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:

Submitted by [redacted] on behalf of:

Name of your organisation

NCRI/RCP/RCR/ACP/JCCO

Comments coordinated by [redacted]

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?

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.

Oestrogen receptor positive metastatic breast cancer is largely treated with endocrine therapies. However when these have failed chemotherapy is sometimes used.

There is no significant geographical variation in current practice.

On the whole non-steroidal aromatase inhibitors such as letrozole and anastrazole are used as first-line therapy followed by steroidal aromastase inhibitor exemestane on progression. Tamoxifen is used less than previously. It is sometimes used in the adjuvant setting and occasionally as second or third-line endocrine therapy. The optimal sequencing of these endocrine therapies has not been defined and there is some variation in current practice. There is also some variation as to at what stage chemotherapy is used rather then second, third or fourth-line endocrine therapy.

Alternatives to faslodex include other endocrine therapies, such as the non-steroidal aromatase inhibitors anastrozole and letrozole, the steroidal aromatase inhibitor exemestane as well as anti-oestrogen tamoxifen and progestogens such as megace. A further alternative is chemotherapy. The main advantage of the other endocrine therapies over faslodex is that they are orally administered and also cheaper. Chemotherapy is usually administered intravenously, although oral options are available for some of the drugs. On the whole, chemotherapy has more side effects than endocrine therapy, including faslodex.

Patients with visceral metastasis (such as lung and liver metastasis) have a poorer prognosis and those with bone metastasis or soft tissue relapse have a better outcome. Patients with a long disease-free time since their diagnosis and adjuvant therapy have a better outcome as do patients with strongly hormone receptor positive tumours. No sub-groups will be put at risk by faslodex. It is the drugs given

by deep intramuscular injection that those with abnormalities of clotting may experience large haematoma, but this is easily prevented by measurement of a simple blood test prior to commencement of treatment.

Faslodex is initiated by a consultant oncologist or surgeon. It is administered by deep intramuscular injection monthly and this is done either in the hospital setting or in primary care by a district nurse.

There is currently a variation across the NHS in the use of faslodex. In the absence of NICE approval some of us and PCTs approve it for any patient while in other cases it is approved for selected patients.

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?

The alternatives to faslodex or other endocrine treatments including non-steroidal aromatase inhibitors anastrozole and letrozole and if used as first-line endocrine therapy, or the steroidal aromatase inhibitor exemestane if used as seond-line endocrine therapy, on progression on a non-steroidal aromatase inhibitor. The aromatase inhibitors are oral medications and are self-administered by patients while faslodex is given by deep intramuscular injection requiring this to be given by a trained nurse. However, patients do not find this particularly troublesome and district nurses can easily be trained to give this injection. The fact that the treatment is given intramuscularly insures high compliance rate. It is known that the compliance rate with oral aromatase inhibitors is of the order of 70-80%, hence reducing their efficacy in clinical practice.

Initiation of treatment is on disease progression on other endocrine therapy and the treatment with faslodex should be discontinued on disease progression. Assessment

of response is done as current practice either by clinical or radiological assessment as is appropriate for the individual patient.

There are very few side effect of faslodex, these largely being a local discomfort at the site of injection. They do not affect patient's quality of life and for patients is a readily acceptable treatment. No adverse effects have come to light during subsequent routine clinical practice that were not apparent from the clinical trials.

Faslodex has been tested in a variety of studies. The initial studies compared it with with tamoxifen while subsequent studies compared it with non-steroidal aromatase inhibitor anastrozole or with the steroidal aromatase inhibitor exemestane. The dose used in most studies has been 250mg by deep i.m. injection every month. However, the licence has recently been changed to a high dose of 500mg which has been shown to be superior to 250mg in the CONFIRM study. The settings in which faslodex has been tested reflect the conditions in UK current practice.

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.

The major studies that have been done with faslodex are as follows:

1. First-line metastatic breast cancer double-blind trial of faslodex at a dose of 250mg versus tamoxifen, found to be equivalent.
2. The FIRST trial compared faslodex at a high dose of 500mg once a month versus anastrozole in first-line setting, this was an open-label study. Increased time of progression in favour of faslodex was seen with equal overall response rates and clinical benefit.
3. The FACT trial compared 250mg faslodex and anastrozole versus anastrozole in the first-line metastatic breast cancer setting. In this trial time to progression overall response rates were equivalent.
4. EFECT trial faslodex 250mg compared with exemestane in the second-line setting after failure of a non-steroidal aromatase inhibitor and found to be equivalent.
5. In the CONFIRM trial two doses of faslodex were compared 500mg with 250mg. This was a first-line study and the high dose was found to be superior in terms of progression-free survival and also a trend towards improved overall survival.
6. SOFEA trial has recently closed having recruited 600 patients progressed on anastrozole or letrozole and were randomised to either faslodex versus faslodex plus anastrozole versus exemestane. The result of this study which has completed accrual are awaited with interest and probably will be available within a year.

It is our opinion that the above trials have all been very well conducted with no inherent biases.

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 faslodex delivery of this to patients it will be straightforward requiring only minimal extra education and training for NHS staff. No additional resources will be required in terms of facilities or equipment.