NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Dabigatran etexilate for the prevention of stroke in atrial fibrillation

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost-effectiveness of dabigatran etexilate within its licensed indication for the prevention of stroke in people with atrial fibrillation.

Background

Atrial fibrillation (AF) is the most common atrial tachyarrhythmia and its main characteristic is an erratic and rapid heartbeat. AF leads to deterioration in the mechanical function of the atria and prevents complete expulsion of blood. Stasis of blood in the atria predisposes to thrombus (blood clot) formation and leads to an increased risk of systemic thromboembolism and stroke.

Annually, between 94,000 and 117,000 people experience a stroke episode in England and Wales. More than 20% of these strokes are a complication of AF. Stroke accounts for 11% of deaths in England. It has been estimated that 10% of patients will die within 30 days after experiencing an acute ischaemic episode. Stroke is also the leading cause of adult disability. Nearly 50% of the survivors of an acute ishaemic episode will suffer from mild or severe disabilities persisting beyond six months. Depending on the area of the brain that has been damaged a patient can experience speech and language problems and/or orientation, movement and memory problems.

AF is an independent risk factor for stroke. Additional risk factors for stroke in AF are: age, sex, diabetes mellitus, hypertension, prior cardiovascular events (myocardial infarction, stroke, transient ischaemic attacks (TIA)). The risk of experiencing AF increases with age: 0.5% at age 50-59, to nearly 9% at age 80-89. There is a 30-43% risk of a recurrent stroke within five years after the first stroke.

The risk of stroke in people with AF can be reduced with antithrombotic treatment. The choice of antithrombotic treatment in any individual is based on a balance of the benefits of treatment in terms of a reduction in the risk of stroke and other thromboembolic events versus the increased risk of bleeding associated with anticoagulation or anti-platelet therapy. NICE clinical guideline for the management of atrial fibrillation (36), recommends that people with AF at high risk of stroke should receive anticoagulation with warfarin. In people with AF at low risk of stroke, such as those under the age of 65 years with no other risk factors, the balance may not be in favour of anticoagulation and treatment with aspirin may be preferred. Likewise, anticoagulation may be inadvisable in people with AF at high risk of bleeding.

The technology

Dabigatran etexilate (Pradaxa, Boehringer Ingelheim) is an orally administrated prodrug. It is converted to dabigatran after administration. Dabigatran inhibits the formation of the thrombin enzyme. Thrombin converts fibrinogen into fibrin during the coagulation cascade and is the primary component of thrombus (blood clots). Dabigatran etexilate does not require anticoagulation monitoring.

Dabigatran etexilate is not currently licensed for the prevention of stroke in AF in the UK. It has been studied in clinical trials compared with warfarin in patients with trial fibrillation for the prevention of stroke and systemic embolism. Dabigatran etexilate holds a UK marketing authorisation for the primary prevention of venous thromboembolic events for adults who have undergone total hip and knee replacement surgery.

Intervention(s)	Dabigatran etexilate
Population(s)	People with atrial fibrillation
Comparators	People at high risk of stroke/systemic embolism: • Warfarin People at moderate risk of stroke/systemic embolism or intolerant of warfarin therapy • Antiplatelet therapy such as aspirin
Outcomes	The outcome measures to be considered include: • stroke • non-central nervous system embolism • myocardial infarction • mortality • adverse effects of treatment including haemorrhage • 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	If evidence allows, the following sub-groups should be considered : • people who have had a prior stroke /TIA episode • people who cannot receive anticoagulation therapy • people at increased risk of haemorrhage
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal in development. Dronedarone within its licensed indication for the treatment of atrial fibrillation and atrial flutter (expected date TBC). Related Guidelines: Clinical guideline No. 36, June 2006, The management of Atrial Fibrillation. Expected review date in June 2010.

Questions for consultation

Could clopidogrel plus aspirin combination be considered as an appropriate comparator?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other 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?

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?

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)