

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Pembrolizumab for untreated PD-L1 positive non-small-cell lung cancer with at least 1% tumour proportion score

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for untreated PD-L1 positive non-small-cell lung cancer with at least 1% tumour proportion score.

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 2015, around 33,000 people are estimated to be diagnosed with NSCLC in England.^{1,2} Around 12% have stage IIIA, 9% had stage IIIB and 53% had stage IV disease¹. 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

Cancer cells expressing an immunologic marker called programmed cell death 1 ligand (PD-L1) are believed to suppress certain immune responses and cause increased tumour aggressiveness. The proportion of NSCLC that express PD-L1 in England is unknown.

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. 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 people who are unable to tolerate a platinum combination, the clinical guideline recommends single-agent chemotherapy with docetaxel, gemcitabine, paclitaxel, or vinorelbine.

For non-squamous NSCLC that has not progressed immediately following initial therapy with a NICE-recommended platinum-based chemotherapy regimen, maintenance treatment with pemetrexed is recommended as an option ([NICE technology appraisal guidance 190](#) and [NICE technology appraisal guidance 402](#)). Pembrolizumab is recommended as an option for untreated PD-L1-positive metastatic NSCLC if the tumour expresses PD-L1 with at least 50% tumour proportion score ([NICE technology appraisal guidance 531](#)).

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 PD-L1 positive metastatic NSCLC for tumours that express PD-L1 with at least 1% tumour proportion score with no EGFR or ALK positive tumour mutations. It has been studied in a clinical trial, compared with platinum-based chemotherapy, in adults with PD-L1 positive advanced or metastatic NSCLC who have not had chemotherapy for advanced or metastatic disease. The trial excluded people with EGFR- or ALK-positive tumour mutations.

Pembrolizumab with pemetrexed and platinum chemotherapy has a marketing authorisation for the first-line treatment of metastatic non-squamous NSCLC in adults for tumours that have no EGFR or ALK positive mutations.

Pembrolizumab as 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. Patients with EGFR or ALK positive tumour mutations should also have received targeted therapy before treatment with pembrolizumab.

Intervention(s)	Pembrolizumab
Population(s)	Adults with PD-L1-positive advanced or metastatic non-small-cell lung cancer (NSCLC) with at least 1% tumour proportion score that has not been treated with chemotherapy, and no EGFR- or ALK-positive tumour mutations

Comparators	<ul style="list-style-type: none"> • Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin) <ul style="list-style-type: none"> ○ with (for people with non-squamous NSCLC only) or without pemetrexed maintenance treatment • Pemetrexed in combination with a platinum drug (carboplatin or cisplatin) (for people with adenocarcinoma or large cell carcinoma only) <ul style="list-style-type: none"> ○ with or without pemetrexed maintenance treatment (following cisplatin-containing regimens only)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates • duration of response • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator or subsequent technologies will be taken into account.</p> <p>The use of pembrolizumab is conditional on the presence of programmed cell death 1 ligand (PD-L1). The economic modelling should include the costs associated with diagnostic testing for PD-L1 in people with NSCLC who would not otherwise have been tested.</p>

	<p>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.</p>
<p>Other considerations</p>	<p>If evidence allows, subgroup analysis by tumour histology (squamous or non-squamous) and level of PD-L1 expression will be considered.</p> <p>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.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (2018) NICE technology appraisal 531. Review expected July 2021.</p> <p>Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer (2016) NICE technology appraisals guidance 402. Review expected August 2019.</p> <p>Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010) NICE technology appraisals guidance 190. Static guidance list (review decision December 2014).</p> <p>Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009) NICE technology appraisals guidance 181. Static guidance list (review decision December 2014).</p> <p>Appraisals in development</p> <p>‘Durvalumab with tremelimumab for untreated non-small-cell lung cancer with no EGFR- or ALK-positive mutations’. NICE technology appraisal guidance [ID1143]. Publication expected January 2020.</p> <p>‘Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer’. NICE technology appraisals guidance [ID1173]. Publication expected December 2018.</p> <p>‘Nivolumab with ipilimumab for untreated non-small-cell lung cancer that has a high tumour mutational burden’ NICE technology appraisal [ID1187]. Publication expected May 2019.</p> <p>‘Atezolizumab in combination for treating advanced non-squamous non-small-cell lung cancer’. NICE technology</p>

	<p>appraisal [ID1210]. Publication expected June 2019.</p> <p>‘Pembrolizumab with carboplatin and paclitaxel for untreated squamous non-small-cell lung cancer’. NICE technology appraisal [ID1306]. Publication expected July 2019.</p> <p>‘Nivolumab monotherapy for non-small-cell lung cancer. NICE technology appraisal guidance’ [ID1088]. Suspended.</p> <p>‘Avelumab for untreated PD-L1 positive non-small-cell lung cancer’. NICE technology appraisal guidance [ID1261]. Publication date to be confirmed</p> <p>‘Veliparib with carboplatin and paclitaxel for untreated non-squamous non-small-cell lung cancer’. NICE technology appraisal guidance [ID1277]. Publication date to be confirmed.</p> <p>‘Durvalumab for untreated EGFR-negative, ALK-negative non-small-cell lung cancer’. NICE technology appraisal guidance [ID1331]. Publication date to be confirmed.</p> <p>‘Atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer’. NICE technology appraisal guidance [ID1504]. Publication date to be confirmed.</p> <p>Related Guidelines:</p> <p>Lung Cancer: The diagnosis and treatment of lung cancer (2011). NICE guideline 121. Review in progress.</p> <p>Guidelines in development</p> <p>‘Lung cancer: diagnosis and management (update)’. Publication expected January 2019.</p> <p>Related Quality Standards:</p> <p>Quality standard for lung cancer (2012). NICE quality standard 17</p> <p>https://www.nice.org.uk/guidance/qs17</p> <p>Related NICE Pathways:</p> <p>Lung cancer. Pathway created: Mar 2012.</p> <p>http://pathways.nice.org.uk/pathways/lung-cancer</p>
<p>Related National Policy</p>	<p>Department of Health, Improving Outcomes: A strategy for cancer, fourth annual report, Dec 2014</p> <p>https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report</p> <p>NHS England, Manual for prescribed specialised services, chapter 105: specialist cancer services</p>

	<p>(adults), May 2016. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf</p> <p>Department of Health, NHS Outcomes Framework 2016-2017, April 2016. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p> <p>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</p>
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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.