Appendix G - professional organisation submission template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Ceritinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer [ID729]

Thank you for agreeing to make a submission 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 submission, 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/RCP/RCR/ACP/British Thoracic Oncology Group

Comments coordinated by: x[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.

EML4 Alk translocation lung cancer is a very small subset of adenocarcinomas of the lung representing 4-5% proportionally. These patients tend to be younger and non-smokers. This gene alteration is the driver for the lung cancer and therefore specific Alk inhibitors are the treatment of choice. This is supported by accruing clinical trials data (ASCEND 1 Shaw et al. NEJM 2014). The prognosis with Alk inhibitors is almost double compared to non-mutated patients treated with chemotherapy. These patients are likely to survive long enough and be well enough to receive second or third line treatments.

Ceritinib is the second of the Alk inhibitors, crizotinib being the first to show efficacy in ALK mutated lung cancers. Currently these adenocarcinomas are treated with a platinum doublet chemotherapy in the EU as crizotinib is pending EMA license and has been shown superior to chemotherapy (for progression-free survival) from a randomized phase 3 trial. This has been shown already in studies and real life audits with EGFR mutated lung cancers which are more common and we have more experience in treating. Overall survival differences are unlikely to be demonstrated in trials as all these patients will at some point receive Alk inhibitors.

The place of ceritinib is really following crizotinib resistance, which is inevitable in these advanced cancers. In the phase 1 trial (ASCEND1) median progression free survival (PFS) for all 246 NSCLC patients was 9 months. Crizotinib used 1st line has shown superiority over chemotherapy (PROFILE

1015) and soon will be used in the 1st line setting for Alk positive NSCLC, pending EMA license. This will change the pathway for these patients again, with a real need for 2nd line treatment. Bearing in mind these patients had all had at least one line of chemotherapy before and were all advanced lung cancer patients. The clinical trial testing Ceritinib in third line setting compared to chemotherapy (ASCEND 5) is almost complete and is likely to report in the near future. Again crossover of treatments mean that an overall survival difference is unlikely to be seen in this group of patients.

These ALK mutated patients are quite rare and present in advanced setting, but tend to be younger, nonsmokers. They do tend to survive to second and third line treatments. Ceritinib has been particularly useful in patients with brain metastases with useful clinical efficacy in controlling symptoms. A specific study for patients with CNS disease in planned with ceritinib.

Treatment:
Platinum doublet chemotherapy, crizotinib, ceritinib

With emerging data the paradigm is likely to change to first line treatment with Alk inhibitors. Giving rise to a real need for second generation targeted treatments.

Safety: From the clinical trial data and my own experience in the studies, the main toxicities encountered are common but very tolerable. These are diarrhoea (86% of patients), nausea (82%) and vomiting (61%). The most serious toxicity is of pneumonitis (3%) but there were no treatment related deaths in the studies. This has to be clearly communicated to the clinicians prescribing this drug as in real life pneumonitis is likely to be higher and may be misdiagnosed as infection or disease progression.

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.

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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?

As above

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.

Implementation issues

The NHS is required by the Department of Health 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 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)?

Alk testing is funded in many but not all Centres so delivery of treatment may be affected

Equality
NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could lead to recommendations that have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Currently Ceritinib is available through clinical trial following crizotinib use or in the first line study for ALK positive lung cancers. As ceritinib has an EMA license, the compassionate use programme is likely to be discontinued once drug becomes available commercially. This is a rare subset of a common disease and access for UK patients will be through NICE/NHS or interim cancer

drugs fund like in the case of crizotinib. It was disappointing that crizotinib use was not approved by NICE. Both crizotinib and ceritinib are very effective in this group and are likely to save money by avoiding futile chemotherapy and supportive therapies which would be the alternatives. There is experience of this in real life data and from clinical trials.