

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Vericiguat for treating chronic heart failure with reduced ejection fraction

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of vericiguat within its marketing authorisation for treating 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. Heart failure may be associated with left ventricular systolic dysfunction (where the muscle of the left pumping chamber, or ventricle, does not contract effectively, and therefore less oxygen-rich blood is pumped out to the body). The amount of blood that the left ventricle pumps out is usually measured in terms of an ejection fraction (the percentage of the total amount of blood in the left ventricle pushed out with each contraction). [NICE guideline 106 for chronic heart failure in adults](#) defines heart failure with reduced ejection fraction as heart failure with an ejection fraction below 40%.

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.¹ There were 188,683 hospital admissions in England for heart failure in 2018/19.² 66% of people with heart failure had a reduced left ventricular ejection fraction.³ 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%.⁴

[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

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- 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

Vericiguat (brand name unknown, Bayer) is a stimulator of the soluble guanylate cyclase (sGC) enzyme. sGC stimulation increases the availability of nitric oxide in the body and widens the pulmonary arteries (the blood vessels that connect the heart to the lungs), making it easier for the heart to pump blood through the lungs.

Vericiguat does not currently have a marketing authorisation in the UK for chronic heart failure with reduced ejection fraction. It has been studied in combination with standard care in a randomised controlled trial compared with placebo, in adults with chronic heart failure NYHA Class II-IV, who had a left ventricular ejection fraction of less than 45%.

Intervention(s)	Vericiguat in combination with standard care
Population(s)	Adults with chronic heart failure with reduced ejection fraction of less than 45%.
Comparators	<ul style="list-style-type: none"> • Hydralazine in combination with nitrate • Sacubitril valsartan in combination with beta-blockers, and/or mineralocorticoid receptor antagonists • Individually optimised standard care with or without ivabradine, which may include: <ul style="list-style-type: none"> ○ ACE inhibitors in combination with beta-blockers, and/or mineralocorticoid receptor antagonists ○ ARBs in combination with beta-blockers, and/or mineralocorticoid receptor antagonists

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • symptoms of heart failure • hospitalisation for heart failure • all-cause hospitalisation • mortality • cardiovascular mortality • adverse effects of treatment (including symptomatic hypotension, syncope, diabetic ketoacidosis, genital infections, Fournier's gangrene, amputations and fractures) • health-related quality of life.
Economic analysis	<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>
Other considerations	<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>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction (2016) NICE technology appraisal 388</p> <p>Ivabradine for treating chronic heart failure (2012) NICE technology appraisal guidance 267</p> <p>Appraisals in development (including suspended appraisals)</p> <p>Dapagliflozin for treating heart failure with reduced ejection fraction NICE technology appraisals guidance [ID1656].</p>

	<p>Publication expected February 2021.</p> <p>Related Guidelines: Chronic heart failure in adults: diagnosis and management (2018) NICE guideline NG106</p> <p>Related Quality Standards: Chronic heart failure in adults (2011) NICE quality standard 9</p> <p>Related NICE Pathways: Chronic heart failure (2019) NICE pathway</p>
Related National Policy	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p>

Questions for consultation

The key trial for vericiguat included people with left ventricular ejection fraction of below 45%, are outcomes likely to vary according to left ventricular ejection fraction? If so would this limit who is likely to receive vericiguat in practice?

Is the population defined appropriately? In particular, would vericiguat be offered to people with reduced ejection fraction

- below 40% or
- 35% or less?

Have all relevant comparators for vericiguat been included in the scope? In particular:

- Which treatments are considered to be established clinical practice in the NHS for chronic heart failure with reduced ejection fraction?
- Is standard of care defined appropriately?
- For people with ejection fraction of 40% or more

Are the outcomes listed appropriate?

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

Where do you consider vericiguat 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:

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- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which vericiguat 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 vericiguat 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 vericiguat 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>).

NICE has published an addendum to its guide to the methods of technology appraisal (available at <https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf>), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. British Heart Foundation. Heart statistics, BHF statistics fact sheet England. Accessed July 2020. 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 July 2020. 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 July 2020. 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.