NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Dronedarone for atrial fibrillation and atrial flutter

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost-effectiveness of dronedarone within its licensed indication for the treatment of atrial fibrillation and atrial flutter.

Background

Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia. Atrial flutter is a closely related atrial arrhythmia. The heart rate, while tachycardic in both, is regular in flutter and irregular with fibrillation. While the two arrhythmias have differing underlying mechanisms, they are the result of similar disease processes, lead to similar symptoms and complications and require the same approach with medication. Both atrial fibrillation and flutter are caused by various cardiac and non-cardiac diseases, are common after cardiac surgery and can change from one to the other. Symptoms include breathlessness, palpitations, syncope/dizziness and chest discomfort. Both arrhythmias are associated with an increased risk of thrombus formation and thromboembolism including ischaemic strokes. AF can be classed as paroxysmal, persistent or permanent according to how long it lasts or whether it can be terminated by an intervention.

The prevalence of AF increases with age with a prevalence of 0.5% at age 50-59 years increasing to almost 9% at age 80-89 years. In the UK, more than 46,000 new cases of AF are diagnosed each year. Atrial flutter is much less common than AF and the exact prevalence in the UK is not known. The incidence of atrial flutter is estimated at approximately 88 per 100,000 population per year in the USA.

Management of AF and atrial flutter depends on the type of AF, the presence of concomitant/precipitating conditions, whether a rate-control or rhythm-control strategy is chosen and patient characteristics (age, symptoms, activity levels). In addition anti-coagulation is required depending on the risk of thromboembolism. Commonly used drugs for rate-control include beta-blockers, calcium-channel blockers or digoxin. Electrophysiological or surgical interventions are also an option.

The technology

Dronedarone (Multaq, Sanofi Aventis) is a multi-channel antagonist (potassium, sodium, and calcium channel blocker with anti-adrenergic properties) and is chemically related to amiodarone. Completed clinical trials have compared dronedarone to placebo in AF and there are ongoing clinical trials comparing dronedarone with amiodarone in people with AF.

Intervention(s)	Dronedarone
Population(s)	People with persistent atrial fibrillation or atrial flutter in whom a rhythm-control strategy is preferred and • who have structural heart disease and for whom a standard beta-blocker is ineffective, contraindicated or not tolerated • who do not have structural heart disease and for whom other antiarrhythmic drugs (standard beta-blockers, Class Ic agents, sotalol) are ineffective, contraindicated or not tolerated People with paroxysmal atrial fibrillation or atrial flutter who are symptomatic and • who have no structural heart disease and for whom symptomatic suppression is not achieved with standard beta blockers, Class Ic agents or sotalol • who have coronary artery disease and for whom symptomatic suppression is not achieved with standard beta-blockers or sotalol • who have poor ventricular function and for whom standard beta-blockers do not adequately suppress paroxysms.
Standard comparators	• Amiodarone
Outcomes	The outcome measures to be considered include: • time to recurrence of AF/atrial flutter • symptoms related to AF/atrial flutter • 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	Details of the components of best supportive care should be clearly described. Guidance will only be issued in accordance with the marketing authorisation
Related NICE recommendations	Related Guidelines: Clinical Guideline CG36, June 2006, 'Atrial fibrillation: national clinical guideline for management in primary and secondary care' Related Interventional Procedures: Interventional Procedure Guidance 168, April 2006, 'Percutaneous radiofrequency ablation for atrial fibrillation'

Questions for consultation

Is the patient population, defined according to the NICE clinical guideline for AF (CG36),

a) the population that would be considered for treatment with dronedarone in routine clinical practice?

b) the same population defined in the clinical trials with regard to the nomenclature for atrial fibrillation?

c) the same population as that for atrial flutter?

Would an improved side-effect profile lead to dronedarone replacing other anti-arrhythmic agents used earlier in the treatment pathway?

Has the most appropriate comparator for dronedarone in the treatment of atrial fibrillation and atrial flutter been included in the scope?

a) Are the comparators for atrial fibrillation the same as for flutter?

b) Should non-pharmacological interventions be included as comparators, if so which interventions should be included?

Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately (for example, people with congestive cardiac failure, people with structural heart disease, or those intolerant of amiodarone)?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

Which process would be the most suitable for appraising this technology, the single technology or multiple technology process? (Information on these

processes is available at
http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)