NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

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

Draft scope (pre-referral)

Draft 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 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.

Atrial fibrillation affects about 1.3% of the population in England and Wales. 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 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. This Guideline is being updated. NICE technology appraisal 249 recommends dabigatran etexilate, technology appraisal 256 recommends rivaroxaban, and technology appraisal 275 recommends apixaban as treatment options for people with non-valvular atrial fibrillation with 1 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

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 are comparing edoxaban tosylate with warfarin in adults with non-valvular atrial fibrillation who are at moderate to high risk ($CHAD_2 \geq 2$) of stroke.

Intervention(s)	Edoxaban tosylate
Population(s)	Adults with non-valvular atrial fibrillation who are at risk of stroke or systemic embolism
Comparators	• Apixaban • Dabigatran etexilate • Rivaroxaban • Warfarin (in people for whom warfarin is suitable)
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.
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. 36, June 2006, 'Management of atrial fibrillation.' Currently being updated. Earliest anticipated date of publication June 2014. Related NICE Pathways: NICE Pathway: Stroke, created May 2011: http://pathways.nice.org.uk/pathways/stroke
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

Questions for consultation

Have all relevant comparators for edoxaban tosylate been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation?

- Should vitamin K antagonists be included as a comparator?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which edoxaban tosylate will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

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.

In October 2014, NICE will conduct a review proposal for technology appraisals 275, 256 and 249 (apixaban, rivaroxaban and dabigatran etexilate, respectively). The review proposal will consider whether a multiple technology appraisal should be undertaken to update the guidance on these technologies for the prevention of stroke and systemic embolism in atrial fibrillation. If a multiple technology appraisal takes place, would it be preferable to also include edoxaban tosylate, noting that guidance on this technology would be delayed, compared to if it was considered as a single technology appraisal?

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)