

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

**Remit/evaluation objective**

To appraise the clinical and cost effectiveness of empagliflozin 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.<sup>1</sup> 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.<sup>2</sup> [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.<sup>2,3</sup> There were 94,185 hospitalisations in England for heart failure in 2019/20.<sup>4</sup> 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%.<sup>5</sup>

[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).<sup>2</sup> NICE ([TA902](#)) recommends dapagliflozin as an option for treating symptomatic chronic heart failure with preserved or mildly reduced ejection fraction in adults.

**The technology**

Empagliflozin (Jardiance, Boehringer Ingelheim) has a marketing authorisation for adults with symptomatic chronic heart failure. [NICE technology appraisal guidance 773](#) provides recommendations for the use of empagliflozin in people with chronic

heart failure with reduced ejection fraction of 40% or less. This evaluation covers the remaining population of the marketing authorisation (i.e., people with chronic heart failure with ejection fraction of more than 40%).

<b>Intervention</b>	Empagliflozin in combination with standard care (including loop diuretics and symptomatic treatments for co-morbidities)
<b>Population</b>	Adults with symptomatic chronic heart failure with left ventricular ejection fraction of 40% or more
<b>Comparators</b>	<ul style="list-style-type: none"> <li>Established clinical management without empagliflozin, including but not limited to loop diuretics and symptomatic treatments for co-morbidities</li> <li>Dapagliflozin</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>symptoms of heart failure</li> <li>hospitalisation for heart failure</li> <li>all-cause hospitalisation</li> <li>mortality</li> <li>cardiovascular mortality</li> <li>kidney function</li> <li>adverse effects of treatment</li> <li>health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>

<b>Other considerations</b>	<p>The availability and cost of biosimilar and generic products should be taken into account.</p> <p>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.</p>
<b>Related NICE recommendations</b>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">Dapagliflozin for treating chronic heart failure with preserved or mildly reduced ejection fraction</a> (2023). NICE technology appraisal 907.</p> <p><a href="#">Empagliflozin for treating chronic heart failure with reduced ejection fraction (2022)</a>. NICE technology appraisal 773.</p> <p><a href="#">Dapagliflozin for treating chronic heart failure with reduced ejection fraction</a> (2021) NICE technology appraisal 679.</p> <p><a href="#">Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction</a> (2016) NICE technology appraisal 388.</p> <p><a href="#">Ivabradine for treating chronic heart failure</a> (2012) NICE technology appraisal guidance 267.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">Chronic heart failure in adults: diagnosis and management</a> (2018) NICE guideline NG106</p> <p><b>Related Quality Standards:</b></p> <p><a href="#">Chronic heart failure in adults</a> (2011) NICE quality standard 9</p>
<b>Related National Policy</b>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a></p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a></p>

## 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.