NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Nivolumab for previously treated locally advanced or metastatic non-small-cell lung cancer

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for previously treated locally advanced or metastatic 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. NSCLC can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma. 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 IIIB) or to other parts of the body (metastatic disease; stage IV). In 2012, approximately 27,300 people were diagnosed with NSCLC in England, of whom 2600 (9.6%) had stage IIIB and 12,800 (47%) had stage IV disease.

Lung cancer caused 28,000 deaths in England in 2011. 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.

For the majority of people with NSCLC, the aims of therapy are to prolong survival and improve quality of life. NICE clinical guideline 121 (CG121) recommends platinum-based chemotherapy as an option for people with previously untreated stage III or IV NSCLC and good performance status. For people with locally advanced or metastatic NSCLC whose disease has progressed after non-targeted chemotherapy, NICE recommends docetaxel monotherapy afatinib and erlotinib as options in certain circumstances (CG121, technology appraisal 162 and technology appraisal 310 respectively). In clinical practice, NSCLC tumours that progress after treatment with EGFR-targeted therapies may be treated with platinum in combination with gemcitabine, vinorelbine, pemetrexed or a taxane. Treatment choices may be influenced by the presence of genetic markers (such as mutations in EGFR-TK), histology (squamous or non-squamous) and previous treatment experience. Supportive care may be considered for some people for whom chemotherapy is unsuitable or may not be tolerated.

The technology

Nivolumab (brand name unknown, Bristol-Myers Squibb) is a monoclonal antibody that targets a receptor on the surface of lymphocytes known as PD-1. This receptor is part of the immune checkpoint pathway, and blocking its activity may promote an anti-tumour immune response. Nivolumab is administered by IV infusion.

Nivolumab does not currently have a marketing authorisation in the UK. It is being studied in clinical trials, in comparison with docetaxel, for treating locally advanced or metastatic NSCLC which has progressed or recurred after platinum-based chemotherapy. It is also being studied in non-comparative trials for treating NSCLC which has progressed or recurred after other previous therapies.

Intervention(s)	Nivolumab
Population(s)	People with previously treated locally advanced or metastatic (stage IIIB or IV) non-small cell lung cancer
Comparators	**Non-squamous EGFR-TK mutation positive tumours:** • After one prior therapy: – Platinum therapy (in combination with gemcitabine, vinorelbine, pemetrexed or a taxane) – Afatinib (if no previous EGFR-TKI therapy received due to delayed confirmation of mutation status) – Nintedanib (subject to ongoing NICE appraisal) • After two prior therapies (an EGFR-TKI and one other therapy): – Docetaxel monotherapy – Best supportive care **Non-squamous EGFR-TK mutation negative tumours:** • After one prior therapy: – Docetaxel monotherapy – Erlotinib (subject to ongoing NICE appraisal) – Nintedanib (subject to ongoing NICE appraisal) • After two prior therapies: – Docetaxel monotherapy

	– Erlotinib (if not received previously; subject to ongoing NICE appraisal) – Best supportive care **Squamous tumours:** • After one prior therapy: – Docetaxel monotherapy • After two prior therapies: – 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. Where comparator technologies are available through the Cancer Drug Fund, the cost incurred by the Cancer Drug Fund should be used in any economic analyses, rather than the list price.
Other considerations	If the evidence allows, consideration will be given to subgroups based on cancer histology (for example, squamous or non-squamous) and genetic markers (for example, EGFR-TK, ALK and PD-L1 status). If appropriate, the appraisal should include consideration of the costs and implications of additional testing for genetic markers, but will not make recommendations on specific diagnostic tests or devices.

	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: Technology Appraisal No. 310, Mar 2014, 'Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer'. Review Proposal Date Apr 2017. Technology Appraisal No. 175, Jul 2009, 'Gefitinib for the second-line treatment of locally advanced or metastatic non-small-cell lung cancer (terminated appraisal)'. Review in progress. Technology Appraisal No. 162, Nov 2008, 'Erlotinib for the treatment of non-small-cell lung cancer'. Review in progress. Technology Appraisal No. 124, Nov 2007, 'Pemetrexed for the treatment of non-small-cell lung cancer'. Static list. Technology Appraisal in preparation, 'Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed following prior chemotherapy (Review of TA162 and TA175)' [ID620]. Expected date of publication TBC. Technology Appraisal in preparation, 'Nintedanib for treating previously treated metastatic non-small cell lung cancer' [ID438]. Expected date of publication Apr 2015. Related Guidelines: Clinical Guideline No. 121, Apr 2011, 'The diagnosis and treatment of lung cancer'. Related Quality Standards: Quality Standard No. 17, Mar 2012, 'Quality standard for lung cancer'. 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	Department of Health, Improving Outcomes: A Strategy

Policy	for Cancer, third annual report, Dec 2013 https://www.gov.uk/government/publications/the-national-cancer-strategy-3rd-annual-report--2 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 2013-2014, Nov 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf Department of Health, Cancer commissioning guidance, Dec 2009. http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_110115

Questions for consultation

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

- Which treatments are considered to be established clinical practice in the NHS for locally advanced or metastatic NSCLC that has progressed after prior chemotherapy?
- Should crizotinib and ceritinib for previously treated anaplastic lymphoma kinase (ALK) positive NSCLC be included as comparators?
- How should best supportive care be defined?
- Would nivolumab be used to treat squamous or non-squamous tumours? Or both?

Are the subgroups suggested in 'other considerations' appropriate?

- Are there any other subgroups of people in whom nivolumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?
- Should any other genetic markers be considered?

Where do you consider nivolumab 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 nivolumab 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 nivolumab 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 nivolumab 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)