NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Dacomitinib for untreated EGFR-positive non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dacomitinib within its marketing authorisation for treating epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer that has not previously been treated.

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. NSCLC can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma. 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).

In 2015, around 33,000 people were estimated to be diagnosed with NSCLC in England.[1,2] Around 12% have stage IIIA, 9% had stage IIIB and 53% had stage IV disease[1]. The prognosis for people with non-small-cell lung cancer is generally poor. Between 2011 and 2015 around 39% of people with lung cancer survived for 1 year or longer and only 15% survived for 5 years or longer.[2]

For the majority of people with NSCLC, the aims of therapy are to prolong survival and improve quality of life. Treatment choices may be influenced by the presence of biological markers (such as the checkpoint inhibitor programmed death-ligand 1 [PD-L1] and mutations in epidermal growth factor receptor-tyrosine kinase [EGFR-TK] or anaplastic-lymphoma-kinase [ALK], or), histology (squamous or non-squamous) and previous treatment experience.

For people whose locally advanced or metastatic disease tests positive for the activating EGFR-TK mutation and who have not previously had treatment, NICE guidance recommends the tyrosine kinase inhibitors (TKI) afatinib, erlotinib and gefitinib as treatment options (NICE technology appraisal guidance 310, 258 and 192 respectively).

The technology

Dacomitinib (brand name unknown, Pfizer) is a highly selective inhibitor of the human epidermal growth factor receptor (EGFR) family of tyrosine kinases. It specifically and irreversibly binds to and inhibits multiple EGFR subtypes, resulting in inhibition of proliferation and induction of cell death in NSCLC tumours with activating EGFR mutations. Dacomitinib is administered orally.

Dacomitinib does not currently have a marketing authorisation in the UK for untreated EGFR-positive NSCLC. It has been studied in clinical trials compared with gefitinib in patients with pathologically confirmed NSCLC with EGFR-activating mutations (exon 19 deletion or the L858R mutation in exon 21) with no prior treatment with systematic therapy for NSCLC.

Intervention(s)	Dacomitinib
Population(s)	People with untreated locally advanced or metastatic NSCLC with EGFR activating mutation(s)
Comparators	• Afatinib • Erlotinib • Gefitinib
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • response duration • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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 dacomitinib is conditional on the presence of EGFR mutation status. The economic modelling should include the costs associated with diagnostic testing for EGFR mutation in people with NSCLC 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. 'Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer' (2012) NICE Technology Appraisal 258. Guidance on static list. 'Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer' (2010) NICE Technology Appraisal 192.

	Terminated appraisals: 'Bevacizumab for treating EGFR mutation-positive non-small-cell lung cancer' (terminated appraisal) (2017) NICE Technology Appraisal 436 **Appraisals in development (including suspended appraisals):** 'Osimertinib for untreated EGFR-positive non-small-cell lung cancer' NICE technology appraisals guidance [ID1302]. Publication expected December 2018. **Related Guidelines:** Lung Cancer: The diagnosis and treatment of lung cancer (2011). NICE guideline 121. Review ongoing. **Guidelines in development:** 'Lung cancer: diagnosis and management (update)'. Publication expected March 2019. **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: March 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 2015-2016, Dec 2014. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) Improving outcomes: a strategy for cancer, 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2011) Cancer commissioning services

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for untreated locally advanced or metastatic NSCLC with EGFR activating mutations?

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

Are the outcomes listed appropriate?

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

Where do you consider dacomitinib 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 dacomitinib 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 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 dacomitinib 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 dacomitinib 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?
- 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 National lung cancer audit 2016 (2017). Royal college of Physicians. Accessed October 2017.

2 Cancer survival in England: adult, stage at diagnosis and childhood-patients followed up to 2016 (2017) Office for National Statistics. Accessed October 2017