

Invokana[®] (canagliflozin) Significantly Reduces the Risk of Renal Failure in Patients with Type 2 Diabetes and Chronic Kidney Disease in the Landmark Phase 3 CREDENCE Study

- Invokana[®] (canagliflozin) is the only medicine in nearly 20 years and the first diabetes medicine to demonstrate significant reduction in risk of renal failure, dialysis or kidney transplantation and renal or cardiovascular (CV) death in this high-risk population¹
- Approximately 58 million people in Europe currently live with type 2 diabetes mellitus (T2DM), which is set to rise to 67 million by 2045.² If left untreated, patients are at greater risk of developing serious complications, such as CV disease, chronic kidney disease (CKD) and diabetic kidney disease (DKD)³
- The Mundipharma global network of independent associated companies, which includes Napp in the UK, has a partnership with Janssen to be the exclusive distributor for canagliflozin across 18 countries in the European Economic Area (EEA) and Switzerland where the products currently have Pricing and Reimbursement status. This is with the exception of Spain, where the product is co-promoted by both Janssen and Mundipharma

CAMBRIDGE, UK: 15.04.19 – The Mundipharma network of independent associated companies welcomes the CREDENCE study data which successfully demonstrated that Invokana[®] (canagliflozin) reduces the risk of renal and cardiovascular (CV) events and has an acceptable safety profile consistent with previous studies when added to standard of care in subjects with type 2 diabetes mellitus (T2DM)¹. The study met its primary endpoint showing that canagliflozin reduced the risk of composite doubling of serum creatinine, end-stage kidney disease (ESKD) and renal or CV death by 30% [HR: 0.70; 95% CI: 0.59 to 0.82; p<0.0001].¹ These findings were consistent across the individual components of the primary composite endpoint, as well as across all 15 subgroups tested.¹

In addition, canagliflozin reduced the risk of the secondary renal endpoint composite of doubling of serum creatinine, ESKD, and renal death by 34% [HR: 0.66; 95% CI: 0.53 to 0.81; p<0.0001].¹ The study also showed that canagliflozin reduced the risk of major adverse cardiac events (MACE) (composite of non-fatal myocardial infarction, non-fatal stroke and CV death) by 20% [HR: 0.80; CI: 0.67 to 0.95; p=0.0121], the risk of CV death and hospitalization for heart failure by 31% [HR: 0.69; 95% CI: 0.57 to 0.83; p=0.0001], and the risk of hospitalization for heart failure alone by 39% [HR: 0.61; 95% CI: 0.47 to 0.80; p=0.0003].¹ In regard to safety data, the incidence rates of adverse events and serious

adverse events were numerically lower for patients treated with canagliflozin as compared to placebo. There were no observed differences in the incidence of lower limb amputations (HR: 1.11; 95% CI: 0.79 to 1.56) or adjudicated fractures (HR: 0.98; 95% CI: 0.70 to 1.37).¹

As the first dedicated clinical trial to investigate a SGLT2 inhibitor for renal protection in patients with T2DM with CKD, the data from CREDENCE¹ provides the first significant update in nearly 20 years regarding slowing the progression of CKD for this group of patients. The trial, which was stopped early in July 2018 due to a signal of overwhelming efficacy in the prevention of the primary endpoint, was conducted in more than 4,401 adults with T2DM at 690 sites in 34 countries across North America, Latin America, Europe, South Africa and Asia Pacific.¹

In Europe, canagliflozin is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise. The initiation dose is 100mg once daily in adults with an eGFR of ≥ 60 mL/min/1.73 m² and can be increased to 300mg once daily orally if tighter glycaemic control is needed. Canagliflozin should **not** be initiated if eGFR is < 60 mL/min/1.73 m². In patients tolerating canagliflozin whose eGFR falls persistently below 60 mL/min/1.73 m² the dose should be adjusted to or maintained at 100mg once daily. Canagliflozin should be stopped if eGFR falls persistently below 45 mL/min/1.73 m².⁴

“Canagliflozin is the first medical breakthrough in nearly 20 years proven to slow the progression of chronic kidney disease in patients with diabetes at high risk of developing kidney failure” said Professor Vlado Perkovic, Study Author and Executive Director of The George Institute, Australia, Professor of Medicine at UNSW Sydney. *“These impressive results from the CREDENCE study have significant clinical implications for preventing kidney failure and improving health for millions of people living with chronic kidney disease and type 2 diabetes.”*

Approximately 58 million people in Europe currently live with T2DM, which is set to rise to 67 million by 2045.² If left untreated, patients are at greater risk of developing serious complications, such as CV disease and diabetic kidney disease (DKD).³ DKD is the leading cause for progression to ESKD, accounting for 50% of cases in the developed world.⁵ It is associated with a high risk of CV disease (heart attack, heart failure and stroke) and also amplifies the risk of other diabetes complications including: a reduced quality of life, infections, fatigue, depression, adverse drug reactions and premature death.^{6,7}

“With nearly 24 million type 2 diabetes patients in Europe likely to develop diabetic kidney disease, we are delighted with the results from the CREDENCE study which demonstrated superiority of canagliflozin, when

added to the standard of care,” said Dr Vinicius Gomes de Lima, European Medical Affairs Lead.

“Type 2 diabetes is a growing epidemic in Europe and effective treatments are needed to help reduce the burden of the disease in patients. In particular, treatments are called for to improve renal outcomes which is of real importance in this disease.”

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Notes to the editors:

About the CREDENCE Clinical Trial¹

The CREDENCE (Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation) study was the first dedicated and full recruited renal outcome trial evaluating renal and cardiovascular outcomes in people with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) with a sodium glucose co-transporter 2 (SGLT2) inhibitor. It was a phase 3 randomised, double-blind, event-driven, placebo-controlled, parallel-group, 2 arm multi-centre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and CKD. In particular, it compared the efficacy and safety of canagliflozin versus placebo at preventing clinically important kidney and cardiovascular outcomes in patients with T2DM and CKD when used in addition to standard of care, including a maximum tolerated daily dose of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB).

About Canagliflozin

Canagliflozin is an oral, once-daily medication which belongs to a class of medications called sodium glucose co-transporter 2 (SGLT2) inhibitors. SGLT2 inhibitors work by inhibiting SGLT2, which promotes the loss of glucose via the urine, lowering blood glucose levels in adults with T2DM. Canagliflozin was approved in the European Union by the European Commission in November 2013. It is indicated for the treatment of adults with insufficiently controlled T2DM as an adjunct to diet and exercise, as monotherapy when metformin is considered inappropriate due to intolerance or contraindications and in addition to other medicinal products for the treatment of diabetes. Approval was based on a comprehensive global Phase III clinical trial programme.⁴

About the Mundipharma network

Mundipharma is a global network of privately-owned independent associated companies whose purpose is to move medicine forward. With a high performing and learning organization that strives for innovation and commercial excellence through partnerships, we successfully transformed and diversified our European portfolio of medicines to create value for patients, payers and wider healthcare systems across important therapeutic areas such as Diabetes, Respiratory, Oncology, Pain and Biosimilars.

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³ Update to International Diabetes Federation, 2016, Complications of Diabetes [Online] Available at: <https://www.idf.org/aboutdiabetes/what-is-diabetes/complications.html> Last accessed March 2019.

⁴ Canagliflozin SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/invokana-epar-product-information_en.pdf Last accessed April 2019

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⁶ CDC. National Chronic Kidney Disease Fact Sheet, 2017. Available at: https://www.cdc.gov/kidneydisease/pdf/kidney_factsheet.pdf Last accessed July 2018

⁷ Thomas M., Cooper M., and Zimmer P. Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. *Nature Review Nephrology*. 2015; (12): 73-81.