Professional organisation statement template

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: [redacted]

Name of your organisation: Royal College of Pathologist and BSH/BCSH

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)

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 is a large amount of trial data and guidelines from several organisations (including NICE) to direct anticoagulation in patients with atrial fibrillation (AF). For the group at highest risk of stroke, current standard therapy is anticoagulation with the orally administered anticoagulant, warfarin. There is generally little disagreement about this. The only practical alternative for this group is aspirin but it is less effective in preventing stroke. The principal disadvantage of warfarin is its narrow therapeutic index, numerous interactions with other drugs and diet and the requirement for regular monitoring by blood test (INR) with consequent dose adjustment. All anticoagulant therapies are associated with an increased risk of bleeding but this is accepted as being outweighed by the benefit in preventing stroke.

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?

It is possible to identify subgroups of patients with AF who have different risk of stroke (eg using the CHADS2 score) and different risk of bleeding. Warfarin anticoagulation is given at the same intensity for all patients who require oral anticoagulation. The results of the major trial of this technology (Dabigatran) suggested that it may be possible to treat different groups or patients with different characteristics, differently.

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)?

Historically, anticoagulant therapy was monitored primarily in hospital clinics although the warfarin prescription was written in primary care. In recent years an increasing proportion of anticoagulant monitoring has been performed in primary care. Introduction of this technology is likely also to be predominantly in primary care and to reduce further the number of patients treated in hospital. Because routine monitoring is not required, there should be no additional costs. It is possible that the number of medical and allied workers required to deliver anticoagulation therapy to this group will decrease.

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?

At present this technology is only licensed for prophylaxis of venous thromboembolism in patients undergoing hip or knee replacement. I'm not aware of any use outside this indication.

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.

Clinical Guidelines for anticoagulation in AF are available from:
American College of Chest Physicians (ACCP)
British Committee for Standards in Haematology (BCSH)
NICE
Scottish Intercollegiate Guidelines Network (SIGN) guideline 36 section 3
(An updated version of the SIGN guideline on antithrombotic therapy does allude to the use of dabigatran in AF. This guideline will be published in autumn 2010).

American Heart Association/ American College of Cardiologists (AHA/ACC)

None of these guidelines include evidence regarding Dabigatran, the subject of this appraisal. The evidence base in the BCSH guideline is graded 'Ia' and the recommendation level A. In the ACCP guideline most of the recommendations are graded level 1A or 1B. The NICE guideline makes a level A recommendation for the use of warfarin anticoagulation. Overall, therefore, the evidence base and the recommendations for anticoagulation therapy using currently available therapies are very strong.

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?

Dabigatran offers the advantage of effective anticoagulation without the need for monitoring and with considerably less potential for interactions with other drugs and with dietary components. The lack of monitoring should make it much easier to administer than the current standard therapy using warfarin and should also make it more acceptable to patients.

In general the patient study group in the RE-LY trial is close to the groups for whom anticoagulation is recommended in the various guidelines. The availability of Dabigatran, particularly if both dose regimens are licensed, may alter the balance of risks and benefits for the 'moderate risk' group in the NICE algorithm (Fig 11.1 of that guideline) in which the physician is invited to 'consider aspirin or anticoagulation'. The two dose regimens may allow better balancing of thromboembolic and haemorrhagic risks for subgroups or for individual patients.

The potential for accumulation in patients with renal impairment is a disadvantage that is not present with current therapy with warfarin or aspirin.
In the RE-LY trial there was a greater drop-out rate amongst patients taking Dabigatran which may be related to the higher incidence of dyspeptic symptoms in those groups. (A result of the tartaric acid in the formulation to assist absorption). This may make Dabigatran unsuitable for some patients. It is possible the twice daily regimen as opposed to once daily for warfarin also contributed.

There is the potential for significant drug interactions with amiodarone and other P-glycoprotein inhibitors but the implications for safety are likely on to emerge after license.

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)?

If NICE approves this technology there will be a reduction in the number of people needing to attend anticoagulation clinics (either at hospital or in primary care). However because there are many other indications for oral anticoagulation and because Dabigatran may not be suitable for all patients with AF, it will not be possible to close these clinics. The savings are therefore likely to be only at the rate of the marginal cost.