NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Brigatinib for treating ALK-positive advanced non-small-cell lung cancer after crizotinib

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of brigatinib within its marketing authorisation for treating advanced ALK-positive non-small-cell lung cancer after treatment with crizotinib.

Background

Lung cancer falls into two main histological categories: non-small-cell lung cancers (NSCLC), which account for 88% of all lung cancers[1], and small-cell lung cancers. NSCLC may be grouped by tumour histology into squamous cell carcinoma, adenocarcinoma and large-cell carcinoma, with the latter 2 being collectively referred to as 'non-squamous' lung cancer.

Anaplastic lymphoma kinase (ALK) fusion genes are chromosomal alterations that occur between the tyrosine kinase portion of the ALK gene and other genes. They are believed to be involved in the growth of tumours. ALK translocation can occur in NSCLC of any histology, although it is thought to be most common in tumours with adenocarcinoma histology (that is, non-squamous histology) and is uncommon in tumours with squamous cell carcinoma histology.[2] People with NSCLC who have an ALK fusion gene are unlikely to have epidermal growth factor receptor (EGFR) mutations. Accordingly, people with the ALK fusion gene do not usually receive drugs that inhibit EGFR tyrosine kinase, such as erlotinib, gefitinib and afatinib.

Most lung cancers are diagnosed at an advanced stage, when the cancer has spread to lymph nodes and other organs in the chest (locally advanced disease; stage III) or to other parts of the body (metastatic disease; stage IV). In 2015, approximately 33,000 people were diagnosed with NSCLC in England.[3] Approximately 5% of people with stage III or IV NSCLC have ALK fusion genes, equating to around 1650 people in England.[4]

For the majority of people with NSCLC, the aims of treatment are to prolong survival and improve quality of life. Treatment choices are influenced by the presence of biological markers (such as mutations in EGFR-TK, ALK or PD-L1 status, histology (squamous or non-squamous) and previous treatment experience. NICE technology appraisal guidance 395 recommends ceritinib as a treatment option for treating advanced anaplastic lymphoma kinase positive non‑small‑cell lung cancer in adults who have previously had crizotinib.

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The technology

Brigatinib (Alunbrig, Takeda UK) is an anti-neoplastic agent. Brigatinib acts as an ALK antagonist, EGFR antagonist and ROS1 inhibitor. It is administered orally.

Brigatinib does not currently have a marketing authorisation in the UK for treating ALK-positive advanced non-small-cell lung cancer. A randomised phase II study is currently evaluating the efficacy and safety of two different dosing regimens of brigatinib in adults with advanced ALK+ NSCLC whose disease has progressed after treatment with crizotinib.

Intervention(s)	Brigatinib
Population(s)	People with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib
Comparators	• ceritinib
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.

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Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account. The use of brigatinib is conditional on ALK+ status. The economic modelling should include the costs associated with diagnostic testing for ALK status in people with advanced non-small-cell lung cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Ceritinib for previously treated anaplastic lymphoma kinase positive non-small-cell lung cancer' 2016. NICE technology appraisal guidance 395. Review date: TBC. Related Guidelines: Lung cancer: diagnosis and management (2011) NICE guidelines CG121. Reviewed 2016, next review January 2019. Related Quality Standards: Quality standard for lung cancer. (2012) NICE Quality Standard 17. Reviewed 2016, next review August 2017. Related NICE Pathways: Lung cancer (2017) NICE

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Related National Policy	**National Service Frameworks** Cancer **Department of Health** Department of Health (2013) NHS Outcomes Framework 2014–2015 Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf **NHS England** NHS England (2014) Manual for Prescribed Specialised Services 2013/14. Chapter 105: Specialist cancer services (adults) http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf

Questions for consultation

Have all relevant comparators for brigatinib been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for the treatment of ALK+ NSCLC after crizotinib?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom brigatinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider brigatinib will fit into the existing NICE pathway, Lung cancer?

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 the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which brigatinib will be licensed;

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- 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 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.

Do you consider brigatinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of brigatinib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

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- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Royal College of Physicians (2017) National Lung Cancer Audit Report 2016 (for the audit period 2015). Accessed October 2017

2. Scagliotti G, Stahel RA, Rosell R et al. (2012) ALK translocation and crizotinib in non-small cell lung cancer: An evolving paradigm in oncology drug development. European Journal of Cancer 48: 961-973

3. Office for National Statistics (May 2017) Cancer Statistics Registrations, England: 2015. Accessed October 2017

4. Cancer Research UK (2014) Biological therapy for lung cancer. Accessed October 2017

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