NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Apixaban for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of apixaban within its licensed indication for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation with one or more risk factors for stroke or systemic embolism.

Background

Atrial fibrillation is the most common heart rhythm disturbance and its main characteristic is an erratic and rapid heartbeat. It leads to deterioration in the mechanical function of the atria and prevents complete expulsion of blood. The blood in the atria becomes stagnant which can lead to blood clot formation. These clots can travel throughout the body and cause systemic embolism if they become stuck in an artery and block blood flow. If a blood clot travels to the brain, it can cause a stroke.

Annually in England and Wales, 130,000 people experience a stroke episode and there are 60,000 deaths from stroke. More than 20% of these strokes are attributed to atrial fibrillation. Approximately a third of people who have a stroke are likely to die within the first ten days, about a third are likely to make a recovery within one month and about a third are likely to be left with disabilities needing rehabilitation. Stroke is the leading cause of adult disability. 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.

Stroke is more common in women, older people and people with atrial fibrillation, diabetes mellitus, hypertension and prior cardiovascular events (myocardial infarction, stroke, transient ischaemic attacks). There is a 30-43% risk of a recurrent stroke within five years after the first stroke.

The risk of stroke in people with atrial fibrillation can be reduced with antithrombotic treatment. The choice of antithrombotic treatment is based on a balance between the benefits of treatment (reduction in the risk of stroke and other thromboembolic events) and 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 atrial fibrillation at high risk of stroke should receive anticoagulation with warfarin. In people with atrial fibrillation at low risk of stroke, such as those under the age of 65 years with no other risk factors, treatment with aspirin

may be preferred. Additionally, NICE technology appraisal 249 recommends dabigatran etexilate, and technology appraisal 256 recommends rivaroxaban as alternative treatment options for people with non-valvular atrial fibrillation with one or more risk factors for stroke or systemic embolism. Anticoagulation may be inadvisable in people with atrial fibrillation at high risk of bleeding.

The technology

Apixaban (Eliquis, Bristol-Myers Squibb and Pfizer) is a direct oral factor Xa inhibitor, which prevents the formation of thrombin and fibrin, the key components in blood clot formation.

Apixaban does not currently have a UK marketing authorisation for the prevention of stroke associated with atrial fibrillation. It is being studied in clinical trials for the prevention of stroke and systemic embolism compared with warfarin and aspirin in adults with atrial fibrillation.

Intervention(s)	Apixaban
Population(s)	Adults with non-valvular atrial fibrillation who are at risk of stroke or systemic embolism.
Comparators	• Warfarin (in people for whom warfarin is suitable) • Dabigatran etexilate • Rivaroxaban
Outcomes	The outcome measures to be considered include: • stroke • non-CNS systemic embolism • myocardial infarction • mortality • transient ischaemic attacks • 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, consideration will be given to subgroups defined by • INR time in therapeutic range (TTR) on warfarin • patients with different level of stroke/ thrombo-embolic risks Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No 249, March 2012, 'Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation'. Technology Appraisal No 256, May 2012, 'Rivaroxaban for the prevention of stroke in atrial fibrillation'. Related Guidelines: Clinical Guideline No. 36, June 2006, 'The management of atrial fibrillation'. Related Interventional Procedures: Interventional Procedures Guidance No. 349, June 2010, 'Percutaneous occlusion of the left atrial appendage in non-valvular atrial fibrillation for the prevention of thromboembolism'. Interventional Procedures Guidance No. 400, June 2011 'Thoracoscopic exclusion of the left atrial appendage (with or without surgical ablation) for non-valvular atrial fibrillation for the prevention of thromboembolism'.