NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Final scope

Final 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-based chemotherapy (that is, cisplatin or carboplatin and either docetaxel, gemcitabine, paclitaxel, or vinorelbine) as an option for people with stage III or IV NSCLC if the tumours express PD-L1 with a tumour proportion score between 0% and 49%. 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).

For untreated, metastatic, non-squamous NSCLC people may have atezolizumab plus bevacizumab, carboplatin and paclitaxel (NICE technology

appraisal guidance 584) if the tumours express PD-L1 with a tumour proportion score between 0% and 49%. People with untreated, metastatic NSCLC whose tumours express PD-L1 (with at least a 50% tumour proportion score) and have no epidermal growth factor receptor or anaplastic lymphoma kinase-positive mutations may receive pembrolizumab (NICE technology appraisal guidance 531).

NICE technology appraisal guidance 683 recommended pembrolizumab, with pemetrexed and platinum chemotherapy for people whose tumours have no epidermal growth factor receptor (EGFR)- or anaplastic lymphoma kinase (ALK)-positive mutations. Pembrolizumab with pemetrexed and platinum chemotherapy can be offered whether or not tumours are PD-L1 positive, and regardless of tumour proportion score.

NICE technology guidance 600 recommended pembrolizumab with carboplatin and paclitaxel, as an option for use within the Cancer Drugs Fund for untreated metastatic squamous non-small-cell lung cancer (NSCLC) in adults. This technology appraisal guidance is currently under review.[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 people whose tumours express PD-L1 with at least a 50% tumour proportion score: • Pembrolizumab • Pembrolizumab with pemetrexed and platinum chemotherapy • Atezolizumab (subject to ongoing NICE appraisal) For people with non-squamous NSCLC whose tumours express PD-L1 with a tumour proportion score below 50%: • Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin) o with or without pemetrexed maintenance treatment • Pembrolizumab with pemetrexed and platinum chemotherapy For people with adenocarcinoma or large-cell carcinoma whose tumours express PD-L1 with a tumour proportion score below 50%: • Pemetrexed in combination with a platinum drug (carboplatin or cisplatin) o with (following cisplatin-containing regimens only) or without pemetrexed maintenance treatment For people with squamous NSCLC whose tumours express PD-L1 with a tumour proportion score below 50%: • Chemotherapy (gemcitabine or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin)

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.
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 pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell-lung-cancer (2021) NICE technology appraisals guidance 683. Review date 2024. 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.

	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 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. 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 (2021) 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

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.