NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Erlotinib for the first-line treatment of EGFR-TK mutation positive non-small-cell lung cancer

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] **submitting on behalf of:**

Name of your organisation

NCRI/RCP/RCR/ACP/JCCO

Statement 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)

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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.

Patients with advanced NSCLC and proven EGFR mutation are currently treated with gefitinib as per TA192. Combination pemetrexed and cisplatin chemotherapy (as per TA181) are not appropriate comparators as these are not generally given for patients with proven EGFR mutation over gefitinib.

The clinical data that underpin gefitinib (TA192) have already been reviewed by the committee. Efficacy and toxicity of the technology (erlotinib) is largely based on 2 randomized phase 3 trials, in which patients were randomized between erlotinib and platinum-doublet chemotherapy (OPTIMAL and EURTAC). The primary endpoint of both of these trials was progression-free survival superiority for Erlotinib versus chemotherapy, and in both trials, this was met.

EURTAC represents the only clinical trials-based evidence on patients from a largely Caucasian background. OPTIMAL was a trial run in China, and the randomized phase 3 trials of gefitinib versus platinum based chemotherapy were all based on Far Eastern datasets.

There have been no head-to-head trials between gefitinib and erlotinib, as yet. Therefore it is impossible to make direct comparisons. However cross-trial comparisons indicate similar efficacy between the two agents:

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Median progression-free survival (PFS) for erlotinib or gefitinib in published trials, in months

	ERLOTINIB		GEFITINIB		
TRIAL	OPTIMAL	EURTAC	IPASS	NEJ002	WJTOG3405
PFS	13.1	9.7	9.5	10.8	9.2

In addition, toxicities reported with both gefitinib and erlotinib are broadly similar.

The technology should be used under oncology supervision in the secondary care setting

Erlotinib is recognized alongside gefitinib as a treatment option for its licensed indication according to ESMO 2011 advanced lung cancer clinical guidelines.

The ASCO provisional clinical opinion (April 2011) on EGFR mutation testing for patients with advanced NSCLC considering 1st line EGFR tyrosine kinase inhibitor therapy discusses the use of either gefitinib or erlotinib. This clinical opinion was published prior to presentation of the EURTAC data.

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?

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Erlotinib is associated with typical toxicities of its class: skin rash and diarrhoea. These toxicities are similar to that observed with gefitinib, and as there are not head-to-head trials between the two agents it is difficult to draw meaningful conclusions between cross trial comparisons of the two agents.

Compared with platinum-doublet chemotherapy, the toxicities of erlotinib are mild, and quality of life significantly improved. The OPTIMAL trial has demonstrated improved quality of life for Erlotinib over chemotherapy. Erlotinib is also advantageous in that it is a simple tablet administered as an outpatient compared with chemotherapy requiring day-case / overnight admission and management of toxicities that may require inpatient care. When compared with gefitinib, the different strengths of erlotinib available make dose modification simple. By contrast for gefitinib, only a single strength tablet is available limiting dose modification to reducing dosing frequency. However, for both Erloltinib and gefitinib, a need for dose modification is uncommon.

The EURTAC and OPTIMAL trials were reflective of UK practice at the time the trials were accruing. However, since then, gefitinib has become standard of care for patients with advanced NSCLC and EGFR mutation. There are no robust head-to-head trial data between gefitinib and erlotinib, and cross trial comparisons demonstrate similar efficacy and toxicity. The EURTAC and OPTIMAL trials used progression-free survival as primary endpoint and these are appropriate.

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.

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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)?

This technology would not change existing arrangements for EGFR genotyping and the identification of patients with EGFR mutation. No further training would be required.

Equality

Are there any issues that require special attention in light of the NICE's duties to have due regard to the need to eliminate unlawful discrimination and promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others?

No