UK media only
Press Release

AstraZeneca

European commission approves forxiga (dapagliflozin) for the treatment of symptomatic chronic heart failure with reduced ejection fraction in adults[1,2]

- *Dapagliflozin is the first SGLT2 inhibitor approved in the European Union (EU) for adult patients with symptomatic chronic heart failure with reduced ejection fraction (HFrEF) with and without type 2 diabetes (T2D).*[1,2]
- *Almost one million people are living with heart failure (HF) in the UK, with associated mortality risk being worse than some of the most common cancers.*[3,4]

Luton, UK, 5 November 2020 – AstraZeneca today announced that the European Commission (EC) has approved a change to the terms of the marketing authorisation for Forxiga (dapagliflozin) to include the treatment of symptomatic chronic heart failure (HF) with reduced ejection fraction (HFrEF) in adults.[1,2]

The approval by the EC is based on the positive results from the landmark DAPA-HF Phase III trial, published in *The New England Journal of Medicine*.[5] It follows the recommendation for approval by the Committee for Medicinal Products for Human Use of the European Medicines Agency.

John McMurray, MD, Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, University of Glasgow, UK, said: "Today's approval provides physicians with a completely novel treatment for heart failure with reduced ejection fraction, not only improving symptoms and reducing hospital admissions, but also increasing survival in this life-threatening condition."

HF is a life-threatening, chronic condition where a person's heart is unable pump enough blood to their organs.[6] Almost one million people are living with HF in the UK, with HF mortality risk being worse than some of the most common cancers.[4,5] The COVID-19 pandemic has also had a significant impact on heart failure treatment services, with recent data showing that the number of people presenting to hospitals with heart failure had dropped by 66% by the end of April.[7]

Dapagliflozin is the first SGLT2 inhibitor to have shown a statistically significant reduction in the risk of cardiovascular (CV) death or worsening of HF events (including hospitalisation for HF, hHF) versus placebo, where both components of the primary composite endpoint contributed benefit to the overall effect. The overall safety profile of dapagliflozin in patients with heart failure was consistent with the known safety profile of dapagliflozin.[5,8]

Tom Keith-Roach, President, AstraZeneca UK, said: "This is exciting news for heart failure patients both with and without Type 2 Diabetes. With more effective treatments we see the clear opportunity to help eradicate heart failure as one of the UK's leading causes of hospitalisation and death and we look forward to working with our partners in the NHS to transform standards of care and improve outcomes for these patients."

The DAPA-HF Phase III trial demonstrated that dapagliflozin, in addition to standard of care, reduced the risk of the composite outcome of CV death or the worsening of HF versus placebo by 26% (hazard ratio [HR] = 0.74 [95% confidence interval {CI} 0.65-0.85]; $p < 0.0001$) (absolute risk reduction [ARR] = 4.9% [16.3% vs 21.2% patients with event, respectively]). During the trial, one CV death or hHF or an urgent visit associated with HF could be avoided for every 21 patients treated.[5]

Very common adverse events 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, dizziness, rash, back pain, dysuria,

polyuria, haematocrit increased, creatinine renal clearance decreased during initial treatment and dyslipidaemia.[9]

– ENDS –

CONTACTS
UK Media Enquiries
Tatiana Allan, AstraZeneca: 07385 037254 / tatiana.allan@astrazeneca.com
Alex Larkinson, Edelman: 07980 687255 / alex.larkinson@edelman.com

About Heart Failure
Heart Failure (HF) is a life-threatening disease in which the heart cannot pump enough blood around the body.[6] It affects approximately 64 million people worldwide (at least half of which have a reduced ejection fraction), including one million in the UK. [3,10,11] It is a chronic disease where around half of patients will die within five years of diagnosis.[12]

HF mortality risk is worse than some of the most common cancers (prostate, breast, and bladder cancer).[4] It is the leading cause of hospitalisation for those over the age of 65 and represents a significant clinical and economic burden.[13]

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.[14,15]

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.[5]

About dapagliflozin
Dapagliflozin is a first-in-class, oral, once-daily selective inhibitor of human sodium-glucose co-transporter 2 (SGLT2). It acts by reducing reabsorption of filtered glucose in the kidneys and allowing excretion of excess glucose through urine.

Dapagliflozin is available in 5mg and 10mg tablets. Dapagliflozin is 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.[1] Dapagliflozin is indicated in adults for the treatment of symptomatic chronic heart failure with reduced ejection fraction.[1]

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

AstraZeneca in CVRM
Cardiovascular, renal and metabolic diseases are some of the leading causes of death around the world.[16,17] At AstraZeneca, our vision is to protect the lives of the millions of people in the UK affected by these conditions.[18,19,20] We are committed to delivering innovative solutions that lead directly to better disease management, improved outcomes and decreased mortality rates. In heart failure, our ambition is to improve the lives of more than 50,000 people living with heart failure by 2025.

GB-24684
Date of preparation: November 2020

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.

References

[1] European Medicines Agency. Forxiga. Available at: https://www.ema.europa.eu/en/medicines/human/summaries-opinion/forxiga-1 Last accessed November 2020.
[2] European Commission. Note to standing committee: Adoption of commission implementing decision amending the marketing authorisation by Decision C(2012)8378(final) for "Forxiga – dapagliflozin", a medicinal product for human use.
[3] British Heart Foundation. UK Factsheet. Available at: https://d1qotm6w854ck0.cloudfront.net/Uploads/a/f/a/bhfcvdstatisticsukfactsheet1_343908.pdf Last accessed November 2020.
[4] 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.
[5] McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2019;381:1995-2008.
[6] Savarese G, Lund LH. Global public health burden of heart failure. *Card Fail Rev*. 2017;3:7-11.
[7] NICOR, National CardiacAudit Programme. Rapid cardiovascular data: we need it now (and in the future). Available at: https://www.hqip.org.uk/wp-content/uploads/2020/09/NICOR-COVID-2020-Report-1-3.pdf Last accessed November 2020.
[8] McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2019;381:1995-2008 (Supplementary appendix).
[9] Dapagliflozin 10mg Summary of Product Characteristics. 02 January 2020. Available at: https://www.medicines.org.uk/emc/product/7607/smpc#gref. Accessed November 2020.
[10] Travessa AM, de Menezes Falcao LF. Treatment of heart failure with reduced ejection fraction - recent developments. *Am J Ther*. 2016;23:e531-e549.
[11] GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390:1211–1259.
[12] 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.
[13] Azad N, Lemay G. Management of chronic heart failure in the older population. J Geriatr Cardiol 2014; 11(4):329–37.
[14] Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;37:2129–2200.
[15] National Institute for Health and Care Excellence. Chronic heart failure in adults: diagnosis and management: NICE guideline [NG106]; 2018. Available at: https://www.nice.org.uk/guidance/ng106/resources/chronic-heart-failure-in-adults-diagnosis-and-management-pdf-66141541311685 Last accessed November 2020.
[16] World Health Organization (WHO). The top ten causes of death. Available at: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death Last accessed November 2020.
[17] Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the sustainable development goals. *Bull World Health Organ*. 2018;96:414-422D.
[18] British Heart Foundation. Facts and figures. Available at: https://www.bhf.org.uk/what-we-do/news-from-the-bhf/contact-the-press-office/facts-and-figures Last accessed November 2020.
[19] Diabetes UK. Diabetes prevalence 2019. Available at: https://www.diabetes.org.uk/professionals/position-statements-reports/statistics/diabetes-prevalence-2019 Last accessed November 2020.
[20] Kidney Care UK. Facts and stats. Available at: https://www.kidneycareuk.org/news-and-campaigns/facts-and-stats/ Last accessed October 2020.

GB-24684
Date of preparation: November 2020