The CHMP issues positive opinion to expand INVOKANA® and VOKANAMET® labels to include positive data on cardiovascular and renal outcomes

- *Update based on positive cardiovascular and renal outcomes from CANVAS Programme*
- Janssen has a partnership with the Mundipharma global network of associate companies, who are the exclusive distributor for both **Invokana**® and **Vokanamet**® in 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: 2 August 2018 - As the European distributor of ***Invokana***® (canagliflozin) and **Vokanamet**® (canagliflozin and metformin) Mundipharma welcomes the announcement from the Janssen Pharmaceutical Companies of Johnson & Johnson that the Committee for Medicinal Products for Human Use (CHMP), of the European Medicines Agency (EMA), has issued a positive opinion to update the Invokana® and Vokanamet® labels including changes to the indication statements.

The recommended product information now includes data on the reduction in major adverse cardiovascular events in patients with type 2 diabetes mellitus (T2DB) who had either a history of CV disease or at least two CV risk factors.

The CHMP's positive opinion will now be reviewed by the European Commission, which has the authority to grant approval of the updated label.

"We are pleased with the CHMP's decision to recommend a label update for canagliflozin to include the results of the CANVAS programme. Both improvement in glycaemic control and reduction of cardiovascular (CV) morbidity and mortality as well as improvements of renal outcomes are important in the treatment of type 2 diabetes. If approved by the European Commission, this will provide a more comprehensive overview of the effects of canagliflozin, and further assist clinicians in making informed treatment decisions that are most appropriate for their patients," said Paul Schofield, European Medical Lead, Diabetes.

The Type II variation application is based on the results of the CANVAS programme, the largest completed cardiovascular (CV) outcomes trial to date for an SGLT2 inhibitor. [1] The study, which included over 10,000 patients treated since 2009, met its primary endpoint and showed canagliflozin significantly reduced the combined risk of CV death, myocardial infarction and non-fatal stroke,

versus placebo in adult patients with T2DB who had either a history of CV disease or at least two CV risk factors.[1]

Canagliflozin was approved in the European Union by the European Commission in November 2013 and is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus.[2] Approval was based on a comprehensive global Phase 3 clinical trial programme.

#ENDS#

Notes to editors

About the CANVAS programme

The CANVAS programme (N=10,142) comprises the two large canagliflozin cardiovascular outcome studies, CANVAS and CANVAS-R, and includes a pre-specified integrated analysis of these two studies to evaluate the potential for CV protection of canagliflozin in patients with type 2 diabetes mellitus (T2DM) who had either a prior history of CV disease or at least two CV risk factors. The integrated analysis also evaluated the effects of canagliflozin on renal and safety outcomes.[1]

Canagliflozin met the primary outcome by significantly reducing the rates of the composite of major adverse cardiovascular events (MACE) comprised of CV mortality, non-fatal myocardial infarction (MI), or non-fatal stroke (26.9 vs. 31.5/1000 patient-years, hazard ratio (HR) 0.86; 95% confidence interval (CI 0.75-0.97; P<0.0001 for noninferiority; P=0.0158 for superiority) compared with PBO, respectively. All 3 components of MACE composite (CV death, non-fatal MI, and non-fatal stroke) exhibited point estimates of effect suggesting benefit with canagliflozin.[1]

Adverse events reported in the CANVAS programme were generally consistent with the known safety profile of canagliflozin.[1] However, the study found that, in patients with type 2 diabetes who had established CV disease or at least two risk factors for CV disease, canagliflozin was associated with an approximately 2-fold increased risk of lower limb amputation with the rate of amputation over standard of care being 0.63/100 patient years for canagliflozin versus 0.34/100 patient years for placebo which corresponds to an additional risk of 0.29/100 patient years.[1] The risk of amputations across the class has previously been investigated by the EMA, and this is reflected in a warning in the labelling of all SGLT2 inhibitors.

About INVOKANA®

INVOKANA® (canagliflozin) is an oral, once-daily medication which belongs to a new 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 type 2 diabetes. Canagliflozin was approved in the European Union by the European Commission in November 2013 and is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus. Approval was based on a comprehensive global Phase 3 clinical trial programme.[2]

About VOKANAMET

VOKANAMET® (a fixed-dose combination of canagliflozin and metformin) is approved in the European Union to improve glycaemic control of adult patients with type 2 diabetes as an adjunct to diet and exercise and combines two oral glucose-lowering medicinal products with different and complementary mechanisms of action.[3]

About the Mundipharma network

The Mundipharma global network of privately-owned independent associated companies was founded in 1956 by doctors and now operates in over 120 countries worldwide. We are focused on developing business partnerships to identify and accelerate meaningful technology across an increasingly diverse portfolio of therapy areas including respiratory, oncology, pain, and biosimilars. Consistent with our entrepreneurial heritage, we like to think we see what others don't by challenging conventional wisdom and asking different and challenging questions. By working in partnership with all our stakeholders, the Mundipharma network develops medicines that create value for patients, payers and wider healthcare systems.

For further information please contact:

Tiffany Fretwell, Communications Lead
Telephone: +44 (0) 1223 397 3361
Email: tiffany.fretwell@mundipharma.com)

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