NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

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

Draft scope (Pre-referral)

Draft 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 atrial fibrillation.

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. 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 atrial fibrillation who are at moderate to high risk of stroke or systemic embolism.
Comparators	• Warfarin • Dabigatran (subject to NICE guidance) • Rivaroxaban (subject to NICE guidance) In people for whom warfarin is unsuitable: • Antiplatelet agents • Dabigatran (subject to NICE guidance) • Rivaroxaban (subject to NICE guidance)
Outcomes	The outcome measures to be considered include: • stroke • systemic 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	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal in Preparation, 'Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation'. Expected date of publication December 2011. Technology Appraisal in Preparation, 'Rivaroxaban for the prevention of stroke in atrial fibrillation'. Earliest anticipated date of publication TBC. 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 in Preparation, 'Thoracoscopic exclusion of the left atrial appendage in atrial fibrillation (with or without other cardiac surgery) for the prevention of thromboembolism'. Earliest anticipated date of publication TBC.

Questions for consultation

Is it appropriate for the scope population to be defined as 'adults with atrial fibrillation who are at moderate to high risk of stroke or systemic embolism'? If so, how should 'moderate to high risk' be defined?

Have the most appropriate comparators for the prevention of stroke in atrial fibrillation been included in the scope?

- Are the comparators listed routinely used in clinical practice?
- Which antiplatelet agents are predominantly used?

Are there any other subgroups of people in whom apixaban is expected to be more clinically effective and cost effective or other groups that should be

examined separately, such as people who have not been previously treated with warfarin?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits

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)