NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

LCZ696 for treating chronic heart failure

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of LCZ696 within its marketing authorisation for treating chronic heart failure (NYHA stage II-IV) with reduced left ventricular 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 (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 are classified by the New York Heart Association (NYHA) system from class I (no limitations) to class IV (inability to carry out any physical activity without discomfort), and commonly include breathlessness, fatigue and ankle swelling. Quality of life is affected by the physical limitations imposed by the symptoms.

Around 800,000 people in the UK have heart failure and approximately 42,000 people were admitted to hospital in England with heart failure in 2012/13. 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 ('Chronic heart failure') recommends that that all patients with chronic heart failure due to left ventricular systolic dysfunction be offered beta-blockers and an angiotensin-converting enzyme (ACE) inhibitor unless contraindicated or not tolerated. Angiotensin II receptor inhibitors are alternatively recommended for use in people in whom ACE inhibitors are not tolerated.

The technology

LCZ696 (brand name unknown, Novartis) is an angiotensin receptor neprilysin inhibitor. It includes the neprilysin inhibitor sacubitril (AHU377) and the angiotensin II receptor inhibitor valsartan. Both sacubutril and valsartan lower blood pressure. It is administered orally.

LCZ696 does not currently have a marketing authorisation in the UK. It has been studied in clinical trial compared with the ACE inhibitor enalapril in

people with heart failure (New York Heart Association (NYHA) class II-IV) with a left ventricular ejection fraction of 35% or lower. It is being assessed in an ongoing trial in people with heart failure with a preserved left ventricular fraction of 45% or more, compared with valsartan.

Intervention(s)	LCZ696
Population(s)	People with chronic heart failure (NYHA class II-IV) with reduced left ventricular ejection fraction
Comparators	• ACE inhibitor licensed for heart failure • Angiotensin II receptor inhibitor licensed for heart failure
Outcomes	The outcome measures to be considered include: • symptoms of heart failure • hospitalisation for heart failure • 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: Technology Appraisal No. 267, Nov 2012 ‘Ivabradine for treating chronic heart failure’. Review proposal date Nov 2015

	Technology appraisal No. 314, Jun 2014 'Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure (review of TA95 and TA120)'. Review proposal date May 2017 Related Guidelines: Clinical Guideline No. 108, Aug 2010, 'Chronic heart failure: Management of chronic heart failure in adults in primary and secondary care'. Review in progress. Anticipated publication date to be confirmed. Related Interventional Procedures: Interventional Procedure No. 463, Aug 2013, 'Insertion and use of implantable pulmonary artery pressure monitors in chronic heart failure. Related Quality Standards: Quality Standard No. 9, Jun 2011 'Chronic heart failure'. Update in progress. Related NICE Pathways: NICE pathway: Chronic heart failure, pathway last updated July 2014
Related National Policy	Department of Health National service framework: coronary heart disease. Published Mar 2000. https://www.gov.uk/government/publications/quality-standards-for-coronary-heart-disease-care Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1,2, 3 and 4 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

Questions for consultation

Have all relevant comparators for LCZ696 been included in the scope? Which treatments for heart failure, if any, would be taken at the same point in the treatment pathway alongside LCZ696?

Are there any subgroups of people in whom LCZ696 is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider LCZ696 will fit into the existing NICE pathway, 'chronic heart failure treatment and monitoring'?

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 LCZ696 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 LCZ696 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 LCZ696 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.

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)