

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

**Pembrolizumab with pemetrexed and platinum chemotherapy for untreated metastatic non-squamous non-small-cell lung cancer**

**Final scope**

**Final remit/appraisal objective**

To appraise the clinical and cost effectiveness of pembrolizumab in combination with pemetrexed and platinum chemotherapy within its marketing authorisation for untreated, metastatic, non-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<sup>1,2</sup>. 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, approximately 31,700 people were diagnosed with NSCLC in England, of whom 53% had stage IV disease<sup>2</sup>. Around a third of people with lung cancer survive for more than 1 year after diagnosis<sup>2</sup>, however this is reduced to a fifth of people diagnosed at stage IV<sup>3</sup>.

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 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). 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 402). Pembrolizumab monotherapy is currently recommended for use within the Cancer Drugs Fund as an option for people whose tumours express PD-L1 with at least a 50% tumour proportion score

and have no EGFR- or ALK-positive mutations (NICE technology appraisal guidance 447). Best supportive care may be considered for some people for whom chemotherapy is unsuitable or may not be tolerated.

### 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 in combination with pemetrexed and platinum chemotherapy for untreated metastatic non-squamous NSCLC. The combination has been studied in a randomised clinical trial compared with pemetrexed and platinum chemotherapy alone, in adults with untreated metastatic non-squamous NSCLC.

<b>Interventions</b>	Pembrolizumab in combination with pemetrexed and platinum chemotherapy
<b>Population</b>	Adults with untreated metastatic non-squamous NSCLC
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• 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"> <li>○ with (following cisplatin-containing regimens only) or without pemetrexed maintenance treatment</li> </ul> </li> <li>• Chemotherapy (docetaxel, gemcitabine, paclitaxel or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin) <ul style="list-style-type: none"> <li>○ with or without pemetrexed maintenance treatment</li> </ul> </li> <li>• Pembrolizumab monotherapy (for people whose tumours express PD-L1 with at least a 50% tumour proportion score) (recommended for use within Cancer Drugs Fund; guidance update in progress)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rates</li> <li>• duration of response</li> </ul>

	<ul style="list-style-type: none"> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<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>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 patient access schemes for the intervention or comparator technologies will be taken into account.</p>
<b>Other considerations</b>	<p>If the evidence allows, consideration will be given to subgroups based on cancer histology and biological markers (PD-L1).</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>
<b>Related NICE recommendations and NICE Pathways</b>	<p><b>Related Technology Appraisals</b></p> <p><a href="#">Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer</a> (2017). NICE technology appraisal 447. Review ongoing [<a href="#">ID1349</a>].</p> <p><a href="#">Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin</a> (2016). NICE technology appraisal 402. Review date August 2019.</p> <p><a href="#">Pemetrexed for the maintenance treatment of non-small-cell lung cancer</a> (2010). NICE technology appraisal 190. Static guidance list.</p> <p><a href="#">Pemetrexed for the first-line treatment of non-small-cell lung cancer</a> (2009). NICE technology appraisal 181. Static guidance list.</p> <p><b>Appraisals in development (including suspended appraisals)</b></p> <p>Nivolumab in combination with ipilimumab for untreated non-small-cell lung cancer. NICE technology appraisal</p>

	<p>guidance <a href="#">[ID1187]</a>. Publication date to be confirmed.</p> <p>Nivolumab for untreated non-small-cell lung cancer. NICE technology appraisal guidance <a href="#">[ID1135]</a>. Publication date to be confirmed.</p> <p>Pembrolizumab for untreated PD-L1-positive non-small-cell lung cancer with at least 1% tumour proportion score. NICE technology appraisal guidance <a href="#">[ID1247]</a>. Publication date to be confirmed.</p> <p>Nivolumab monotherapy for non-small-cell lung cancer. NICE technology appraisal guidance <a href="#">[ID1088]</a>. Suspended.</p> <p><b>Related Guidelines</b></p> <p><a href="#">Lung cancer: diagnosis and management</a> (2011). NICE clinical guideline 121. Review in progress.</p> <p><b>Guidelines in development</b></p> <p>Lung cancer: diagnosis and management (<a href="#">update</a>). Publication expected March 2019.</p> <p><b>Related Interventional Procedures</b></p> <p><a href="#">Microwave ablation for treating primary lung cancer and metastases in the lung</a> (2013). NICE interventional procedures guidance 469.</p> <p><b>Related Quality Standards</b></p> <p><a href="#">Lung cancer in adults</a> (2012). NICE quality standard 17.</p> <p><b>Related NICE Pathways</b></p> <p><a href="#">Lung cancer</a> (2017) NICE pathway.</p>
<p><b>Related National Policy</b></p>	<p>Department of Health (2014) <a href="#">Improving outcomes: a strategy for cancer. Fourth annual report</a></p> <p>NHS England (2016) <a href="#">Manual for prescribed specialised services</a>. Chapter 105: Specialist cancer services (adults)</p> <p>Department of Health (2016) <a href="#">NHS Outcomes Framework 2016-2017</a>. Domains 1, 2, 4 and 5.</p> <p>NHS England (2016) <a href="#">Implementing the cancer taskforce recommendations: Commissioning person centred care for people affected by cancer</a></p>

## References

<sup>1</sup> Cancer Research UK (2017) [Lung cancer incidence statistics \(2011 data\)](#). Accessed March 2018.

<sup>2</sup> Royal College of Physicians (2017) [National Lung Cancer Audit annual report 2016 \(for the audit period 2015\)](#). Accessed March 2018.

<sup>3</sup> Cancer Research UK (2017) [Lung cancer survival statistics \(2014 data\)](#). Accessed March 2018.