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New guidance from ADA and EASD recommends use of sodium-glucose co-transporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for patients with type 2 diabetes

- *The SGLT2i class is now recommended in the newly published 2018 American Diabetes Association (ADA)/European Association for the Study of Diabetes (EASD) Consensus Report as a preferred oral treatment after metformin in patients with type 2 diabetes mellitus (T2DM) with established atherosclerotic cardiovascular disease (ASCVD), heart failure (HF) or chronic kidney disease (CKD) and also in patients without cardiovascular disease (CVD) especially where there is a compelling need to minimize weight gain or promote weight loss and need to minimize risk of hypoglycaemia.*[1]
- *As a member of the SGLT2i class, INVOKANA® (canagliflozin) is now included as a treatment option in newly published 2018 guidelines for use in patients with T2DM with established ASCVD, HF, CKD also in patients without cardiovascular disease (CVD) especially where there is a compelling need to minimize weight gain or promote weight loss and need to minimize risk of hypoglycaemia.*[1]
- *The decision to include SGLT2i's as an important treatment option was based on data from completed cardiovascular (CV) outcome trials including the positive CV outcomes data of canagliflozin in the CANVAS programme, the largest completed and published CV outcomes trial to date for an SGLT2i.*[3,4]

CAMBRIDGE, UK: 16 October 2018 - As the European distributor of **INVOKANA®** (canagliflozin) and **VOKANAMET®** (canagliflozin and metformin) Mundipharma welcomes the news that SGLT2i's, including canagliflozin, have now been included as an important treatment option in the newly published 2018 ADA/EASD Consensus Report in the early management of T2DM patients with established ASCVD, HF, CKD and also in patients without cardiovascular disease (CVD) especially where there is a compelling need to minimize weight gain or promote weight loss or a need to minimize the risk of hypoglycaemia. The new guidance was co-published in Diabetologia, the journal of EASD, and Diabetes Care, the journal of the ADA, during the annual meeting of EASD in Berlin, Germany on October 5.[1]

Updates to the guidance took into consideration recent evidence from large CV outcome trials (CVOTs), which included the CANVAS programme, the largest completed and published CV outcomes trial to date for an SGLT2i, which has shown that canagliflozin reduces the risk of major adverse cardiovascular events (MACE) including CV mortality, non-fatal myocardial infarction or non-fatal stroke in patients with T2DM who had either a history of CV disease or at least two CV risk factors, as well as reducing hospitalisation for heart failure (HHF) and demonstrating improved renal outcomes.[2]

"The new guidance puts patients at the centre of care and helps clinicians to make informed treatment decisions that are aligned to the needs of each individual and emphasise the importance of clinicians providing personalised treatment options. There is a lot of excitement to see the future potential of this class of drugs in improving outcomes for patients with type 2 diabetes," said Paul Schofield, European Medical Lead, Diabetes.

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The positioning of canagliflozin within the Consensus Report has been supported by the recent European Commission approval to expand the canagliflozin label which was based on the positive results from the CANVAS Programme.[2] The study included 10,142 patients with a history of CV disease or at least two risk factors of a CV event and showed canagliflozin met the primary outcome demonstrating a reduction in the combined risk of major adverse CV events (MACE) by 14% and, as a secondary outcome, a HHF reduction of 33%. In addition, there were renal outcomes benefits, seen as a reduction in the doubling of serum creatinine, the need for renal-replacement therapy and renal death by 47%. The study also demonstrated a 27% reduction in the progression of albuminuria in people with T2DM with either a history of CV disease or at least two CV risk factors.[3,4] Canagliflozin provided sustained positive effects on glycaemic and blood pressure control, as well as weight reduction, demonstrating wide-ranging durability.

#ENDS#

Notes to editors

About the new guidance

The American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) convened a panel to update the position statements, published in 2012 and 2015, on the management of T2DM in adults. The updated consensus paper was co-published in Diabetologia, the journal of EASD, and Diabetes Care, the journal of the ADA, during the annual meeting of EASD in Berlin, Germany on 5th October 2018.[1]

The major changes from prior consensus reports are based on new evidence from large CV outcome trials which have shown that specific SGLT2 inhibitors or glucagon-like peptide-1 (GLP-1) receptor agonists improve CV outcomes, as well as secondary outcomes such as HF and progression of renal disease, in patients with established CVD or CKD.

About the CANVAS programme

The CANVAS programme (N=10,142) comprised the two large canagliflozin cardiovascular outcome trials, CANVAS and CANVAS-R, and included 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.[3,4]

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 non-inferiority; 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.[3,4]

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Adverse events reported in the CANVAS programme were generally consistent with the known safety profile of canagliflozin.[3] 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. 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.[3,4]

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 T2DM. 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 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.[2]

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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[1] Davies, M et al. Management of hyperglycaemia in type 2 diabetes. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care, October 2018; Volume 41, Issue 10; 1-33. Last accessed October 2018.

[2] INVOKANA SmPC. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002649/WC500156456.pdf Last accessed October 2018.

[3] Perkovic, V et al. Canagliflozin and renal outcomes in type 2 diabetes: results from the CANVAS Programme randomised clinical trials, 2018; The Lancet Diabetes & Endocrinology. Last accessed October 2018.

[4] Neal B et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes: The New England Journal of Medicine. 2017; 377:644-657. Last accessed October 2018.

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