

**NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE**

**Proposed Health Technology Appraisal**

**Ivabradine for the treatment of chronic heart failure**

**Draft scope (Pre-referral)**

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of ivabradine within its licensed indication for the treatment of chronic heart failure.

**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 due to 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.

Signs in heart failure can be due to pulmonary and systemic congestion, the structural abnormalities causing heart failure, the structural abnormalities resulting from heart failure, or from complications of therapy. 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. Overall, the quality of life in people with heart failure declines as the severity of the disease increases.

Around 900,000 people in the UK have heart failure and approximately 68,000 people are diagnosed with heart failure each year. Both the prevalence and incidence of heart failure increase with age. About 3% of people aged 65 to 74 years have heart failure, this rate increases to about 7% of those aged 75-84 years and to over 14% of those aged 85 and above. The risk of heart failure is higher in men than in women in all age groups, but there are more women than men with heart failure due to population demographics.

Annually, over 24,000 deaths in the UK (nearly 4% of all deaths) are a result of heart failure. Thirty to forty percent of patients diagnosed with heart failure die within the first year. In the UK, heart failure accounts for approximately 2% of all NHS inpatient bed-days and 5% of all emergency medical admissions to the hospital.

The primary goals of the management of heart failure are to improve patients' life expectancy and enhance quality of life. Current strategies include pharmacological management, implantation of devices, and surgical treatment, as well as management of any co-morbid conditions.

Current pharmacological treatment for chronic heart failure due to left ventricular systolic dysfunction includes a number of options. NICE clinical guideline 108 ('Chronic heart failure') recommends that that all patients be considered for first-line treatment with beta-blockers and an angiotensin-converting enzyme (ACE) inhibitor unless contraindicated or not tolerated. Aldosterone antagonists, angiotensin-II receptor antagonists, or hydralazine in combination with nitrate are recommended for second-line use in people who remain symptomatic despite first-line treatment. Angiotensin-II receptor antagonists are alternatively recommended for first-line use for patients in whom ACE inhibitors are not tolerated. Coronary resynchronisation (NICE technology appraisal 120, 'Cardiac resynchronisation therapy for the treatment of heart failure') and cardiac transplantation are options for severe symptoms unmanageable by pharmacological treatment.

### The technology

Ivabradine (Procoralan, Servier Laboratories) is a sino-atrial modulator with bradycardiac activity. It selectively inhibits inward sodium and potassium ion cardiac current, slowing the onset of the next action potential and therefore the next heart beat. It is administered orally.

Ivabradine does not have a UK marketing authorisation for the treatment of chronic heart failure. It has been studied in clinical trials, in comparison with placebo, in adults with symptomatic chronic heart failure, and left ventricular systolic dysfunction. Ivabradine is intended as an adjunct to current therapies.

<b>Intervention(s)</b>	Ivabradine
<b>Population(s)</b>	Adults with chronic heart failure due to left ventricular systolic dysfunction
<b>Comparators</b>	Standard treatment without ivabradine
<b>Outcomes</b>	The outcome measures to be considered include: <ul style="list-style-type: none"> <li>• cardiovascular mortality</li> <li>• all-cause mortality</li> <li>• hospitalisation due to heart failure</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life</li> </ul>

<b>Economic analysis</b>	<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>
<b>Other considerations</b>	<p>Guidance will only be issued in accordance with the marketing authorisation.</p>
<b>Related NICE recommendations</b>	<p>Related Technology Appraisals:</p> <p>Technology Appraisal No. 120, May 2007, 'Cardiac resynchronisation therapy for the treatment of heart failure', Review Date Jul 2010.</p> <p>Technology Appraisal in Preparation, 'Review of NICE Technology Appraisal Guidance No. 95; Implantable cardioverter defibrillators (ICDs) for the treatment of arrhythmias and No. 120; Cardiac resynchronisation therapy (CRT) for the treatment of heart failure'. Earliest anticipated date of publication TBC.</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'.</p>

### Questions for consultation

In what population is ivabradine expected to be used?

At what point in the pathway of care is ivabradine expected to be used?

What are the most appropriate comparators for ivabradine for the treatment of chronic heart failure?

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

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the

assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology 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 the technology 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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology\\_appraisal\\_process\\_guides.jsp](http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp))