NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Rivaroxaban for treating chronic heart failure

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of rivaroxaban within its marketing authorisation for treating heart failure in people with coronary heart disease.

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 (that is, reduced left ventricular ejection fraction, where the left pumping chamber's ability to pump is impaired) but may also be associated with preserved ejection fraction (minimum ejection fraction of 45%).

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

Over 440,000 people in England have heart failure.[1] Approximately 169,756 people were admitted to hospital in England with heart failure in 2016/17.[2] 68% of people with heart failure had a reduced left ventricular ejection fraction.[3] Both the prevalence and incidence of heart failure increase with age. Thirty to forty percent of patients diagnosed with heart failure die within the first year.

NICE clinical guideline 108 for chronic heart failure recommends that all patients with chronic heart failure due to left ventricular systolic dysfunction should be offered beta-blockers and an angiotensin-converting enzyme (ACE) inhibitor unless contraindicated or not tolerated. Angiotensin II receptor inhibitors (ARBs) are alternatively recommended for use in people in whom ACE inhibitors are unsuitable. In clinical practice, an aldosterone antagonist is usually administered alongside beta-blockers with ACE inhibitors or ARBs. Clinical guideline 108 also recommends offering hydralazine in combination with nitrate to people for whom both ACE inhibitors and ARBs are unsuitable. NICE technology appraisal guidance 388 recommends sacubitril valsartan as a second-line treatment for people who remain symptomatic on standard of care.

The technology

Rivaroxaban (Xarleto, Bayer) is an anticoagulant which acts by direct inhibition of activated factor X (Factor Xa). Inhibition of Factor Xa reduces the formation of thrombin, which plays a role in the pathophysiological processes which occur in coronary artery disease after heart failure. It is administered orally.

Rivaroxaban does not currently have a marketing authorisation in the UK for treating heart failure. It is being studied in a clinical trial, compared with placebo, in people with heart failure and significant coronary artery disease following an episode of decompensated heart failure.

Intervention(s)	Rivaroxaban with standard of care (including an ACE inhibitor or ARB)
Population(s)	People with heart failure and coronary artery disease
Comparators	• Standard of care • Sacubrital valsartan with standard of care
Outcomes	The outcome measures to be considered include: • symptoms of heart failure • hospitalisation for heart failure • all-cause hospitalisation • mortality • cardiovascular mortality • 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.
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:** Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction (2016) NICE technology appraisal guidance 388. Last reviewed July 2018: on static list. Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure (2014) NICE technology appraisal guidance 314. Last reviewed June 2017: on static list. Ivabradine for treating chronic heart failure (2012) NICE technology appraisal guidance 267. Last reviewed March 2018: on static list. **Appraisals in development (including suspended appraisals):** Nesiritide for the treatment of heart failure. NICE technology appraisal. Publication date to be confirmed. Status: suspended Implantable Vagus Nerve Stimulator in Heart Failure. NICE technology appraisal. Publication date to be confirmed. Status: suspended **Related Guidelines:** Cardiovascular disease: risk assessment and reduction, including lipid modification (2014, updated September 2016) NICE guideline CG181 Chronic heart failure in adults: management (2010) NICE guideline CG108 To be updated by Chronic heart failure in adults: diagnosis and management NICE guideline. Publication expected September 2018 **Related Quality Standards:** Chronic heart failure in adults (2011) NICE quality standard 9 **Related NICE Pathways:** Chronic heart failure (2017) NICE pathway http://pathways.nice.org.uk/
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. see: 7. Adult specialist cardiac

	services (pp31-35) Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1–5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

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

- Is 'Sacubrital valsartan with standard of care' an appropriate comparator?

Is there overlap between the population included in the scope and the population indicated for treatment with rivaroxaban for atrial fibrillation?

Which treatments are considered to be established clinical practice in the NHS for heart failure and coronary artery disease?

Are the outcomes listed appropriate?

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

Where do you consider rivaroxaban will fit into the existing NICE pathway, Chronic heart failure (2017)?

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 rivaroxaban 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 rivaroxaban 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 rivaroxaban 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. NHS Digital (2017) Quality and Outcomes Framework – Prevalence, Achievements and Exceptions Report, England 2016-17. Accessed June 2018. Available at: https://files.digital.nhs.uk/publication/c/r/qof-1617-rep.pdf
2. NHS Digital (2017) Hospital admitted patient care activity, 2016-17: Primary diagnosis 3 character. Accessed June 2018. Available at: https://files.digital.nhs.uk/publication/7/d/hosp-epis-stat-admi-diag-2016-17-tab.xlsx
3. National Institute for Cardiovascular Outcomes Research (2017) National heart failure audit April 2015–March 2016. Accessed june 2018. Available at: http://www.ucl.ac.uk/nicor/audits/heartfailure/documents/annualreports/annual-report-2015-6-v8.pdf