

Mundipharma Announces the Licence Extension Submission for Invokana[®] (canagliflozin) and Vokanamet[®] (canagliflozin and metformin) to the European Medicines Agency

- *The licence extension submission for Invokana[®] (canagliflozin) and Vokanamet[®] (canagliflozin and metformin) to treat type 2 diabetes mellitus (T2DM) patients with chronic kidney disease (CKD) will now be reviewed by the Committee for Medicinal Products for Human Use (CHMP)*
- *The CREDENCE renal outcomes study, which was stopped early due to positive efficacy findings, served as the basis for the licence extension submission*
- *If approved, Invokana will be the first therapy in nearly 20 years indicated to reduce the risk of end-stage renal disease when added to current standard of care for this group of T2DM patients*
- *Mundipharma has a partnership with Janssen to be the exclusive distributor for Invokana 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 products are co-promoted by both Janssen and Mundipharma*

CAMBRIDGE, UK: 22.08.19 – As the European distributor of Invokana[®] (canagliflozin) and Vokanamet[®] (canagliflozin and metformin), Mundipharma welcomes the news that the European Medicines Agency (EMA) has accepted the licence extension submission for these two medicines to treat stage 2 or stage 3 chronic kidney disease (CKD) and albuminuria as an adjunct to standard of care in adults with type 2 diabetes mellitus (T2DM). The submission is based on the results from the landmark Phase III CREDENCE study¹ which evaluated the efficacy and safety of canagliflozin versus placebo in this high-risk patient population when used in addition to standard of care.

“Chronic kidney disease is a serious complication of type 2 diabetes, which can increase patients’ risk of developing end-stage renal disease and may reduce their life expectancy by several years.” said Dr Vinicius Gomes de Lima, European Medical Affairs Lead, Mundipharma. *“If approved, this licence extension would be a significant step forward to help reduce the associated burden of chronic kidney disease and improve patients’ quality of life.”*

Approximately 24 million T2DM patients in Europe are likely to develop diabetic kidney disease (DKD),² which is projected to rise in line with the increasing prevalence of diabetes. DKD has a major

impact on patients' physical, emotional and financial wellbeing and amplifies the risk of diabetes complications including; cardiovascular disease, a reduced quality of life, infections, fatigue, depression, adverse drug reactions and premature death.^{3,4}

In Europe, Invokana is currently indicated for the treatment of adults with insufficiently controlled T2DM 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 m².⁵

The dose of glucose-lowering therapy with Vokanamet should be individualised on the basis of the patient's current regimen, effectiveness, and tolerability, using the recommended daily dose of 100 mg or 300 mg canagliflozin and **not** exceeding the maximum recommended daily dose of metformin orally.⁶

Invokana and Vokanamet have been approved in the European Union since 2013 and 2014 respectively. In July 2018, the treatment labels were updated to include positive cardiovascular and renal outcomes from the CANVAS programme which show a reduction in morbidity and mortality.⁷

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Notes to the editors:

About the **CREDESCENCE** Clinical Trial¹

The CREDESCENCE (**C**anagliflozin and **R**enal **E**vents in **D**iabetes with **E**stablished **N**ephropathy **C**linical **E**valuation) 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 III 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). The study was stopped early in July 2018 due to positive efficacy findings.

About Invokana^{®5}

Invokana (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. Invokana 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.

About Vokanamet^{®6}

Vokanamet (a fixed-dose combination of canagliflozin and metformin) is approved in the European Union for the treatment of adults with insufficiently controlled type 2 diabetes as an adjunct to diet and exercise. Vokanamet combines two oral glucose-lowering medicinal products with different and complementary mechanisms of action.

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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² Alicic R., et al. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. *Clin J Am Soc Nephrol*. 2017; 12(12): 2032-2045.

³ CDC. National Chronic Kidney Disease Fact Sheet, 2017. Available at: https://www.cdc.gov/kidneydisease/pdf/kidney_factsheet.pdf. Last accessed July 2019

⁴ Thomas M., Cooper M., and Zimmet P. Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. *Nature Review Nephrology*. 2016; (12): 73-81

⁵ Invokana SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/invokana-epar-product-information_en.pdf Last accessed July 2019

⁶ Vokanamet SmPC. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/SGLT2_inhibitors_20/European_Commission_final_decision/WC500206514.pdf. Last accessed July 2019

⁷ Neal B et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. *The New England Journal of Medicine*. 2017; 377:644-657