NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Cemiplimab for untreated PD-L1-postive advanced or metastatic non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of cemiplimab within its marketing authorisation for untreated PD-L1 positive advanced or metastatic non-small cell lung cancer with no EGFR, ALK or ROS-1 mutations.

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[1]. NSCLC can be further classified into squamous cell carcinoma and non-squamous cell carcinoma. Approximately 70% of NSCLC are of non-squamous histology and can be either large-cell undifferentiated carcinoma or adenocarcinoma[2]. 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 2017, 39,205 people were diagnosed with NSCLC in England & Wales, and around 65% had stage IIIB or stage IV disease[3]. Around a third of people with lung cancer survive for more than 1 year after diagnosis[4], however this is reduced to a fifth of people diagnosed at stage IV[3].

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.

NICE guideline 122 recommends platinum-combination 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. Alternatively, people may receive pemetrexed in combination with cisplatin if the histology of the tumour has been confirmed as adenocarcinoma or large-cell carcinoma (NICE technology appraisal guidance 181). NICE technology appraisal guidance 584 recommends atezolizumab with bevacizumab, carboplatin and paclitaxel as an option for untreated non-squamous NSCLC if the tumour expresses PD-L1 with less than 50% tumour proportion score and has no EGFR- or ALK-

positive mutations. NICE technology appraisal guidance 531 recommends pembrolizumab monotherapy as an option for untreated PD-L1-positive metastatic NSCLC if the tumour expresses PD-L1 with at least 50% tumour proportion score and has no EGFR- or ALK-positive mutations. NICE technology appraisal guidance 557 recommends pembrolizumab combination therapy for use within the Cancer Drugs Fund, as an option for metastatic untreated non-squamous NSCLC if the tumour has no EGFR- or ALK-positive mutations[a]. NICE technology appraisal guidance 600 recommends pembrolizumab with carboplatin and paclitaxel for use within the Cancer Drugs Fund, as an option for metastatic untreated squamous NSCLC[a].

The technology

Cemiplimab (Libtayo, Sanofi) is a fully human immunoglobulin G4 (IgG4) monoclonal antibody that binds to the programmed cell death-1 (PD-1) receptor and blocks its interaction with its ligands PD-L1 and PD-L2, thereby activating the patient's immune system to attack the cancer.

Cemiplimab does not currently have a marketing authorisation for untreated PD-L1-postive advanced or metastatic NSCLC. It has been studied in a clinical trial compared with standard-of-care chemotherapy (pemetrexed, paclitaxel or gemcitabine, with platinum therapy) alone in adults with untreated advanced or metastatic NSCLC without EGFR, ALK or ROS1 mutations.

[a] Products recommended for use in the Cancer Drugs Fund after 1 April 2016 should not be considered as comparators, or appropriately included in a treatment sequence, in subsequent relevant appraisals. https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisal-guidance/cancer-drugs-fund/CDF-comparator-position-statement.pdf

Intervention(s)	Cemiplimab
Population(s)	Adults with untreated PD-L1 positive advanced or metastatic NSCLC with no EGFR, ALK or ROS-1 mutations.

Comparators	For adults with non-squamous histology:
	• Pemetrexed in combination with a platinum drug (carboplatin or cisplatin) (for people with adenocarcinoma or large-cell carcinoma only)
	  ○ with (following cisplatin-containing regimens only) or without pemetrexed maintenance treatment
	• Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin)
	  ○ with or without pemetrexed maintenance treatment
	• Atezolizumab with bevacizumab, carboplatin and paclitaxel (for people whose tumours express PD-L1 with less than 50% tumour proportion score)
	• Pembrolizumab (for people whose tumours express PD-L1 with at least a 50% tumour proportion score)
	
	For adults with squamous histology:
	• Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin)
	• Pembrolizumab (for people whose tumours express PD-L1 with at least a 50% tumour proportion score)

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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 and cost of biosimilar products of should be taken into account. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The economic modelling should include the costs associated with diagnostic testing for biological markers or mutations (PD-L1, EGFR ALK and ROS1) 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 the evidence allows, consideration will be given to subgroups based on biological markers (PD-L1). The availability and cost of biosimilar and generic products should be taken into account. 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:** Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (2019) NICE technology appraisals guidance 600. Review date to be confirmed. Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (2019) NICE technology appraisal 584. Review date June 2022. Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer (2019) NICE technology appraisals guidance 557.

	Review date to be confirmed. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018) NICE technology appraisal guidance 531. Review date July 2021. Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin (2016) NICE technology appraisal guidance 402. Review date to be confirmed. Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010, updated 2017) NICE technology appraisals guidance 190. Static guidance list. Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009, updated 2014) NICE technology appraisal 181. Static guidance list. **Appraisals in development (including suspended appraisals)** Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer. NICE technology appraisal guidance [ID1678]. Expected publication date June 2021. Atezolizumab with carboplatin and nab-paclitaxel for untreated advanced non-squamous non-small-cell lung cancer. NICE technology appraisal guidance [TA618]. Suspended. Atezolizumab with carboplatin and nab-paclitaxel for untreated advanced non-squamous non-small-cell lung cancer. NICE technology appraisal guidance [ID1513]. Suspended. Atezolizumab with carboplatin or cisplatin and pemetrexed for untreated advanced non-squamous non-small-cell lung cancer. NICE technology appraisal [ID1495]. Suspended. Avelumab for untreated PD-L1 positive non-small-cell lung cancer. NICE technology appraisal [ID1261]. Suspended. Durvalumab + Tremelimumab + standard chemotherapy for non-small cell lung cancer (NSCLC) lacking activating EGFR mutations and ALK fusions. NICE technology appraisals guidance [ID1538]. Publication date to be confirmed. Durvalumab for untreated advanced non-small-cell lung cancer with no EGFR or ALK mutations and high PD-L1 expression. NICE technology appraisal guidance

	[ID3762]. Publication date to be confirmed. Durvalumab for untreated EGFR-negative, ALK-negative non-small-cell lung cancer. NICE technology appraisal guidance [ID1331]. Suspended. Durvalumab with tremelimumab for untreated non-small-cell lung cancer with no EGFR- or ALK-positive mutations. NICE technology appraisal guidance [ID1143]. Suspended. Nivolumab in combination with ipilimumab for untreated PD-L1-positive non-small-cell lung cancer. NICE technology appraisal guidance [ID1187]. Suspended. Nivolumab in combination with platinum-doublet chemotherapy for untreated PD-L1-negative non-small-cell lung cancer. NICE technology appraisal guidance [ID1135]. Suspended. Nivolumab monotherapy for non-small-cell lung cancer. NICE technology appraisal guidance [ID1088]. Suspended. Nivolumab with ipilimumab and chemotherapy for untreated advanced non-small-cell lung cancer NICE technology appraisal guidance [ID1566]. Expected publication date June 2021. Pembrolizumab for untreated PD-L1 positive non-small-cell lung cancer with at least 1% tumour proportion score. NICE technology appraisal guidance [ID1247]. Suspended. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (CDF Review TA600) NICE technology appraisal guidance [ID1683]. Expected publication date to be confirmed. Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer (CDF Review of TA557) NICE technology appraisal guidance [ID1584]. Expected publication date December 2020. Veliparib with carboplatin and paclitaxel for untreated non-squamous non-small-cell lung cancer. NICE technology appraisal guidance [ID1277]. Publication date to be confirmed. **Related Guidelines:** Lung cancer: diagnosis and management (2019) NICE guideline 122

	Related Interventional Procedures: Microwave ablation for treating primary lung cancer and metastases in the lung (2013). NICE interventional procedures guidance 469 **Related quality standards:** Lung cancer in adults (2019) NICE quality standard 17 **Related NICE Pathway:** Lung cancer (2019) NICE pathway.
Related National Policy	**NHS England:** The NHS England (2019) NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105: specialist cancer services (adults) **Department of Health:** Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for cemiplimab for people with untreated PD-L1 positive advanced or metastatic non-small cell lung cancer with no EGFR, ALK or ROS-1 mutations been included in the scope?

Are the outcomes listed appropriate?

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

Where do you consider cemiplimab will fit into the existing NICE pathway for non-small-cell 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 durvalumab with chemotherapy 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 cemiplimab 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 cemiplimab 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 comparators 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] Lung cancer incidence by morphology. Cancer Research UK. Accessed November 2020

[2] Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, et al. SEER Cancer Statistics Review, 1975-2012, National Cancer Institute. 2015 [Available from: https://seer.cancer.gov/csr/1975_2012/.

[3] National Lung Cancer Audit: Annual report 2018 (for the audit period 2017) (2019). Royal College of Physicians. Accessed November 2020.

[4] Lung cancer survival statistics (2010-11). Cancer Research UK. Accessed November 2020.