NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism

Thank you for agreeing to give us a statement on your 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 statement, 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: [redacted]

Name of your organisation Derriford Hospital

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.)?
- 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?

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?

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)?

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?

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.

Current treatment with Warfarin, LMWH or Rivaroxaban generally.
I am led to believe there is a geographical variation in practice with some areas allowed to use Rivaroxaban liberally and others not so.
Yes there is a difference in opinion between professionals about which drug to use and when.
Current alternatives as above:
Warfarin requires a period of LMWH for immediate anticoagulant effect until the INR is in the therapeutic range. Not the case for Apixaban or Rivaroxaban. The use of LMWH either at the start of anticoagulation or throughout, is painful for patients and more expensive and sometimes logistically difficult to administer, especially at the start of treatment.

Cancer patients may have a different prognosis, partly because of the underlying cancer but are also more prone to bleeding. Patients with APS have a significantly greater thrombotic risk and it is not clear how many of these were in the trials.

Apixaban could be used in primary or secondary or specialist clinics. Our current experience with rivaroxaban, demonstrates the feasibility of this. No need for increased staffing. If anything less input from HCPs as no need to monitor or teach to give injections.

Apixaban is not currently available for use but Rivaroxaban is a very similar drug and is readily available and very easy to use. No clinical guidelines that currently include

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apixaban for VTE treatment, but again, there are a number of local guidelines that include rivaroxaban.

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?

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.

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?

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?

There is little doubt that Apixaban will be easier to use than the currently used LMWH +/- Warfarin (or other vitamin K antagonist, VKAs). Our experience with Rivaroxaban has provided the evidence for making such a statement. There are concerns however, that patients do need to be carefully counselled about the relative differences between the treatment options, together with the fact that Rivaroxaban and Apixaban cannot be reversed. By comparison with Apixaban, there is no requirement to monitor as the pharmacokinetics are far more predictable. Also, when a VTE event is suspected, there may well be a delay in access to radiological investigation. Apixaban is very much easier to organise as an anticoagulant until the scan has proven or otherwise the event in question, particularly in primary care.

To my knowledge the main rules to be adhered to when commencing apixaban:

1) Ensure GFR is >30 ml/min (says 15 ml/min in licence but we adopt more cautious stance locally for rivaroxaban).

2) Check renal function regularly if GFR close to 30ml/min.

3) Ensure LFTs are not significantly deranged.

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4) Ensure patient is not already taking an anticoagulant as one would with any anticoagulant. Acknowledge increased bleeding risk if using apixaban in association with antiplatelet drugs and NSAIDs.

5) Inform patient to watch out for evidence of bruising, bleeding etc

As with any trial, they are performed in a select group of patients who do not have the spectrum of comorbidities present in the general public. Therefore, there is likely to be an increased bleeding risk in some patients over those in the trials, although the trials demonstrated significantly less bleeding than warfarin. As far as possible, the trial can be extrapolated to a UK setting. The most important outcomes are prevention of recurrent VTE, which was significantly better than warfarin in the trial. The other very important outcome is the safety, in particular the bleeding risk, which as already stated, was significantly better than warfarin. No surrogate outcome measures were used in trial.

I am not aware of any reproducible side effects of apixaban which are evident from is use in patients with stroke currently.

Equality and Diversity

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

The only people obviously ruled out from using this drug from my experience locally with rivaroxaban, would be those with GFR's <30ml/min and ALT >3 ULN.
Also, I would not use apixaban on people who are being considered to switch because they are poorly compliant with warfarin. The significantly shorter half-life of apixaban means that poor compliance would suggest even worse anticoagulation concerns.

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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.

I know of no such evidence.
I do have some anecdotal evidence from the use of rivaroxaban which is a very similar drug. I have concerns that junior hospital doctors in particular are unaware of the nature of these drugs, such that they may give a more traditional drug together with them. Also they tend not to understand that rivaroxaban does not need monitoring or that it will increase both PT & APTT.

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)?

Generally, the introduction of apixaban should be easier than rivaroxaban as the latter has ‘paved the way’. It should be very much easier to use apixaban than LMWH +/- VKA, acknowledging the absence of an injectable anticoagulant to commence anticoagulation and the lack of monitoring needs.
There are some concerns about introducing a new drug after the relative experience with the previous options but this should be readily overcome.
I believe that patients should be properly counselled about the relative benefits or otherwise of using the various anticoagulant options and this will become increasing difficult, particularly in busy GP clinics. It may be that secondary care clinics are a better option for the introduction of anticoagulation for VTE in the months to come, which may have resource implications.

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