NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel for untreated metastatic squamous non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab in combination with carboplatin and paclitaxel or nab-paclitaxel within its marketing authorisation for untreated metastatic squamous 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 III) or to other parts of the body (metastatic disease; stage IV).

In 2016, around 37,000 people were diagnosed with NSCLC in England.[1] Around 12% had stage IIIA, 8% had stage IIIB and 53% had stage IV disease[1]. The prognosis for people with non-small-cell lung cancer is generally poor. For people with stage III and stage IV disease respectively, around 43% and 16% survive for 1 year or longer.[1]

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 epidermal growth factor receptor-tyrosine kinase (EGFR-TK), anaplastic-lymphoma-kinase (ALK) or PD-L1 status), histology (squamous or non-squamous) and previous treatment experience.

NICE clinical guideline 121 (CG121 'Lung cancer') recommends platinum-based chemotherapy (that is, cisplatin or carboplatin and either docetaxel, gemcitabine, paclitaxel, or vinorelbine) as an option for people with previously untreated stage III or IV NSCLC and good performance status.

Pembrolizumab monotherapy is currently recommended within the Cancer Drugs Fund as a treatment option for untreated PD-L1-positve metastatic NSCLC if the tumour expresses PD-L1 with at least 50% tumour proportion score (NICE technology appraisal guidance 447). The company for pembrolizumab was required to collect data from the KEYNOTE-024 trial in

line with the managed access agreement. This guidance is currently under review.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, anti-programmed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Pembrolizumab does not have a marketing authorisation in the UK for untreated metastatic squamous NSCLC when used in combination with carboplatin and paclitaxel or nab-paclitaxel. It has been studied in a clinical trial in combination with carboplatin and investigator's choice of paclitaxel or nab-paclitaxel, compared with carboplatin and investigator's choice of paclitaxel or nab-paclitaxel alone, in adults with metastatic squamous NSCLC who have not had chemotherapy for metastatic disease.

Pembrolizumab monotherapy has a marketing authorisation in the UK for:

- first line treatment of metastatic NSCLC for tumours that express PD-L1 with at least 50% tumour proportion score with no EGFR or ALK positive tumour mutations
- treating locally advanced or metastatic NSCLC for tumours that express PD-L1 with at least 1% tumour proportion score after at least one prior chemotherapy regimen.

Interventions	Pembrolizumab in combination with: • carboplatin and paclitaxel • carboplatin and nab-paclitaxel
Population	Adults with untreated metastatic squamous non-small-cell lung cancer (NSCLC)
Comparators	• Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin) • Pembrolizumab monotherapy (for people with at least 50% tumour proportion score with no EGFR or ALK positive tumour mutations only [subject to ongoing NICE appraisal , funded by the CDF in the interim])

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. 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 commercial access agreements for the intervention or comparator technologies will be taken into account. If appropriate, the economic modelling should include the costs associated with diagnostic testing for biological markers (PD-L1) 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	If evidence allows, consideration will be given to subgroups based on the biological marker PD-L1. 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	**Related Technology Appraisals:** 'Necitumumab for untreated advanced or metastatic squamous non-small-cell lung cancer' NICE technology

Pathways	appraisal 411. Review date September 2019. 'Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer' NICE technology appraisal 447. Review in progress [ID1349]. Related Technology Appraisals in development (including suspended appraisals) 'Nivolumab in combination with ipilimumab for untreated PD-L1-positive non-small-cell lung cancer' NICE technology appraisals guidance [ID1187]. Publication date to be confirmed. 'Nivolumab in combination with platinum-doublet chemotherapy for untreated PD-L1-negative non-small-cell lung cancer' NICE technology appraisals guidance [ID1135]. Publication date to be confirmed. Terminated appraisals Paclitaxel as albumin-bound nanoparticles with carboplatin for untreated non-small-cell lung cancer (terminated appraisal) (2015) NICE technology appraisals guidance 362 **Related Guidelines:** Lung Cancer: The diagnosis and treatment of lung cancer (2011). NICE guideline 121. Review in progress. **Guidelines in development** 'Lung cancer: diagnosis and management (update)'. Publication expected January 2019. **Related Quality Standards:** Quality standard for lung cancer (2012). NICE quality standard 17 https://www.nice.org.uk/guidance/qs17 **Related NICE Pathways:** Lung cancer. Pathway created: Mar 2012. http://pathways.nice.org.uk/pathways/lung-cancer
Related National Policy	Department of Health, Improving Outcomes: A strategy for cancer, fourth annual report, Dec 2014 https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report NHS England, Manual for prescribed specialised services, chapter 105: specialist cancer services (adults), May 2016. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-

	may16.pdf Department of Health, NHS Outcomes Framework 2016-20167, April 2016. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 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 pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for untreated metastatic squamous NSCLC?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel 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 pembrolizumab 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 pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel 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 pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel 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 technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 National lung cancer audit 2017 (2018). Royal college of Physicians. Accessed May 2018.