STRICTLY EMBARGOED UNTIL THURSDAY 18 MAY 2023 09:00 BST

FORXIGA (DAPAGLIFLOZIN) IS THE FIRST AND ONLY TREATMENT RECOMMENDED BY NICE FOR CHRONIC HEART FAILURE WITH AN EJECTION FRACTION >40%, POTENTIALLY IMPACTING UP TO HALF A MILLION PATIENTS IN ENGLAND AND WALES

- *AstraZeneca estimates that up to half a million people who are living with this type of heart failure (HF), may be impacted by this recommendation.*[1,2]
- *Approximately half of all patients with HF die within 5 years of diagnosis;*[3] *HF is the leading cause of UK hospital admissions in people aged 65 years or older.*[4]
- *Previously, treatment options for this condition were limited to symptom management only.*[5,6]

London, UK, Thursday 18 May 2023 – AstraZeneca announced today that the National Institute for Health and Care Excellence (NICE) has published Final Draft Guidance (FDG) recommending dapagliflozin as an option for treating symptomatic chronic HF with preserved or mildly reduced ejection fraction (left ventricular ejection fraction [LVEF] of more than 40%) in adults.[7] Dapagliflozin has previously been recommended by NICE as a treatment option for HF patients with reduced ejection fraction (LVEF ≤40%) meaning that dapagliflozin is therefore now recommended for patients with HF regardless of ejection fraction.[7]

Today's decision by NICE is based on results from the DELIVER Phase III trial, which showed that dapagliflozin met its primary endpoint in reducing the composite outcome of cardiovascular (CV) death or worsening HF by 18% (16.4% in the dapagliflozin group and 19.5% in the placebo group over a median follow-up of 2.3 years [hazard ratio {HR} =0.82 {95% CI 0.73-0.92}; p<0.001, absolute risk reduction {ARR} 3.1%]).[8]

In the DELIVER Phase III trial, data was only collected on serious adverse events (AEs) that led to discontinuation of dapagliflozin or placebo and other select AEs, as a result of the extensive safety data on dapagliflozin and established safety profile. Overall, serious AEs, including death, were reported in 43.5% of patients (n=1361) in the dapagliflozin group and in 45.5% of patients (n=1423) in the placebo group. AEs that led to discontinuation of dapagliflozin or placebo were reported in 5.8% of patients (n=182) in the dapagliflozin group and in 5.8% of patients (n=181) in the placebo group.[8]

Professor John McMurray, Professor of Medical Cardiology at the University of Glasgow, and honorary Consultant Cardiologist at the Queen Elizabeth University Hospital, Glasgow, UK, said: Dapagliflozin has the potential to help patients and help ease the pressures on the health service in the UK, as demonstrated in DELIVER, the largest randomised clinical trial in patients with heart failure and mildly reduced or preserved ejection fraction. This is great news for patients and an exciting turning point in the battle against heart failure given the unmet treatment need and the absence, until now, of treatments reducing mortality/ morbidity endpoints in these patients.

An estimated 920,000 people live with HF in the UK[2], with more than 550,000 patients having a confirmed diagnosis in England alone.[1] HF accounts for more than 100,000 hospitalisations each year and admissions have risen by nearly a third in the past five years.[9] Around half of all patients die within five years of diagnosis.[3] The number of people in the UK with heart failure is growing by 10,000 per year and the condition costs the NHS more than £2 billion per year, with 60–70% related to the costs of hospitalisation.[10] In addition to the greater risk of death and hospitalisations, HF significantly impacts patients' physical, mental and social wellbeing.[11,12]

Heart failure with LVEF >40% affects approximately 50% of patients with HF[1], of which HF with preserved ejection fraction (HFpEF) is the more prevalent type.[13] HFpEF, also commonly known

as diastolic HF, is a complex and serious heart condition which occurs when the left ventricle is unable to fill up properly with blood.[14] HFpEF is often associated with diabetes, chronic kidney disease, hypertension or obesity.[1,15] Previously, the only therapies recommended for HFpEF have been diuretics, used to manage symptoms by removing fluid, alongside management of comorbidities.[5,6] This NICE recommendation means that patients have access to disease-modifying therapy for the first time.[7]

Nick Hartshorne-Evans, CEO, Pumping Marvellous said: "This is welcome news that dapagliflozin has been recommended by NICE to treat chronic heart failure with preserved or mildly reduced ejection fraction. This is important for all those people who now have their treatment recommended by NICE to target this type of heart failure. For a condition that's both physically debilitating and severely limits an individual's quality of life, this is a critical step in treating people living with the disease. We hope today's decision can be a catalyst for the long-overdue prioritisation of care for all types of heart failure in the UK, and results in new guidelines, improved treatment pathways, and how we look at the whole picture of treating heart failure."

Tom Keith-Roach, President AstraZeneca UK, said: "We are pleased that NICE has recommended dapagliflozin for routine use within NHS England for patients with chronic heart failure with preserved or mildly reduced ejection fraction. Dapagliflozin now has NICE recommendations for patients with chronic heart failure regardless of ejection fraction. This represents an important step forward in this setting and reflects our ongoing commitment to eradicate unplanned hospital admissions across the full spectrum of heart failure (inclusive of reduced and preserved ejection fraction), in turn reducing potential health service burden at a time when it is needed most."

At AstraZeneca UK, we believe in forming ambitious purpose-led partnerships with government, with the NHS and with academia to transform outcomes at the population level and to continue developing the UK as a global life sciences powerhouse. We are inspired by what science can do and are focused on accelerating the delivery of life-changing medicines that create enduring value for patients and society.

AstraZeneca is a global, innovation-driven biopharmaceutical business with a primary focus on the discovery, development, and commercialisation of prescription medicines for gastrointestinal, cardiovascular, neuroscience, respiratory and inflammation, oncology, and infectious disease. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.

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NOTES TO EDITORS

About Heart Failure

Heart Failure (HF) is a life-threatening chronic disease in which the heart cannot pump enough blood around the body.[15,16] An estimated 920,000 people live with HF in the UK[2] – in England alone, there are more than 550,000 patients diagnosed with HF.[1] Around half of all patients will die within five years of diagnosis.[3] HF mortality risk is worse than some of the most common cancers including, prostate, breast, and bladder cancer.[17]

About HF with Ejection Fraction

There are three main types of HF related to ejection fraction (EF),[18] a measurement of the percentage of blood leaving the heart each time it contracts[14], including:

- HF with reduced ejection fraction (HFrEF) classified as LVEF ≤40%.[7]
- HF with mildly reduced ejection fraction (HFmrEF) classified as LVEF 41-49%.[7]
- HF with preserved ejection fraction (HFpEF) classified as LVEF ≥50%.[7]

About dapagliflozin

Dapagliflozin is an oral, once-daily selective inhibitor of human sodium-glucose co-transporter 2 (SGLT2).[19] Dapagliflozin is indicated in adults for the treatment of symptomatic chronic HF.[19]

Common (frequency ≥1/100 to <1/10) adverse events (AEs) associated with dapagliflozin in placebo-controlled clinical studies and post-marketing experience include genital infections; genital fungal infections; urinary tract infection; dizziness; rash; back pain; dysuria; polyuria; haematocrit increased, and creatinine renal clearance decreased during initial treatment; and dyslipidaemia.[19]

For complete information on dapagliflozin the summary of product characteristics, including a full list of side effects and adverse reactions is available here:
https://www.medicines.org.uk/emc/product/7607/smpc#gref

About DELIVER

DELIVER (Dapagliflozin Evaluation to Improve the LIVEs of Patients with Preserved Ejection Fraction Heart Failure) was an international, randomised, double-blind, parallel-group, placebo-controlled, event-driven Phase III trial designed to evaluate the efficacy of dapagliflozin, compared with placebo, in the treatment of HF patients with LVEF greater than 40%, with or without type 2 diabetes (T2D).[8] DELIVER is the largest clinical trial to date in HF patients with LVEF above 40%, with 6,263 randomised patients.[8]

Results from the DELIVER Phase III trial showed that dapagliflozin met its primary endpoint in reducing the composite outcome of cardiovascular (CV) death or worsening HF by 18% (16.4% in the dapagliflozin group and 19.5% in the placebo group over a median follow-up of 2.3 years [hazard ratio {HR} =0.82 {95% CI 0.73-0.92}; p<0.001, ARR 3.1%]).[8]

About AstraZeneca

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. AstraZeneca operates in over 100 countries and its medicines are used by millions of patients worldwide.

With a proud 100-year heritage in advancing UK science, today AstraZeneca is the UK's leading biopharmaceutical company. AstraZeneca is based in six separate locations across the UK, with its global headquarters in Cambridge. In the UK, around 8,600 employees work in research and development, manufacturing, supply, sales, and marketing. We supply around 35 different medicines to the NHS.

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

References

[1] National Institute of Health and Care Excellence. Health Technology Evaluation. TA10942. Available at: https://www.nice.org.uk/guidance/gid-ta10942/documents/final-scope. Last accessed May 2023.

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[2] Conrad N, Judge A, Tran J, et al. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. *The Lancet*. 2018;391:10120:572–580. Elsevier BV.
[3] Taylor CJ, Ordóñez-Mena JM, Roalfe AK, et al. Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population-based cohort study. *BMJ*. 2019;364:l223.
[4] National Institute for Health and Care Excellence. Clinical guideline [CG187]. Updated November 2021. Available at: https://www.nice.org.uk/guidance/cg187/chapter/Introduction. Last accessed May 2023.
[5] Jasinska-Piadlo A, & Campbell P. Management of patients with heart failure and preserved ejection fraction. *Heart*. 2023;109:11:874–883. BMJ.
[6] Taylor CJ, Moore J, & O'Flynn N. Diagnosis and management of chronic heart failure: NICE guideline update 2018. *British Journal of General Practice.* 2019;69:682:265–266. Royal College of General Practitioners.
[7] National Institute for Health and Care Excellence. Final Draft Guidance. Issued May 2023.
[8] Solomon SD, McMurray JJV, Claggett B, et al. Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. *N Engl J Med*. 2022;387:1089-1098.
[9] British Heart Foundation. New report warns disjointed heart failure care is needlessly costing lives. Online. Available at: https://www.bhf.org.uk/what-we-do/news-from-the-bhf/news-archive/2020/october/heart-failure-report-finds-disjointed-care-costing-lives. Last accessed May 2023.
[10] Hickey, D. A., & Beecroft, S. (2018). PCV124 – Hospital admissions for heart failure in England; an increasing burden on NHS resources and the focus of effective cost containment. *Value in Health* (Vol. 21, p. S113). Elsevier BV.
[11] Freedland KE, et al. Improving quality of life in heart failure. *Curr Cardiol Rep*. 2021;23(11):159.
[12] NHS Inform. Adjusting to life with a heart condition. Available at: https://www.nhsinform.scot/illnesses-and-conditions/heart-and-blood-vessels/living-with-a-heart-condition/adjusting-to-life-with-a-heart-condition. Last accessed May 2023.
[13] AstraZeneca UK Ltd. Data on File. ID: REF-155912. July 2022.
[14] Heart.org. Types of heart failure. Online. Available at: https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/types-of-heart-failure. Last accessed: May 2023.
[15] Dunlay SM, et al. Epidemiology of heart failure with preserved ejection fraction. *Nat Rev Cardiol.* 2017;14:591–602.
[16] British Heart Foundation. UK Factsheet. Available at: https://d1qotm6w854ck0.cloudfront.net/Uploads/a/f/a/bhfcvdstatisticsukfactsheet1_343908.pdf. Last accessed: May 2023.
[17] Mamas MA, Sperrin M, Watson MC, et al. Do patients have worse outcomes in heart failure than in cancer? A primary care-based cohort study with 10-year follow-up in Scotland. *Eur J Heart Fail*. 2017;19:1095-1104.
[18] Hajouli S and Ludhwani. Heart failure and ejection fraction. 2022 Dec 23. *StatPearls Publishing*. PMID: 31971755.
[19] Electronic Medicines Compendium (EMC). Forxiga 10 mg film-coated tablets. Summary of Product Characteristics (SmPC). Available at: https://www.medicines.org.uk/emc/product/7607/smpc#gref. Last accessed May 2023.

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