NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

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

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of rivaroxaban within its licensed indication for the prevention of stroke and non-central nervous system (CNS) systemic embolism in people with non-valvular 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, if they travel to the brain, they can cause a stroke.

Annually in England and Wales, 130,000 people experience a stroke episode and there are 60,000 deaths due to 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. In people with atrial fibrillation a stroke is associated with greater mortality, morbidity and longer hospital stays than in those without atrial fibrillation.

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). The annual risk of stroke is five to six times greater in people with atrial fibrillation than in people with normal heart rhythm. 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 should be 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 atrial fibrillation at high risk of stroke should receive anticoagulation with

warfarin. People with atrial fibrillation at a moderate risk of stroke can be considered for anticoagulation with warfarin or prescribed aspirin, with the decision made on an individual basis. 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

Rivaroxaban (Xarelto, Bayer HealthCare) is an anticoagulant which acts by direct inhibition of activated factor X (factor Xa). Factor Xa is a key component in the formation of blood clots. It is administered orally.

Rivaroxaban does not currently have a UK marketing authorisation for the prevention of stroke and systemic embolism in atrial fibrillation. It is being studied in clinical trials compared with warfarin in adults with non-valvular atrial fibrillation who are moderate to high risk of stroke and non-CNS systemic embolism.

Intervention(s)	Rivaroxaban
Population(s)	Adults with non-valvular atrial fibrillation who are at moderate to high risk of stroke and non-CNS systemic embolism
Comparators	• Warfarin • Dabigatran[1] In people for whom warfarin is unsuitable • Antiplatelet agents • Dabigatran[1]
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

[1] subject to ongoing NICE technology appraisal

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 subgroups should be considered: • people who have not been previously treated with warfarin Consideration should be given to the potential advantage of rivaroxaban in terms for its lower requirement for therapeutic monitoring and its fewer drugs interactions compared with warfarin. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 197, Aug 2010. 'Dronedarone for the treatment of atrial fibrillation.' Review date Mar 2013. Technology Appraisal in preparation. 'Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation.' Expected date of publication Dec 2011. Related Guidelines: Clinical guideline No. 36, June 2006, 'The management of Atrial Fibrillation.' Review date June 2011.