

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Appraisal**

**Atezolizumab in combination for treating advanced non-squamous non-small-cell lung cancer**

**Final scope**

**Final remit/appraisal objective**

To appraise the clinical and cost effectiveness of atezolizumab in combination within its marketing authorisation for treating advanced non-squamous non-small-cell lung cancer.

**Background**

Lung cancer falls into 2 main histological categories: 85-90% are non-small-cell lung cancers (NSCLC) and 10-15% are small-cell lung cancers<sup>1</sup>. 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<sup>2</sup>. 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, approximately 32,500 people were diagnosed with NSCLC in England, and around 61% had stage IIIB or stage IV disease<sup>3</sup>.

Lung cancer caused over 35,620 deaths in England in 2016<sup>4</sup>. Thirty two percent of people with lung cancer survive for more than 1 year after diagnosis<sup>5</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-based chemotherapy (that is, cisplatin or carboplatin and either docetaxel, gemcitabine, paclitaxel, or vinorelbine) as an option for people with 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 TA 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 TA 190 and 402).

For untreated, advanced, non-squamous NSCLC that is epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation-positive, people may receive afatinib (NICE TA 310), erlotinib (NICE TA 258) or gefitinib (NICE TA 192). For untreated, advanced, non-squamous NSCLC that is anaplastic lymphoma kinase (ALK)-positive, people may receive ceritinib (NICE TA 500) or crizotinib (NICE TA 406).

NICE technology appraisal guidance 447 recommended pembrolizumab with a managed access agreement through the Cancer Drugs Fund for people whose tumours express PD-L1 with at least a 50% tumour proportion score and have no epidermal growth factor or anaplastic lymphoma kinase- positive mutations. A review of this guidance is in progress; the Final Appraisal Determination recommends pembrolizumab for routine commissioning [ID1349].

**The technology**

Atezolizumab (Tecentriq, Roche) is a humanised, anti-programmed cell death ligand-1 (PD-L1) monoclonal antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Atezolizumab in combination does not currently have a marketing authorisation in the UK for NSCLC. It is being studied in phase 3 clinical trials in combination with carboplatin plus paclitaxel (with or without bevacizumab), compared with carboplatin plus paclitaxel (with or without bevacizumab), in people with advanced, non-squamous NSCLC who had not had chemotherapy and people with EGFR- or ALK-positive advanced, non-squamous NSCLC who were previously treated with targeted therapy.

<b>Intervention(s)</b>	Atezolizumab in combination with carboplatin plus paclitaxel with or without bevacizumab
<b>Population(s)</b>	<ul style="list-style-type: none"> <li>• People with untreated advanced, non-squamous NSCLC</li> <li>• People with EGFR- or ALK-positive advanced, non-squamous NSCLC who were previously treated with targeted therapy (or cannot have a targeted therapy)</li> </ul>

<b>Comparators</b>	<p>For untreated advanced, non-squamous NSCLC:</p> <ul style="list-style-type: none"> <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>• Pemetrexed in combination with cisplatin (adenocarcinoma or large cell carcinoma only) <ul style="list-style-type: none"> <li>○ with or without pemetrexed maintenance treatment</li> </ul> </li> <li>• Pembrolizumab (for people whose tumours express PD-L1 with at least a 50% tumour proportion score); subject to ongoing appraisal (review of TA447).</li> </ul> <p>For EGFR- or ALK-positive advanced, non-squamous NSCLC previously treated with targeted therapy*:</p> <ul style="list-style-type: none"> <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>• Pemetrexed in combination with cisplatin (adenocarcinoma or large cell carcinoma only) <ul style="list-style-type: none"> <li>○ with or without pemetrexed maintenance treatment</li> </ul> </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 rate</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>

\* The comparators for the EGFR- or ALK-positive advanced, non-squamous NSCLC previously treated with targeted therapy have been updated following the first appraisal committee meeting to correct for an inaccuracy.

<p><b>Economic analysis</b></p>	<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 patient access schemes for the intervention or comparator technologies will be taken into account.</p>
<p><b>Other considerations</b></p>	<p>If evidence allows, subgroup analysis by 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><b>Related NICE recommendations and NICE Pathways</b></p>	<p><b>Related technology appraisals:</b></p> <p><a href="#">Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer</a> (2014) NICE technology appraisal 310.</p> <p><a href="#">Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer</a> (2010) NICE technology appraisal 192. Static guidance list.</p> <p><a href="#">Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer</a> (2017) NICE technology appraisal 447. Review in progress.</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>Terminated appraisals:</b></p> <p><a href="#">Bevacizumab for treating EGFR mutation-positive non-small-cell lung cancer (terminated appraisal)</a> (2017)</p>

	<p>NICE technology appraisal 436</p> <p><a href="#">Bevacizumab for the treatment of non-small-cell lung cancer (terminated appraisal)</a> (2008) NICE technology appraisal 148</p> <p><b>Appraisals in development (including suspended appraisals):</b></p> <p><a href="#">Avelumab for untreated PD-L1 positive non-small-cell lung cancer</a>. NICE technology appraisal guidance [ID1261]. Publication date to be confirmed.</p> <p><a href="#">Cimavax for treating wild-type EGFR-positive non-small-cell lung cancer</a>. NICE technology appraisal guidance [ID1259]. Publication date to be confirmed.</p> <p><a href="#">Durvalumab with tremelimumab for untreated non-small-cell lung cancer with no EGFR- or ALK-positive mutations</a>. NICE technology appraisal guidance [ID1143]. Publication expected January 2019.</p> <p><a href="#">Nivolumab in combination with ipilimumab for untreated PD-L1-positive non-small-cell lung cancer</a>. NICE technology appraisal guidance [ID1187]. Publication date to be confirmed.</p> <p><a href="#">Nivolumab in combination with platinum-doublet chemotherapy for untreated PD-L1-negative non-small-cell lung cancer</a>. NICE technology appraisal guidance [ID1135]. Publication date to be confirmed.</p> <p><a href="#">Nivolumab monotherapy for non-small-cell lung cancer</a>. NICE technology appraisal guidance [ID1088]. Suspended.</p> <p><a href="#">Pembrolizumab for untreated PD-L1 positive metastatic non-small-cell lung cancer (CDF review of TA447)</a>. NICE technology appraisal guidance [ID1349]. Publication expected July 2018.</p> <p><a href="#">Pembrolizumab for untreated PD-L1 positive non-small-cell lung cancer with at least 1% tumour proportion score</a>. NICE technology appraisal guidance [ID1247]. Publication date to be confirmed.</p> <p><a href="#">Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer</a>. NICE technology appraisal guidance [ID1173]. Publication date to be confirmed.</p> <p><a href="#">Veliparib with carboplatin and paclitaxel for untreated non-squamous non-small-cell lung cancer</a>. NICE technology appraisal guidance [ID1277]. Publication date to be confirmed.</p>
--	---

	<p><b>Related Guidelines:</b></p> <p><a href="#">Lung cancer: diagnosis and management</a> (2011). NICE guideline CG121. Review in progress.</p> <p><b>Guidelines in development:</b></p> <p><a href="#">Lung cancer: diagnosis and management (update)</a>. Publication expected March 2019</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> (2018) NICE pathway</p>
<p><b>Related National Policy</b></p>	<p>NHS England (2017) <a href="#">Manual for prescribed specialised services 2017/18</a> Chapter 105: Specialist cancer services (adults).</p> <p>Department of Health, <a href="#">NHS Outcomes Framework 2016-2017</a> (published 2016): Domain 1.</p>

## References

- 1 [Lung cancer incidence by morphology](#). Cancer Research UK. Accessed July 2018
- 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/](https://seer.cancer.gov/csr/1975_2012/)].
- 3 [National Lung Cancer Audit: Annual report 2017 \(for the audit period 2016\)](#) (2018). Royal College of Physicians. Accessed July 2018.
- 4 [Lung cancer mortality statistics \(2016\)](#). Cancer Research UK. Accessed July 2018.
- 5 [Lung cancer survival statistics \(2010-11\)](#). Cancer Research UK. Accessed July 2018.