NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Rivaroxaban for the treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism

Thank you for agreeing to give us a statement 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 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:

Name of your organisation RCPath, BSH

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? **Yes**
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? **Yes**
- 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.)? **Yes**
- 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?

Standard treatment at present is immediate therapy with a LMWH overlapping with VKA (warfarin) until the INR is therapeutic. VKA are then continued for (usually) three months. At this point a decision regarding long term anticoagulation or not, is made. There are high level evidence based guidelines from the BCSH and the ACCP which are in broad agreement and practice is relatively uniform. Many patients with DVT and some with PE can be treated as an outpatient with this regimen. There is less certainty regarding the safety of outpatient treatment for PE.
The advantages of this therapy are:
No transition from one anticoagulant to another.
Oral therapy throughout
No monitoring of anticoagulation required.

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?

Acute
The answer to this question is largely defined by the trial populations. The CHMP is slightly unclear as to whether Rivaroxaban should be used for primary treatment of PE. Patients with symptomatic PE were excluded from the EINSTEIN trial. This was discussed at the scoping exercise.
At present, patients with cancer and thrombosis are treated with continuation of LMWH and not converted to warfarin. Although some patients in EINSTEIN had cancer, there is no evidence that this should be changed for Rivaroxaban.
Long term
Patients with a definite indication for long term anticoagulation were not studied in the extension study.

The technology is likely to be of particular benefit for those with limited mobility, multiple co-morbidities and medications, irregular dietary intake and poor INR control.

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 diagnosis of DVT and PE are most likely to be made in hospital and it is here that treatment would be initiated. Initiation of long term therapy is also likely to be in hospital following consultant advice. However, in both cases the continued prescription will be in primary care.
Overall, with no need for monitoring, the technology is likely to reduce the amount of ancillary and supportive care required (eg: clinics for monitoring, home visits to take samples for monitoring).

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?

Not currently available for this indication. Off label use is rare. Use for licensed indications is still relatively limited.

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.

There are no guidelines relating to the use of Rivaroxaban for VTE.

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?

In general, Rivaroxaban will be easier to use because it does not require monitoring, is given orally and has few drug or diet interactions. Overall, many fewer blood tests will be required. However, the appropriate blood tests to detect the presence of Rivaroxaban (eg prior to surgery) are not yet defined. These are currently in development. There is limited understanding of how, or if, Rivaroxaban anticoagulation can be reversed in an emergency: whereas the approach to reversal of warfarin anticoagulation is well established.

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.

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Current protocols for these indications are well established for heparin and warfarin. They are based on a considerable amount of data describing the efficacy or warfarin and the associated haemorrhagic risks. If Rivaroxaban's therapeutic index is better, then these potocols will require revision and the number of patients who will benefit from receiving long term anticoagulation may rise.
Patients with high risk of recurrence of VTE and who would benefit from long term anticoagulation are currently identified on largely clinical grounds and it is unlikely that new tests would be needed.

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?

The key outcomes are recurrence, mortaility (efficacy) and bleeding (safety). These were addressed in the trials. Although there were several exclusions, the population base otherwise reflected UK practice. An important factor in the comparison is the quality of INR control in the in control group. This was 58% and many patients in the UK achieve better control than this.
The long term extension trial studied anticoagulation of a group who would not normally be anticoagulated.

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?

Side effects were not a major or significant problem. Rivaroxaban is likely to have less impact on lifestyle than warfarin does.

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.

None

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)?

There is unlikely to be a need for additional physical resource in terms of staff or facilities. The costs of Rivaroxaban itself are likely to be more than warfarin.

Equality

Are there any issues that require special attention in light of the NICE's duties to have due regard to the need to eliminate unlawful discrimination and promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others?

No