Clinical Specialist 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: Dr Clive Mulatero

Name of your organisation: Royal College of Physicians

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 – member of the National Cancer Research Institute Lung Cancer Studies Group

- other? (please specify)

Appendix D – Clinical specialist statement template

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.

It would be fair to say that in the UK there remains wide variation in opinion regarding the value of maintenance therapy in advanced Non-Small Cell Lung Cancer (NSCLC). However it is increasingly accepted that those who receive a second line of therapy for NSCLC fare better than those who do not.

Presently less than 10 percent of NSCLC patients in the UK receive second line therapy. If we are to effect a significant improvement in outcomes for these lung cancer patients where the majority present with advanced disease (~25,000 each year) it is important that we improve on this situation.

There are a number of factors that contribute to the low take up rate for second line treatment:

1. Some patients are too unwell at diagnosis to receive any systemic treatment.

2. A number of patients will progress on first line therapy and be too unwell to be offered second line treatment.

3. Some patients who have benefited from first line therapy will be too unwell when their relapse is diagnosed to receive second line treatment.

Improving the first of these categories would rely heavily upon improving patient awareness and speeding up the diagnostic pathway. The second relies upon developing new treatments that would improve response rates. Both of these remain long term goals and are beyond the scope of this appraisal.

There remains scope however to make an impact upon the outcomes in NSCLC by improving the percentage of patients who, having benefited from first line treatment, are offered a second line whilst well enough to tolerate it. This technology appraisal relates directly to this issue.

In the UK NSCLC patients are commonly reviewed at intervals of between 6 and 12 weeks after completing first line treatment. Unfortunately the current reality is that the majority of patients will show evidence of progression of their disease within 12 weeks of completing first line therapy. Many patients are therefore already too unwell to receive a second line of therapy when they are reviewed at their next outpatient appointment.

This situation could be improved in at least two ways:

a. By an increase the frequency of follow up in order to detect relapses sooner whilst the patients are still fit.

b. Through the offer the treatment immediately after first line chemotherapy has been completed.

Given that the average patient relapses within 12 weeks of completion of their first line therapy it is a somewhat arbitrary whether this is referred to as 'maintenance' or 'early second line' therapy.

Offering erlotinib as maintenance therapy would therefore almost certainly improve the uptake of treatment and hence be likely to improve the outcome for the group as a whole.

The patients most likely to benefit from EGFR inhibitors such as erlotinib have an acquired mutation in the EGFR gene. It is estimated that in Western populations around 12 % of NSCLC patients have such a mutation. If these patients receive an EGFR inhibitor their mean duration of response is around 8 months with a tail of patients who do significantly better. This is bourne out by the fact that in the Saturn study there was a 10 % difference in overall survival bewtween placebo and erlotinib groups at 36 months. It may therefore be argued that a major benefit of offering erlotinib as maintenance therapy would be that patients with EGFR mutations would be more likely to receive the drug before they became too unwell to do so. Of course there are also some patients without an EGFR mutation who would also benefit. These facts are in line with the observation that in the Saturn study the disease control rate (those who had completeresponse, partial response or stable disease) at 12 weeks from completion of first line therapy copmpared to placebo was increased by 13.4 %, from 27.4 % to 40.8 % - slightly higher than the number of patients who would be expected to have an EGFR mutation.

Erlotinib is already prescribed as second line therapy for NSCLC according to the NICE FAD of September 2008.

Erlotinib will continue to be prescribed by oncologists in the hospital setting.

Implementation of this policy would not require any additonal allied health professional input.

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?

Erlotinib is already available as second line treatment for NSCLC and so there would be no practical implications for the introduction of this technology.

Cost effective stopping rules for the use of erlotinib involve comparing a baseline CT scan and CXR with a CXR performed after one month of therapy (to detect those with obvious progression in the face of the drug) and a CT scan at two months. Patients continue therapy if they have achieved CR, PR or SD. Patients are then generally assessed by CT scan at 3 monthly intervals thereafter.

Use of erlotinib as maintenance therapy would preclude the need for a CT baseline scan as the end of treatment CT scan could be used for this purpose.

The Saturn study reflects UK practice reasonably and a number of UK centres including my own at the time recruited to this study.

The side effect profile of erlotinib is well established. It is unlikely that new significant and common side effects will come to light, as it is already in widespread clinical use internationally.

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 would be no significant implementation issues for this technology that would make provision within 3 months of publication of guidance an issue.

The only extra resource that would be required for this technology relates to an increase in outpatient visits for patients on treatment and an increase in the the number of imaging investigations that would be needed in this group.