NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

AZD9291 for previously treated locally advanced or metastatic, EGFR and T790M mutation positive non-small-cell lung cancer

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of AZD9291within its marketing authorisation for previously treated locally advanced or metastatic, EGFR and T790M mutation positive non-small-cell lung cancer.

Background

Lung cancer falls into two main histological categories: around 85–90% are non-small-cell lung cancers (NSCLC) and the remainder are small-cell lung cancers. The majority of 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). People with NSCLC can be either epidermal growth factor receptor (EGFR)-positive or EGFR-negative and those with EGFR-positive disease can receive EGFR tyrosine kinase inhibitor (EGFR-TKI) treatment. A mutation can occur at the 790 position of the EGFR, T790M, causing resistance to EGFR-TKI treatment. The T790M mutation accounts for approximately 50% of EGFR-TKI resistance[1].

In 2013, approximately 26,800 people were diagnosed with NSCLC in England, of whom 23% had stage III and 46% had stage IV disease[2]. Lung cancer caused 28,000 deaths in England in 2012[3]. The median survival with lung cancer (all stages) is approximately 6 months; 35% of people with lung cancer, and 14% of people with stage IV disease, survive for more than 1 year[3,4].

Afatinib, erlotinib and gefitinib are recommended as options for people who test positive for the EGFR-TK mutation and who have not previously received treatment (NICE technology appraisal guidance 310, 258 and 192). Erlotinib is also recommended as a second-line treatment option for patients with NSCLC (NICE technology appraisal guidance 162). NICE clinical guideline 121 ‘Lung cancer’ recommends that people with stage III or IV NSCLC and good performance status should be offered chemotherapy to improve survival, disease control and quality of life. The guideline states that docetaxel monotherapy should be considered, if second-line treatment is appropriate,

[1] NIHR Horizon Scanning Centre briefing note
[2] Cancer Research, Biological therapy for lung cancer. Accessed May 2015
[3] Health and Social Care Information Centre (2014) National Lung Cancer Audit: 2013 patient cohort. Accessed June 2015.
[4] Cancer Research UK (2014) Lung cancer statistics. Accessed June 2015

for patients with locally advanced or metastatic NSCLC in whom relapse has occurred.

The technology

AZD9291 (brand name unknown, AstraZeneca) is a small molecule inhibitor that targets the sensitising and T790M mutant forms of the EGFR-TK. It is administered orally.

AZD9291 does not currently have a marketing authorisation in the UK for treating metastatic, EGFR and T790M mutation positive NSCLC after EGFR-TKI therapy. It is currently being studied in a trial comparing AZD9291 with platinum-based doublet chemotherapy (pemetrexed plus carboplatin or pemetrexed plus cisplatin) in adults with EGFR-TKI previously treated EGFR and T790M mutation positive NSCLC.

Intervention(s)	AZD9291
Population(s)	People with locally advanced or metastatic, EGFR and T790M mutation positive non-small-cell lung cancer that has progressed after treatment with an EGFR tyrosine kinase inhibitor
Comparators	• Docetaxel monotherapy • Platinum therapy (in combination with gemcitabine, vinorelbine, pemetrexed or a taxane) • Nintedanib in combination with docetaxel • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.
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 should be taken into account. The use of AZD9291 is conditional on the presence of the T790M mutation in the EGFR gene. The economic modelling should include the costs associated with diagnostic testing for T790M mutations in people with 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: 'Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer' (2014) NICE Technology Appraisal 310. Review date April 2017 'Erlotinib for the treatment of non-small-cell lung cancer' (2008) NICE Technology Appraisal 162. Currently undergoing review 'Nintedanib for treating previously treated metastatic non-small cell lung cancer' (2015) NICE Technology Appraisal 347. Review date July 2018 'Pemetrexed for the first-line treatment of non-small-cell lung cancer' (2009) NICE Technology Appraisal 181. Guidance on static list Appraisals in development (including suspended appraisals): Suspended appraisal. 'Afatinib for the treatment of locally advanced or metastatic non-small cell lung cancer after previous platinum containing chemotherapy and gefitinib or erlotinib' NICE Technology Appraisal [ID357]. Publication date TBC Related Guidelines:

	The diagnosis and treatment of lung cancer (2011). NICE guideline. Review date June 2015. Related Quality Standards: Quality standard for lung cancer. (2012). NICE Quality Standard No. 17 http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: NICE Pathway: Lung cancer. Pathway created: Mar 2012. http://pathways.nice.org.uk/pathways/lung-cancer
Related National Policy	NHS England, Manual for prescribed specialised services, service 105: specialist cancer services (adults), Jan 2014. http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf 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 Department of Health (2013) Improving outcomes: a strategy for cancer, 3rd annual report Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf

Questions for consultation

Have all relevant comparators for AZD9291 been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for locally advanced or metastatic EGFR mutation positive non-small-cell lung cancer?
- In current clinical practice, is a second EGFR-TK inhibitor given to patients whose disease has progressed despite treatment with a first EGFR TKI therapy? If so, which treatments are given?
- How should best supportive care be defined?

Have all relevant outcomes been included in the scope?

Are there any subgroups of people in whom AZD9291 is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider AZD9291 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 AZD9291will 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 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 AZD9291 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 AZD9291 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.

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)