NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

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

Thank you for agreeing to make a submission on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your submission, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name:
Name of your organisation: Clinical Leaders of Thrombosis
Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?

- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?

- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc)?

  Education Secretary, Clinical Leaders of Thrombosis

- other? (please specify)

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

There are local variations in the ease of access to anticoagulant testing with warfarin/sinthrome which is the existing alternative for patients with AF. The most significant disadvantage to the current treatment is the requirement for frequent monitoring.

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

Patients who are poorly controlled on warfarin may benefit from treatment with Edoxaban. However if the poor control is due to non-compliance, this may be a problem as Edoxaban is not routinely monitored which could result in these patients being at risk of stroke.

Patients who have difficulty with regular blood tests would also benefit from Edoxaban.

Patients with poor renal fuction should be identified as unsuitable for treatement with edoxaban.

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

The treatment could be used in Primary or Secondary care. There may be a requirement for monitoring patients renal function at intervals. No additional professional input beyond that already in place for anticoagulant monitoring would be anticipated.

New laboratory assays may be required for monitoring plasma drug levels.

A protocol for the management of patients with bleeding whilst on edoxaban would be required in each area where the drug was used, similar to those being trialled for rivaroxaban.

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

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Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

Edoxaban would be easier to use than Vitamin K antagonists for both patients and healthcare professionals as it does not require monitoring and dose adjustment. Once-daily dosing is an advantage.

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

Edoxaban should not be administered without a full assessment of the patient's renal function. An education session with a healthcare professional regarding the use of the drug prior to starting therapy would be advisable.

Patients will require regular checks for renal function, particularly the older age groups >75 yrs.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

In the published trials, it appears that Edoxaban is non-inferior to well-controlled warfarin for the prevention of stroke.

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

The lack of an effective proven antidote is a matter of concern in the event of bleeding or emergency surgery. In addition, the lack of a specific assay for the drug

readily available in routine laboratories is an issue which may cause problems under these circumstances.

Increased rates of gastro-intestinal bleeding reported in the trials may be a concern.

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

Anticoagulant trained healthcare professionals would be well placed to offer advice on the use of edoxaban. Staff would require education and training in appropriate use of the drug. No other additional facilities would be needed.

A new laboratory assay for drug levels would need to be developed and implemented in case of overdosage.

Equality

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 this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/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 lead to recommendations that 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.

No issues.