a history of cardiovascular disease (14 per cent had a history of heart failure).¹⁵ The study assessed the cardiovascular efficacy and safety of INVOKANA[®] relative to placebo in patients receiving commonly-used diabetes agents.¹⁶ The primary endpoint was defined as major adverse cardiovascular events (MACE), composed of cardiovascular death, nonfatal heart attack and nonfatal stroke.

In addition to MACE, other cardiovascular clinical outcomes of the CANVAS Program included a 33 per cent reduction in hospitalization due to heart failure and a 30 per cent reduction in the composite of death or hospitalization due to heart failure.¹⁷ With respect to renal function, patients treated with INVOKANA[®] over a period of 6.5 years experienced an initial fall in mean eGFR (estimated glomerular filtration

rate) that thereafter stabilized, whereas patients treated with placebo experienced a progressive decline in eGFR.¹⁸

The mean duration of treatment was approximately 2.9 years,¹⁹ and the mean follow-up time was approximately 3.6 years.²⁰

Overall, adverse events seen in the CANVAS Program were generally consistent with the known safety profile of INVOKANA[®]²¹; however, an increased risk of amputation with canagliflozin was seen. The risk of amputation in CANVAS was 0.59/100 patient-years vs. 0.28/100 patient-years in the INVOKANA[®] arm and the placebo arm, respectively. The risk of amputation in CANVAS-R was 0.75/100 patient-years vs. 0.42/100 patient-years in the INVOKANA[®] arm and the placebo arm, respectively.²²

The risk of amputation was highest in patients with a baseline history of prior amputation, peripheral vascular disease and neuropathy.

About INVOKANA[®]

INVOKANA[®] is an oral, once-daily prescription treatment used to lower blood glucose (sugar) levels in adults with type 2 diabetes.²³ INVOKANA[®] belongs to a class of medications called sodium glucose co-transporter 2 (SGLT2) inhibitors, which offer a novel approach to treating diabetes by increasing the excretion of glucose in the urine, resulting in greater loss of calories.²⁴

INVOKANA[®] was approved by Health Canada on May 23, 2014. The treatment is indicated as monotherapy or in combination with other antihyperglycemic agents as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus. INVOKANA[®] is also approved to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction and nonfatal stroke) in adults with type 2 diabetes mellitus and established

cardiovascular disease. INVOKANA® is currently approved as a single agent in 79 countries.

Common side effects reported with INVOKANA® include vaginal yeast infection, hypoglycemia, yeast infection of the penis, urinary tract infection, increased urination, constipation, skin ulcer, nausea and thirst.²⁵ For a complete list of side effects, please refer to the INVOKANA® Product Monograph available [here](#).

INVOKANA® has been studied in more than 18,000 patients with type 2 diabetes across 14 double-blind, controlled Phase 3 and Phase 4 clinical trials.^{26,27}

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At the Janssen Pharmaceutical Companies of Johnson & Johnson, we are working to create a world without disease. Transforming lives by finding new and better ways to prevent, intercept, treat and cure disease inspires us. We bring together the best minds and pursue the most promising science.

We are Janssen. We collaborate with the world for the health of everyone in it. Learn more at www.janssen.com/canada. Follow us at [@JanssenCanada](https://twitter.com/JanssenCanada). Janssen Inc. is part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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*** Dr. Woo was not compensated for any media work. He has been a paid consultant to Janssen Inc.*

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References

¹ INVOKANA® Product Monograph, October 15, 2018.

² INVOKANA® Product Monograph, October 15, 2018.

³ INVOKANA® Product Monograph, October 15, 2018.

⁴ Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. *N Engl J Med*. 2017.

⁵ INVOKANA® Product Monograph, October 15, 2018.

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- ⁶ INVOKANA® Product Monograph, October 15, 2018.
- ⁷ INVOKANA® Product Monograph, October 15, 2018.
- ⁸ Diabetes Canada. 2018 National Backgrounder. Available at: http://www.diabetes.ca/getmedia/6960f8d5-0869-4233-8ac2-6c669dae7c59/2018-Backgrounder-Canada_KH_AB_KB-edited-13-March-2018_2.pdf.aspx. Accessed August 29, 2018.
- ⁹ Diabetes Canada. 2018 National Backgrounder. Available at: http://www.diabetes.ca/getmedia/6960f8d5-0869-4233-8ac2-6c669dae7c59/2018-Backgrounder-Canada_KH_AB_KB-edited-13-March-2018_2.pdf.aspx. Accessed August 29, 2018.
- ¹⁰ Diabetes Canada. Heart Disease and Stroke. Available at: <https://www.diabetes.ca/diabetes-and-you/complications/heart-disease-stroke>. Accessed August 26, 2018.
- ¹¹ Public Health Agency of Canada. (2011). Diabetes in Canada: Facts and figures from a public health perspective. Ottawa, Ont.: Public Health Agency of Canada. Retrieved from <https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/cdmc/publications/diabetes-diabete/facts-figures-faits-chiffres-2011/pdf/facts-figures-faits-chiffres-eng.pdf>. Accessed August 29, 2018.
- ¹² Institute for Clinical Evaluative Sciences. (2003). Diabetes in Ontario: An ICES Practice Atlas. Retrieved from <http://www.ices.on.ca/Publications/Atlases-and-Reports/2003/Diabetes-in-Ontario.aspx>. Accessed August 29, 2018.
- ¹³ Asif M. The prevention and control the type-2 diabetes by changing lifestyle and dietary pattern. *J Educ Health Promot.* 2014;3:1.
- ¹⁴ INVOKANA® Product Monograph, October 15, 2018.
- ¹⁵ Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. *N Engl J Med.* 2017.
- ¹⁶ Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. *N Engl J Med.* 2017.
- ¹⁷ INVOKANA® Product Monograph, October 15, 2018.
- ¹⁸ INVOKANA® Product Monograph, October 15, 2018.
- ¹⁹ INVOKANA® Product Monograph, October 15, 2018.
- ²⁰ INVOKANA® Product Monograph, October 15, 2018.
- ²¹ Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. *N Engl J Med.* 2017.
- ²² INVOKANA® Product Monograph, October 15, 2018.
- ²³ INVOKANA® Product Monograph, October 15, 2018.
- ²⁴ INVOKANA® Product Monograph, October 15, 2018.
- ²⁵ INVOKANA® Product Monograph, October 15, 2018.
- ²⁶ INVOKANA® Product Monograph. October 15, 2018.
- ²⁷ Data on file. Janssen Pharmaceuticals, Inc., Titusville, NJ.