Healthcare professional group/clinical specialist statement

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: Dr Nicholas Brooks

Name of your organisation (if applicable): British Cardiovascular Society

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)

Consultant cardiologist and President of the British Cardiovascular Society

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.

Smoking cessation occurs both in primary and in secondary care. It is usually (when designed as a service rather than developing ad. Hoc.) run by trained councillors with a nursing background with subsequent prescription of nicotine replacement therapy and/or buproprion made by general practitioners or hospital doctors appropriate to the base of service. The main pharmacological support used is with nicotine replacement therapy (NRT). To maximise effect, this should always be given with supportive counselling as part of a holistic service, and this applies to varenicline as well.

The major disadvantage to all current therapies is their lack of success in the general population long term and the high relapse rates. Varenicline appears to be more effective (22 – 23% continuous smoking cessation rates) than placebo (8 – 10% continuous smoking cessation rates) and buproprion (15 – 16% continuous smoking cessation rates) but has not been compared directly with NRT alone nor with NRT plus buproprion. The pharmacology of varenicline suggests that using it in conjunction with NRT will not be effective.

Research has shown that patients with a new onset of a smoking related illness are likely to achieve higher smoking cessation rates than the normal population, with long term cessation rates of up to 70% in acute myocardial infarction. Unfortunately none of the current pharmacological adjuvants have been trialled in acute myocardial infarction and only NRT has been shown to be safe in chronic stable angina. In addition, only NRT has any evidence of safety in pregnancy and breast feeding and even here some individual products are contra-indicated. Varenicline has not been tested in this area and has a class C classification in pregnancy and breast feeding. Therefore more research with all currently available products is required as this is a particularly targeted area in smoking cessation.

Varenicline can be used in both primary and secondary care settings in the context of current smoking cessation services with full counselling and support from trained professionals. No absolute guidelines for its use are currently available, but it has

got approval already from both the FDA in the United States of America and the European Commission.

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?

Varenicline in three phase 3 trials has clearly shown that it is superior to placebo in smoking cessation and probably superior to buproprion (significant in one trial (1), trend towards in a second (2) – the third was different in nature (3)). It also offers an entirely new class of drug (4), providing clinicians and patients who have previously failed in smoking cessation attempts a valuable alternative to current therapies. With the current set up of services it will be relatively easy to use, although ease of use will remain greatest with NRT, which is available 'over the counter'. It should only be used in conjunction with smoking cessation counselling and professional support.

Additional research needs to be undertaken in pregnancy and breast feeding, stable and unstable coronary artery disease and chronic obstructive pulmonary disease as these groups were all excluded in the clinical trials.

Provided that varenicline is instituted through current smoking cessation services with full counselling, the trials reasonably represent clinical practice. It should not be prescribed as a stand alone therapy, as its efficacy is not proven. However the outcome of continuous smoking cessation at 52 weeks with exhaled carbon monoxide measurement was adequately measured and proven in the three phase 3 trials.

The most common side effect of varenicline is that of nausea, which was reported by 30% of participants. This was generally mild to moderate and only caused 3% of patients to discontinue treatment prematurely. 10% also had abnormal dreams. Other side effects were similarly common in either placebo or buproprion groups (or

both) and can probably be attributed to nicotine withdrawal. All groups put on a similar amount of weight.

Overall, and provided that varenicline is used within full smoking cessation services (i.e. with proper support and counselling) it will be a valuable addition to current available therapies.

References:

1 Efficacy of varenicline, an a4b2 nicotinic acetylcholine receptor partial agonist, versus placebo or sustained release buproprion for smoking cessation. Jorenby DE, Hays JT, Rigotti NA et al. JAMA July 5, 2006 Vol 296;1:56-63

2 Varenicline, an a4b2 nicotinic acetylcholine receptor partial agonist, versus sustained release buproprion and placebo for smoking cessation. Gonzales D, Rennard SI, Nides M et al. JAMA July 5, 2006 Vol 296;1:47-55

3 Effect of maintenance therapy with varenicline on smoking cessation. Tonstad S, Tonnesen P, Hajek P et al. JAMA July 5, 2006 Vol 296;1:64-71

4 Varenicline: An a4b2 nicotinic receptor partial agonist for smoking cessation. Coe JW, Brooks PR, Vetelino MG et al J. Med. Chem. 2005;48:3474-3477

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 not readily available, although many more references were assessed in making this judgement.

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)?

As smoking cessation services in both primary and secondary care have already been established, it should be fairly straightforward to implement the introduction of varenicline with no additional resources required beyond the cost of the drug itself. This is approximately £160 for a full 12 week course as used in the clinical trials (1,2). The numbers needed to treat to gain one additional ex-smoker at one year over placebo are approximately 9 and over buproprion are approximately 14. As 50% of smokers die of a smoking related disease then in the healthy population studied, 19 patients would require varenicline versus placebo to prevent one smoking related death and 29 versus buproprion. This is a cost per life saved of £3,040 versus placebo and therefore indicates that varenicline is likely to be very cost effective.