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European Commission expands labelling for Janssen's INVOKANA® and VOKANAMET® to include positive data on cardiovascular outcomes

INVOKANA® (canagliflozin) and VOKANAMET® (canagliflozin and metformin) labelling now approved to include positive cardiovascular outcomes from CANVAS Program which show a reduction in morbidity and mortality

BEERSE, BELGIUM XX, 2018 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the European Commission (EC) has granted approval to update the INVOKANA® (canagliflozin) and VOKANAMET® (canagliflozin and metformin) labelling to include changes to the indication statement for the treatment of adults with insufficiently controlled type 2 diabetes mellitus (T2DM) as an adjunct to diet and exercise. The decision means that the product information now includes data on the reduction in major adverse cardiovascular (CV) events (cardiovascular mortality, non-fatal myocardial infarction, or non-fatal stroke) in patients with type 2 diabetes mellitus (T2DM) who had either a history of CV disease or at least two CV risk factors, in addition to the existing study results on improving glycemic control.

"We hope this approval will not only provide clinicians with a more detailed overview of canagliflozin but also help them when making informed treatment decisions which are most appropriate for their patients. Type 2 diabetes mellitus is one of the most common forms of diabetes and accounts for the majority of diabetes cases worldwide so it is extremely important that we continue improving outcomes for these patients," said Dr. Jose Antonio Buron, Vice-President Medical Affairs EMEA, Janssen-Cilag Farmacêutica, Lda.

The EC's decision follows a recommendation from the Committee for Medical Products for Human Use (CHMP) that was based on data from the CANVAS Program, the largest completed CV outcomes trial to date for an SGLT2 inhibitor.[1] The study, which included over 10,000 patients started in 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 T2DM who had either a history of CV disease or at least two CV risk factors.[1]

Canagliflozin also significantly lowered the risk of hospitalisation for heart failure and demonstrated improved renal outcomes.[1] Adverse events reported in the CANVAS Program were generally consistent with the known safety profile of canagliflozin.[1] However, the study found that, in patients with T2DM 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 SGLT2 inhibitors.

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.

Janssen has a partnership with Mundipharma, who is 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. Mundipharma has exclusive rights to promote, distribute, and sell both products through its network of independent associated companies. This is with the exception of Spain, where the product is co-promoted by both Janssen and Mundipharma.

#ENDS#

Notes to editors

About the CANVAS Program
The CANVAS Program (N=10,142) comprises the two large canagliflozin CV 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 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 CV 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 placebo, 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 Program were generally consistent with the known safety profile of canagliflozin. 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 Invokana 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 SGLT2 inhibitors.

These results served the basis for Janssen's submission to the European Medicines Agency (EMA), seeking to expand labelling for INVOKANA® and VOKANAMET® to include positive data on cardiovascular morbidity and mortality.

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. INVOKANA® is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise. 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 for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise. VOKANAMET® combines two oral glucose-lowering medicinal products with different and complementary mechanisms of action.[3]

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/emea. Follow us at www.twitter.com/JanssenEMEA.

Janssen-Cilag International N.V. is part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding INVOKANA® and VOKANAMET® labelling. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen-Cilag International N.V., any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 31, 2017, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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References

[1] Neal B et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes, 2017; The New England Journal of Medicine
[2] INVOKANA SmPC. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002649/WC500156456.pdf Last accessed August 2018.
[3] VOKANAMET SmPC. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002656/WC500166670.pdf Last accessed August 2018.