NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Dronedarone for atrial fibrillation and atrial flutter

Final scope

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. Both atrial fibrillation and flutter are caused by various cardiac and non-cardiac diseases, are common after cardiac surgery. 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 flutterL 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.

Atrial flutter is often amenable to ablation which may be considered in the first instance. Atrial flutter which cannot be managed by ablation is managed in the same manner as AF. Management of AF depends on the type, the presence of concomitant/precipitating conditions, whether a rate-control or rhythm-control strategy is chosen and patient characteristics (age, symptoms, activity levels).

Standard baseline therapy for AF may include drugs to maintain sinus rhythm, where beta-blockers are usually the first choice. Where standard baseline therapy with a beta-blocker is ineffective, contraindicated or not tolerated, second line therapy is chosen according to various factors including whether the person has structural heart abnormalities. Either flecainide or sotalol may be chosen if there are no structural abnormalites and amiodarone may be used in people with structural heart disease. Standard baseline therapy also includes antithrombotic therapy where the risk of thromboembolism is considered high enough to warrant it and provided that there are no contraindications. (see NICE Clinical Guideline 36)

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. CHMP opinion on dronedarone is expected in Q3 2009.

Intervention(s)	Dronedarone
Population(s)	People with either a recent history of, or current paroxysmal or persistent atrial fibrillation or atrial flutter, who are currently receiving standard baseline treatment, with or without beta blockers
Standard comparators	As a first line treatment or as an adjunct to standard baseline therapy, dronedarone will be compared with • standard baseline therapy with or without beta blockers As a second line therapy, dronedarone will be compared to the following drugs according to their indications • Class 1c anti arrhythmic agents (flecainide) • sotalol • amiodarone
Outcomes	The outcome measures to be considered include: • time to recurrence of atrial fibrillation/atrial flutter • symptoms related to atrial fibrillation/atrial flutter • stroke • 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 If data are available the following subgroups will be considered • based on cardiovascular risk • people with atrial flutter
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'