NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Empagliflozin for treating chronic heart failure with preserved ejection fraction

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of empagliflozin within its marketing authorisation for treating symptomatic chronic heart failure with preserved 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; ischaemic heart disease, atrial fibrillation, valve disease, hypertension, diabetes, chronic obstructive pulmonary disease, and asthma. Heart failure may be associated with impaired filling of the left ventricle when the heart muscle is thickened, often as a result of long-standing high blood pressure. This is called heart failure with preserved ejection fraction.[1] The European Society of Cardiology suggests that a left ventricular ejection fraction of 50% or more should be used to define preserved ejection fraction.[6]

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 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]

NICE guideline 106 for chronic heart failure in adults recommends low to medium dose loop diuretics for people with chronic heart failure and preserved ejection fraction. Specialist advice is needed if the disease does not respond. The guideline also recommends calcium-channel blockers, amiodarone (in consultation with a specialist) and anticoagulants to treat all types of heart failure.

The technology

Empagliflozin (Jardiance, Boehringer Ingelheim) is a sodium-glucose co-transporter 2 (SGLT2) inhibitor. The mechanism of action of empagliflozin in heart failure with preserved ejection fraction is not yet fully understood. It is administered orally.

Empagliflozin has a marketing authorisation for treating symptomatic chronic heart failure with reduced ejection fraction. It does not currently have a marketing authorisation in the UK for treating symptomatic chronic heart failure with preserved ejection fraction. It is being studied in randomised controlled trials compared with

placebo, in adults with symptomatic chronic heart failure (NYHA functional class II-IV) with a left ventricular ejection fraction of more than 40% and evidence of structural heart disease.

Intervention	Empagliflozin
Population	Adults with symptomatic chronic heart failure with preserved ejection fraction
Comparators	Established clinical management without empagliflozin, including but not limited to loop diuretics, calcium-channel blockers, amiodarone and anticoagulants
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	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 and NICE Pathways	**Related Technology Appraisals**: Dapagliflozin for treating chronic heart failure with reduced ejection fraction (2021) NICE technology appraisal 679.

	Review date 2024. Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction (2016) NICE technology appraisal 388. Reviewed 2018. Ivabradine for treating chronic heart failure (2012) NICE technology appraisal guidance 267. Reviewed 2018. **Appraisals in development (including suspended appraisals)** Empagliflozin for treating chronic heart failure with reduced ejection fraction [ID3826]. NICE technology appraisal. Publication expected February 2022. Dapagliflozin for treating heart failure with preserved ejection fraction [ID1648]. NICE technology appraisal. Publication 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 NICE Pathways**: Chronic heart failure (2021) NICE pathway
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

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for chronic heart failure with preserved ejection fraction?

Have all relevant comparators for empagliflozin been included in the scope?

Which treatments would empagliflozin be used in combination with?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom empagliflozin is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider empagliflozin will fit into the existing NICE pathway, Chronic heart failure?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which empagliflozin will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider empagliflozin to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of empagliflozin can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

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. NHS Digital (2019) Quality and Outcomes Framework, Achievement, prevalence and exceptions data 2018-19. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/quality-and-outcomes-framework-achievement-prevalence-and-exceptions-data/2018-19-pas. Accessed Nov 2021.

3. Dunlay SM, Roger VL, Redfield MM. (2017) Epidemiology of heart failure with preserved ejection fraction. Nature Reviews Cardiology.14:591-602. Available from: https://www.nature.com/articles/nrcardio.2017.65.

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 November 2021.

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.

6. 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. Available from: https://academic.oup.com/eurheartj/article/42/36/3599/6358045?login=true. Accessed November 2021.