NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Edoxaban tosylate for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of edoxaban tosylate within its licensed indication for preventing stroke and 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 heartbeat that is often abnormally fast. 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.

Atrial fibrillation affects about 2.0% of the population in England. Men are more commonly affected than women and the prevalence increases with age. The risk of stroke in people with atrial fibrillation is 5 times higher than in people with a normal heart rhythm. In the UK, about 12,500 strokes a year are attributed to atrial fibrillation. Depending on the area of the brain that has been damaged, people who survive a stroke may experience problems with communication, cognition, movement, vision, fatigue, anxiety, and/or depression. In people with atrial fibrillation, a stroke is associated with greater mortality and morbidity than in those without atrial fibrillation.

The risk of stroke and systemic embolism in people with atrial fibrillation can be reduced with anticoagulation treatment. The choice of anticoagulant 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. NICE clinical guideline 180 on the management of atrial fibrillation recommends that people with non-valvular atrial fibrillation with 1 or more risk factors for stroke or systemic embolism should be offered anticoagulation with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist (such as warfarin). Anticoagulation may be inadvisable in people with atrial fibrillation at high risk of bleeding.

The technology

Edoxaban tosylate (brand name unknown, Daiichi Sankyo) is an anticoagulant that acts by direct inhibition of activated factor X (factor Xa). Factor Xa is a key component in the formation of blood clots. Edoxaban tosylate is administered orally.

Edoxaban tosylate does not currently have a UK marketing authorisation for preventing stroke and systemic embolism in people with atrial fibrillation. Clinical trials have compared edoxaban tosylate with warfarin in adults with non-valvular atrial fibrillation who are at moderate to high risk of stroke (with a $CHADS_2$ score of 2 or above).

Intervention(s)	Edoxaban tosylate
Population(s)	Adults with non-valvular atrial fibrillation who are at risk of stroke or systemic embolism
Comparators	• Warfarin • Apixaban • Dabigatran etexilate • Rivaroxaban
Outcomes	The outcome measures to be considered include: • stroke • systemic embolism • myocardial infarction • transient ischaemic attacks • 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, consideration will be given to subgroups defined by: • time in therapeutic range on warfarin. • level of stroke/thromboembolic risk. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 275, Feb. 2013, 'Apixaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation.' Review proposal date Oct. 2014, to be considered alongside Technology Appraisals 256 and 249. Technology Appraisal No. 256, May 2012, 'Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation.' Review proposal date Oct. 2014. Technology Appraisal No. 249, Mar. 2012, 'Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation.' Review proposal date Oct. 2014. Related Guidelines: Clinical Guideline No. 180, June 2014, 'Atrial fibrillation: the management of atrial fibrillation.' Review proposal date to be confirmed. Related NICE Pathways: NICE Pathway, Stroke: http://pathways.nice.org.uk/pathways/stroke NICE Pathway, Atrial fibrillation: http://pathways.nice.org.uk/pathways/atrial-fibrillation/
Related National Policy	Specialised Services Commissioning policy, Adult specialist cardiac services (section 8): http://www.england.nhs.uk/wp-content/uploads/2012/12/pss-manual.pdf