NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation

Final scope

Remit/appraisal objective

To appraise the clinical and cost-effectiveness of dabigatran etexilate within its licensed indication for the prevention of stroke and systemic embolism 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 antiplatelet therapy. NICE clinical guideline 36 for the management of atrial fibrillation 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 administered prodrug (a drug that is administered in an inactive or less active form) which is converted to dabigatran after administration. Dabigatran is an anticoagulant that 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 and systemic embolism in AF in the UK. It has been studied in clinical trials compared to warfarin for the prevention of stroke and systemic embolism in patients with AF who are at moderate to high risk of stroke or systemic embolism. Dabigatran etexilate holds a UK marketing authorisation for the primary prevention of venous thromboembolic events in adults who have undergone total hip and knee replacement surgery.

Intervention(s)	Dabigatran etexilate
Population(s)	People with AF who are at moderate to high risk of stroke or systemic embolism
Comparators	• Warfarin In people for whom warfarin is unsuitable: • Antiplatelet agents (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 subgroup should be considered: • people who have not been previously treated with warfarin. Consideration should be given to the potential advantage of dabigatran in terms of its lower requirement for therapeutic monitoring. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal in preparation. Dronedarone for the treatment of atrial fibrillation. Expected date of issue June 2010. Technology Appraisal in preparation. Clopidogrel in combination with aspirin for the prevention of vascular events in people with atrial fibrillation. Expected date of issue: tbc. Related Guidelines: Clinical guideline No. 36, June 2006, The management of Atrial Fibrillation. Review date June 2011.