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; NCRI Breast Group, JCCO, RCR, ACP and RCP

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.)?

- **X** other? (please specify)

Registrar, Royal College of Physicians

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?

The technology relates to the treatment of HER2+ advanced breast cancer that has progressed despite or following previous chemotherapy with trastuzumab. Current standard practice is to give further palliative chemotherapy alone.

The role of continuation of trastuzumab with chemotherapy on progression as an alternative to the technology under review is unknown. Despite the lack of evidence, many clinicians continue trastuzumab beyond progression and simply change the chemotherapy. This variation in practice is base on clinical opinion and availability of funding to continue trastuzumab; the latter varies around the country.

Current alternatives are thus chemotherapy agents alone including oral treatment with capecitabine or similar chemotherapy plus continuation of trastuzumab . Introduction of the new technology would standardise the approach to this clinical situation in an evidence-based manner.

Lapatinib is an oral agent and is thus easier to administer than trastuzumab. The risk of cardiotoxicity may also be less although this is the subject of ongoing research. Lapatinib may also be active against metastatic disease in the brain, a site that is `"protected" from the effects of other agents including trastuzumab due to the blood-brain barrier.

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?

This technology is only relevant for patients with HER2 + disease (i.e. 3+ on IHC testing or evidence of gene amplification on FISH testing of tumour tissue; see NICE evidence reviews on trastuzumab). Such patients generally have aggressive disease with a high incidence of visceral disease. The prognosis is typically short and measurable in months.

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)?

Advanced metastatic breast cancer managed by oncologists in dedicated oncology facilities with specific expertise in breast cancer. Minimal additional professional input over and above standard chemotherapy and supportive care. Regular checks on cardiac function are recommended by echocardiography (ECHO) or radionuclide (MUGA) scans.

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 routinely available although a named patient compassionate use programme supervised by GSK is in progress in some cancer centres.

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.

No specific clinical guidelines exist. Specialists are aware of the findings of the registration study and would propose to use lapatinib as in the trial. Use of single agent lapatinib or in combination with other chemotherapy agents may need to be considered. Individual cancer networks are currently developing their own guidelines.

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?

The technology will offer an evidence based effective palliative treatment to women with far advanced breast cancer and provide on average a few extra months of disease control.

The technology is simple to administer and side effects relatively mild. There are some restrictions on concomitant medications that can be administered with lapatinib because of its metabolism within the liver.

The technology will only be suitable for (as for trastuzumab) women with adequate cardiac function as defined by estimation of left ventricular ejection fraction (LVEF) by appropriate imaging techniques.

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.

The technology should be started alongside chemotherapy following progression of metastatic breast cancer on trastuzumab. It should be discontinued at the next episode of progression. Response should be monitored at least 3 monthly and cardiac function monitored at regular intervals.

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?

The phase III evidence base revolves around a single well conducted trial of capecitabine +/- lapatinib (Geyer et al NEJM 2006 355:2733-43). Capecitabine is a NICE recommended treatment for patients with advanced breast cancer and is widely used and thus the technology is entirely consistent with UK practice.

The most important outcome measures are time to progression (TTP), survival, toxicity and symptom control. Time to progression was the primary endpoint and some assessment of the other endpoints have been made. Any positive impact on survival was inevitably diminished by crossover to lapatinib on progression. This occurred in a significant proportion of patients following a recommendation by the trial DMSB and in light of the positive findings within the trial.

TTP is an accepted robust outcome in advanced cancer, and a good surrogate for survival. Central radiological review enhances the confidence in the results.

Adverse events from lapatinib were generally mild and predominantly limited to skin changes and diarrhoea. The vast majority of patients would find that the potential benefits of lapatinib considerably outweigh any increase in toxicity.

No new important toxicities have come to light. Careful assessment of effects of lapatinib on cardiac function continue and monitoring of LVEF will be recommended. However, early indications suggest that cardiotoxicity is very rare and probably even less frequently encountered than with trastuzumab.

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.

Not aware of any important new data to emerge since the Geyer et al publication in NEJM that are of direct relevance.

Abstract publications of single agent lapatinib, use in brain metastases and use in combination with other agents are emerging

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)?

Minimal additional resources required over and above those already required for delivery of chemotherapy and trastuzumab. Education needs regarding this new compound are relatively straightforward as this is a generally well tolerated oral medication that should be restricted to specialist oncology clinics.