STRICTLY EMBARGOED UNTIL 00.01 ON THURSDAY 24 DECEMBER

NICE RECOMMENDS FORXIGA (dapagliflozin) FOR THE TREATMENT OF SYMPTOMATIC CHRONIC HEART FAILURE WITH REDUCED EJECTION FRACTION IN ADULTS[1]

- *Dapagliflozin is the first SGLT2 inhibitor recommended by NICE as an option for the treatment of adult patients with symptomatic chronic heart failure with reduced ejection fraction (HFrEF), as an add-on to optimised standard care.*[1]
- *Almost one million people are living with heart failure (HF) in the UK,*[2] *of those, approximately 250,000 patients in England and Wales could be eligible for treatment.*[3,4,5,6,7]
- *HF is the cause of approximately 65,000 unplanned hospital admissions per year and the risk of death associated with HF is worse than some of the most common cancers.*[7,8]

Luton, UK, Thursday 24 December 2020 – AstraZeneca today announced that the National Institute for Health and Care Excellence (NICE) has issued a positive Final Appraisal Document (FAD) recommending dapagliflozin as an option for treatment of symptomatic chronic heart failure (HF) with reduced ejection fraction (HFrEF) in adults, as an add-on to optimised standard care. NICE recommends that treatment is started on the advice of a heart failure specialist, and that monitoring should be done by the most appropriate healthcare professional.[1]

Dapagliflozin is in a class of medicines called SGLT2 inhibitors, and is the first medicine of this kind to be licensed and recommended for use in HF. In the DAPA-HF clinical trial, dapagliflozin, on top of standard of care, reduced the risk of cardiovascular (CV) death, being hospitalised by HF or needing an urgent visit to hospital for HF by 26% (relative risk reduction [RRR], absolute risk reduction [ARR] = 4.9%), when compared to placebo (hazard ratio [HR] = 0.74 [95% confidence interval {CI} 0.65-0.85]; $p < 0.001$) ([16.3% vs 21.2% patients with event, respectively]).[9] The trial data showed that for every 21 patients treated with dapagliflozin, one CV-related death, urgent visit to hospital for HF, or hospitalisation for HF could be avoided.[10] The overall safety profile of dapagliflozin in patients with heart failure was consistent with the known safety profile of dapagliflozin.[10]

John McMurray, MD, Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, University of Glasgow, UK, said: "This is great news for people with heart failure with reduced ejection fraction, as they will now be able to receive a completely novel treatment for their condition, which, when added to existing therapy, improves symptoms, reduces the need for hospital admission and increases survival. Dapagliflozin can make a huge difference for those suffering from this life-restricting and life-threatening condition."

HF is a life-threatening, chronic condition where a person's heart is unable pump enough blood around their body.[11] Almost one million people are living with HF in the UK, and the risk of death associated with HF is worse than some of the most common cancers.[2,8] HF is also the cause of approximately 65,000 unplanned hospital admissions per year,[7] and with COVID-19 placing such a large burden on the health system, it is critical that heart failure patients have access to care options to help them reduce the risk of their symptoms worsening and need for admission to hospital.[12,13]

Nick Hartshorne-Evans, CEO of the Pumping Marvellous Foundation, said: "Despite the high mortality risk for people living with heart failure in the UK and the dramatic impact on their quality of life as a whole, the condition is often under-recognised and misdiagnosed. COVID-19 has also placed greater strain on both people living with the condition and healthcare services. This has highlighted a clear and urgent need for multiple treatment options that minimise contact with healthcare professionals. We are therefore pleased with NICE's decision to provide access through both GP care settings on the advice of specialists and hospitals. This will support better

health outcomes and reduce the risk of people living with heart failure needing to be hospitalised, which is critical during this pandemic."

This recommendation is based on the positive results from the landmark DAPA-HF Phase III trial, published in *The New England Journal of Medicine*.[9] It follows approval for use in adults with symptomatic chronic heart failure with reduced ejection fraction from the European Commission (EC) in November 2020.[14]

Tom Keith-Roach, President, AstraZeneca UK, said: "This final NICE recommendation is exciting news for people living with heart failure, with and without type-2 diabetes. Importantly, primary care physicians will be able to prescribe dapagliflozin in heart failure following agreement with a heart failure specialist. This treatment has the potential to improve symptoms and extend the lives of hundreds of thousands of people in the UK. Working closely with our partners in the NHS, we are determined to help eradicate heart failure as one of the leading causes of hospitalisation and death in this country."

The very common adverse event associated with dapagliflozin in placebo-controlled clinical studies and post-marketing experience is hypoglycaemia (when used with sulphonylurea or insulin). Common associated adverse events are genital infections, urinary tract infections, dizziness, rash, back pain, dysuria, polyuria, haematocrit increased, creatinine renal clearance decreased during initial treatment and dyslipidaemia.[14]

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About Heart Failure
Heart Failure (HF) is a life-threatening disease in which the heart cannot pump enough blood around the body.[11] It affects approximately 64 million people worldwide (at least half of which have a reduced ejection fraction), including almost one million in the UK.[2,15,16] It is a chronic disease where around half of patients will die within five years of diagnosis.[17]

HF mortality risk is worse than some of the most common cancers (prostate, breast, and bladder cancer).[8] The rate of hospital admission for HF is growing three times as quickly as all other hospital admissions and represents a significant clinical and economic burden.[18,19,20]

There are two main categories of HF related to ejection fraction (EF), a measurement of the percentage of blood leaving the heart each time it contracts: HFrEF and HFpEF. HFrEF occurs when the left ventricle (LV) muscle is not able to contract adequately and therefore, expels less oxygen-rich blood into the body.[21,22]

About DAPA-HF
DAPA-HF (Dapagliflozin And Prevention of Adverse-outcomes in HF) is an international, multi-centre, parallel-group, randomised, double-blinded Phase III trial in 4,744 people with HFrEF (LVEF ≤ 40%), with and without T2D, designed to evaluate the effect of dapagliflozin 10mg, compared with placebo, given once daily in addition to standard of care. The primary composite endpoint was time to the first occurrence of a worsening HF event (hospitalisation or equivalent event; i.e. an urgent HF visit), or CV death. The median duration of follow-up was 18.2 months.[9]

About dapagliflozin
Dapagliflozin is an oral, once-daily selective inhibitor of human sodium-glucose co-transporter 2 (SGLT2). Dapagliflozin is indicated in adults for the treatment of symptomatic chronic heart failure with reduced ejection fraction.[14] In addition to this, dapagliflozin is also indicated in adults for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise, as monotherapy when metformin is considered inappropriate due to intolerance, and in addition to other medicinal products for the treatment of type 2 diabetes.[14]

For further information on dapagliflozin the summary of product characteristics for dapagliflozin is available here: https://www.medicines.org.uk/emc/product/7607/smpc#gref

About AstraZeneca
AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, Cardiovascular, Renal & Metabolism and Respiratory & Immunology. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.

With its global headquarters in Cambridge, AstraZeneca operates in five different locations in the UK, where around 8,300 employees work in research and development, manufacturing, supply, sales and marketing. We supply 40 different medicines to the NHS. The UK is also an important location for AstraZeneca's clinical trials; in 2018, we undertook 201 trials in the UK, involving 376 centres and over 7,000 patients.

For more information, please visit www.astrazeneca.co.uk and follow us on Twitter @AstraZenecaUK.

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