NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Dapagliflozin for treating chronic heart failure with preserved or mildly reduced ejection fraction

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dapagliflozin within its marketing authorisation for treating symptomatic chronic heart failure with a left ventricular ejection fraction of 40% or more.

Background

Heart failure is a complex clinical syndrome of signs and symptoms, generally defined as the inability of the heart to supply sufficient blood flow to meet the body's needs. It is caused by structural or functional abnormalities of the heart, commonly resulting from coronary artery disease. Other conditions that can increase the risk of heart failure include; ischaemic heart disease, atrial fibrillation, valve disease, hypertension, diabetes, chronic obstructive pulmonary disease, and asthma.[1] The European Society of Cardiology (ESC) defines 3 types of chronic heart failure based on left ventricular ejection fraction (LVEF), a measurement of how much blood the left ventricle pumps out with each contraction. The ESC defines heart failure with reduced ejection fraction as a LVEF of 40% or less; mildly reduced ejection fraction as a LVEF between 41% and 49%; and preserved ejection fraction as a LVEF of 50% or more.[2] NICE guideline 106 for chronic heart failure in adults (NG106) states that heart failure with preserved ejection fraction is usually associated with impaired left ventricular relaxation, rather than left ventricular contraction, and is characterised by normal or preserved LVEF with evidence of diastolic dysfunction. Symptoms of heart failure commonly include breathlessness, fatigue and ankle swelling. Quality of life is affected by the physical limitations imposed by the symptoms.

More than 550,000 people in England have heart failure and around 50% have preserved or mildly reduced ventricular ejection fraction.[2,3] There were 94,185 hospitalisations in England for heart failure in 2019/20.[4] Both the prevalence and incidence of heart failure increase with age. Around 24% of people diagnosed with heart failure die within the first year, with a 5-year mortality rate of about 55%.[5]

NG106 recommends low to medium dose loop diuretics for people with chronic heart failure with preserved ejection fraction. Specialist advice is needed if the disease does not respond. Most people with chronic heart failure with preserved ejection fraction also have symptomatic treatments for comorbidities, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), beta-blockers or mineralocorticoid receptor antagonists (MRAs).[2]

The technology

Dapagliflozin (Forxiga, AstraZeneca), is a sodium-glucose co-transporter 2 (SGLT2) inhibitor. It is administered orally.

Dapagliflozin does not currently have a marketing authorisation in the UK for treating symptomatic chronic heart failure with preserved or mildly reduced ejection fraction.

Dapagliflozin does have a marketing authorisation in the UK for treating symptomatic chronic heart failure with reduced ejection fraction. It is being studied in a randomised controlled trial compared with placebo, in adults with symptomatic heart failure (New York Heart Association class II-IV) with a left ventricular ejection fraction of 40% or more and evidence of structural heart disease.

Intervention	Dapagliflozin in combination with standard care (including loop diuretics and symptomatic treatments for co-morbidities)
Population	Adults with symptomatic chronic heart failure with a left ventricular ejection fraction of 40% or more
Comparators	Established clinical management without dapagliflozin, including but not limited to loop diuretics and symptomatic treatments for co-morbidities
Outcomes	The outcome measures to be considered include: • symptoms of heart failure • hospitalisation for heart failure • all-cause hospitalisation • mortality • cardiovascular mortality • kidney function • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

Other considerations	The availability and cost of biosimilar and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related Technology Appraisals:** Dapagliflozin for treating chronic heart failure with reduced ejection fraction (2021) NICE technology appraisal 679. Empagliflozin for treating chronic heart failure with reduced ejection fraction. NICE technology appraisal 773. Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction (2016) NICE technology appraisal 388. Ivabradine for treating chronic heart failure (2012) NICE technology appraisal 267. **Appraisals in development (including suspended appraisals)** Empagliflozin for treating chronic heart failure with preserved ejection fraction [ID3945]. NICE technology appraisal. Publication date to be confirmed. **Related Guidelines:** Chronic heart failure in adults: diagnosis and management (2018) NICE guideline NG106 **Related Quality Standards:** Chronic heart failure in adults (2011) NICE quality standard 9
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. National Institute for Cardiovascular Outcomes Research (2019) National heart failure audit 2017/18. Available at: https://www.hqip.org.uk/wp-

content/uploads/2019/09/Ref-129-Cardiac-Heart-Failure-Summary-Report-2019-FINAL.pdf. Accessed November 2021.

2. McDonagh, Theresa A., et al. (2021) ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal 42.36: 3599-3726.

3. NHS Digital (2021) Quality and Outcomes Framework, 2020-21. Prevalence at regional and national level. Available at: https://digital.nhs.uk/data-and-information/publications/statistical/quality-and-outcomes-framework-achievement-prevalence-and-exceptions-data/2020-21. Accessed March 2022.

4. NHS Digital (2020) Hospital admitted patient care activity, 2019-20: Primary diagnosis 3 character. Available at: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2019-20. Accessed March 2022.

5. Taylor CJ, Ordonez-Mena JM, Roalfe AK et al. (2019) Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population based cohort study. BMJ 364:l223.