

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Proposed Health Technology Appraisal**

**Sacubitril valsartan for treating chronic heart failure**

**Final scope**

**Remit/appraisal objective**

To appraise the clinical and cost effectiveness of sacubitril valsartan within its marketing authorisation for treating heart failure (NYHA stage II-IV) with systolic dysfunction.

**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%). Severe systolic dysfunction is usually associated with an ejection fraction of 35% or lower.

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 900,000 people in the UK have heart failure. Approximately 42,000 people were admitted to hospital in England with heart failure in 2012/13 and 72% of these people had a reduced left ventricular ejection fraction<sup>1</sup>. 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 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 are alternatively recommended for use in people in whom ACE inhibitors are unsuitable. In clinical practice, an aldosterone antagonist is usually administered alongside the other treatments.

**The technology**

Sacubitril valsartan (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 sacubitril and valsartan lower blood pressure. It is administered orally.

Sacubitril valsartan does not currently have a marketing authorisation in the UK. It has been studied in a clinical trial compared with the ACE inhibitor enalapril in adults 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 adults with heart failure with a preserved left ventricular fraction of 45% or more, compared with valsartan.

<b>Intervention(s)</b>	Sacubitril valsartan in combination with standard care (including treatment with a beta blocker and an aldosterone antagonist)
<b>Population(s)</b>	People with chronic heart failure (NYHA class II-IV) with systolic dysfunction.
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• ACE inhibitor in combination with standard care</li> <li>• Angiotensin II receptor blocker in combination with standard care (for people in whom an ACE inhibitor is unsuitable).</li> </ul> <p>Standard care includes treatment with a beta blocker and an aldosterone antagonist.</p>
<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</li> <li>• health-related quality of life</li> </ul>

<p><b>Economic analysis</b></p>	<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>Standard care includes treatment with a beta blocker and an aldosterone antagonist.</p> <p>The cost of background therapies, such as diuretics, should also be included in cost effectiveness analyses.</p>
<p><b>Other considerations</b></p>	<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>
<p><b>Related NICE recommendations and NICE Pathways</b></p>	<p>Related Technology Appraisals:</p> <p>Technology Appraisal No. 267, Nov 2012 'Ivabradine for treating chronic heart failure'. Review proposal date Nov 2015.</p> <p>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.</p> <p>Related Guidelines:</p> <p>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.</p> <p>Related Interventional Procedures:</p> <p>Interventional Procedure No. 463, Aug 2013, 'Insertion and use of implantable pulmonary artery pressure monitors in chronic heart failure.</p> <p>Related Quality Standards:</p> <p>Quality Standard No. 9, Jun 2011 'Chronic heart failure'. Update in progress.</p> <p>Related NICE Pathways:</p>

	NICE pathway: Chronic heart failure, pathway last updated July 2014.
<b>Related National Policy</b>	<p>Department of Health National service framework: coronary heart disease. Published Mar 2000.  <a href="https://www.gov.uk/government/publications/quality-standards-for-coronary-heart-disease-care">https://www.gov.uk/government/publications/quality-standards-for-coronary-heart-disease-care</a></p> <p>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1,2, 3 and 4  <a href="https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf">https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf</a></p>

<sup>1</sup>The National Heart Failure Audit April 2012-March 2013. Available from:  
<http://www.hqip.org.uk/assets/NCAPOP-Library/NCAPOP-2013-14/UCL-HF-2013-Report-2013-ONLINE-v2.pdf>