

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Appraisal

### Dapagliflozin for treating heart failure with reduced ejection fraction

#### Final scope

##### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dapagliflozin within its marketing authorisation for treating adults with chronic heart failure with reduced ejection fraction.

##### 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; ischemic heart disease, atrial fibrillation, valve disease, hypertension, diabetes, chronic obstructive pulmonary disease and asthma. Heart failure may be associated with left ventricular systolic dysfunction (that is, reduced left ventricular ejection fraction, where the left pumping chamber's ability to pump is impaired) but may also be associated with reduced ejection fraction, defined as an ejection fraction below 40% in [NICE guideline 106 for chronic heart failure in adults](#).

Symptoms of heart failure commonly include breathlessness, fatigue and ankle swelling. Quality of life is affected by the physical limitations imposed by the symptoms.

Nearly 500,000 people in England have heart failure.<sup>1</sup> There were 188,683 hospital admissions in England for heart failure in 2018/19.<sup>2</sup> 66% of people with heart failure had a reduced left ventricular ejection fraction.<sup>3</sup> Both the prevalence and incidence of heart failure increase with age. About 20 percent of people diagnosed with heart failure die within the first year, with a 5-year mortality rate of about 50%.<sup>4</sup>

[NICE guideline 106 for chronic heart failure in adults](#) recommends offering an angiotensin-converting enzyme (ACE) inhibitor and a beta-blocker for people with heart failure with reduced ejection fraction. If ACE inhibitors are contraindicated or not tolerated, an angiotensin receptor blocker (ARB) should be considered. A mineralocorticoid receptor antagonist (MRA) in addition to an ACE inhibitor (or ARB) and beta-blocker should be offered if symptoms continue. If neither ACE inhibitors or ARBs are tolerated, specialist advice should be sought and treatment with hydralazine in combination with nitrate can be considered.

NICE [technology appraisal guidance 388](#) recommends sacubitril valsartan as an option for treating symptomatic chronic heart failure with reduced ejection fraction, only in people:

- with New York Heart Association (NYHA) class II to IV symptoms and
- with a left ventricular ejection fraction of 35% or less and
- who are already taking a stable dose of ACE inhibitors or ARBs

NICE [technology appraisal guidance 267](#) recommends ivabradine in combination with standard therapy for people:

- with New York Heart Association (NYHA) class II to IV stable chronic heart failure with systolic dysfunction and
- who are in sinus rhythm with a heart rate of 75 beats per minute or more and
- who are given ivabradine in combination with standard therapy including beta-blocker therapy, angiotensin-converting enzyme (ACE) inhibitors and aldosterone antagonists, or when beta-blocker therapy is contraindicated or not tolerated and
- with a left ventricular ejection fraction of 35% or less.

### The technology

Dapagliflozin (Forxiga, AstraZeneca) is a sodium-glucose co-transporter 2 (SGLT-2) inhibitor. The mechanism of action of dapagliflozin in heart failure with reduced ejection fraction is not yet fully understood. It is administered orally.

Dapagliflozin does not currently have a marketing authorisation in the UK for chronic heart failure with reduced ejection fraction. It is being studied in combination with individually optimised standard care in randomised controlled trials compared with placebo, in adults with an established documented diagnosis of symptomatic heart failure with reduced ejection fraction (NYHA functional class II-IV) for at least 2 months, who had a left ventricular ejection fraction of 40% or less.

<b>Intervention</b>	Dapagliflozin in combination with standard care (including treatment with an ACE inhibitor, ARB, mineralocorticoid receptor antagonist, beta blocker and sacubitril valsartan).
<b>Population</b>	Adults with chronic heart failure with reduced ejection fraction.
<b>Comparators</b>	Individually optimised standard care without dapagliflozin.  Standard care is defined as: <ul style="list-style-type: none"> <li>• ACE inhibitors in combination with beta-blockers, and/or mineralocorticoid receptor antagonists</li> </ul>

	<ul style="list-style-type: none"> <li>• ARBs in combination with beta-blockers, and/or mineralocorticoid receptor antagonists</li> <li>• Sacubitril valsartan in combination with beta-blockers, and/or mineralocorticoid receptor antagonists</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>• adverse effects of treatment (including diabetic ketoacidosis, genital infections, Fournier's gangrene, amputations and fractures)</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>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> <p>The cost of background therapies, such as diuretics for people with oedema, should also be included in cost effectiveness analyses.</p>
<b>Other considerations</b>	<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 and NICE Pathways</b>	<p>Related Technology Appraisals:</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</p>

	<p>technology appraisal guidance 267</p> <p>Related Guidelines:</p> <p><a href="#">Chronic heart failure in adults: diagnosis and management</a> (2018) NICE guideline NG106</p> <p>Related Quality Standards:</p> <p><a href="#">Chronic heart failure in adults</a> (2011) NICE quality standard 9</p> <p>Related NICE Pathways:</p> <p><a href="#">Chronic heart failure</a> (2019) NICE pathway</p>
<p><b>Related National Policy</b></p>	<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, 2.</p> <p><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. British Heart Foundation. Heart statistics, BHF statistics fact sheet England. Accessed September 2019. Available at: <https://www.bhf.org.uk/what-we-do/our-research/heart-statistics>
2. NHS Digital (2019) Hospital admitted patient care activity, 2018-19: Primary diagnosis 3 character. Accessed September 2019. Available at: <https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2018-19>
3. National Institute for Cardiovascular Outcomes Research (2018) National heart failure audit 2016/17. Accessed September 2019. Available at: <https://www.nicor.org.uk/wp-content/uploads/2018/11/Heart-Failure-Summary-Report-2016-17.pdf>
4. 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.