

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

**Atezolizumab monotherapy for untreated PD-L1 positive metastatic non-small-cell lung cancer**

**Final scope**

**Remit/appraisal objective**

To appraise the clinical and cost effectiveness of atezolizumab monotherapy within its marketing authorisation for untreated PD-L1 positive metastatic 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 2017, 39,205 people were diagnosed with NSCLC in England & Wales, and around 65% had stage IIIB or stage IV disease<sup>3</sup>. Lung cancer caused over 28,000 deaths in England in 2017<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 aim 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 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 557 recommended pembrolizumab, with pemetrexed and platinum chemotherapy with a managed access agreement through the Cancer Drugs Fund for people whose tumours have no epidermal growth factor receptor (EGFR)- or anaplastic lymphoma kinase (ALK)-positive mutations. This technology appraisal guidance is currently under review.

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.

**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 monotherapy for untreated metastatic NSCLC does not currently have a marketing authorisation in the UK. It has been studied in a clinical trial which compared atezolizumab monotherapy with platinum chemotherapy and either gemcitabine or pemetrexed in adults with untreated PD-L1 positive non-squamous or squamous metastatic NSCLC.

<b>Intervention(s)</b>	Atezolizumab
<b>Population(s)</b>	Adults with non-squamous or squamous untreated metastatic NSCLC with PD-L1 positive tumour expression and without EGFR- or ALK-positive mutations
<b>Comparators</b>	<p>For people whose tumours express PD-L1 with at least a 50% tumour proportion score:</p> <ul style="list-style-type: none"> <li>• Pembrolizumab</li> </ul> <p>For people with non-squamous NSCLC whose tumours express PD-L1 with a tumour proportion score below 50%:</p> <ul style="list-style-type: none"> <li>• Atezolizumab plus bevacizumab, carboplatin and paclitaxel</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</li> </ul> </li> </ul>

	<p style="text-align: center;">treatment</p> <p>For people with adenocarcinoma or large-cell carcinoma whose tumours express PD-L1 with a tumour proportion score below 50%:</p> <ul style="list-style-type: none"> <li>• Pemetrexed in combination with a platinum drug (carboplatin or cisplatin) <ul style="list-style-type: none"> <li>○ with (following cisplatin-containing regimens only) or without pemetrexed maintenance treatment</li> </ul> </li> </ul> <p>For people with squamous NSCLC whose tumours express PD-L1 with a tumour proportion score below 50%:</p> <ul style="list-style-type: none"> <li>• Chemotherapy (gemcitabine or vinorelbine) in combination with a platinum drug (carboplatin or cisplatin)</li> </ul>
<p><b>Outcomes</b></p>	<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>
<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>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>If the use of atezolizumab is conditional on any relevant diagnostic tests which would not have otherwise been tested for, the economic modelling should include the costs associated with the relevant diagnostic tests. A sensitivity analysis should be provided without the cost of the diagnostic tests. <a href="#">See section 5.9 of the Guide to the Methods of Technology Appraisals</a>.</p> <p>The availability of any commercial arrangements 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</p> <ul style="list-style-type: none"> <li>• Level of PD-L1 expression</li> <li>• Squamous and non-squamous status</li> </ul> <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="#">Pembrolizumab with carboplatin and paclitaxel for untreated squamous non-small-cell lung cancer</a> (2019) NICE technology appraisals guidance 600.</p> <p><a href="#">Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer</a> (2019) NICE technology appraisals guidance 584.</p> <p><a href="#">Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-squamous non-small-cell lung cancer</a> (2019) NICE technology appraisals guidance 557.</p> <p><a href="#">Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer</a> (2018) NICE technology appraisals guidance 531. Review date July 2021.</p> <p><a href="#">Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin</a> (2016) NICE technology appraisal guidance 402. Review date April 2019..</p> <p><a href="#">Pemetrexed for the maintenance treatment of non-small-cell lung cancer</a> (2010) NICE technology appraisals guidance 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><a href="#">Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer</a> (CDF Review of TA557) NICE technology appraisal ID1584. Expected publication date June 2020</p> <p><a href="#">Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer</a> (CDF Review TA600) NICE technology appraisal</p>

	<p>ID1683. Expected publication date August 2020</p> <p><a href="#">Atezolizumab with carboplatin or cisplatin and pemetrexed for untreated advanced non-squamous non-small-cell lung cancer</a> NICE Technology Appraisal Guidance [ID1495] Publication date to be confirmed.</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="#">Durvalumab with tremelimumab for untreated non-small-cell lung cancer with no EGFR- or ALK-positive mutations</a>. NICE technology appraisal guidance [ID1143]. Suspended.</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]. Suspended.</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]. Suspended.</p> <p><a href="#">Nivolumab with ipilimumab and chemotherapy for untreated advanced non-small-cell lung cancer</a> NICE technology guidance [ID1566] Publication 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 non-small-cell lung cancer with at least 1% tumour proportion score</a>. NICE technology appraisal guidance [ID1247]. Suspended.</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><a href="#">Atezolizumab with carboplatin and nab-paclitaxel for untreated advanced non-squamous non-small-cell lung cancer</a>. NICE technology appraisal guidance [ID1513]. Suspended.</p> <p><a href="#">Durvalumab for untreated EGFR-negative, ALK-negative non-small-cell lung cancer</a>. NICE technology appraisal guidance [ID1331]. Suspended.</p>
<b>Related National</b>	The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a>

<b>Policy</b>	<p>NHS England (2018) <a href="#">Manual for prescribed specialised services 2018/19</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>
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## References

1. [Lung cancer incidence by morphology](#). Cancer Research UK. Accessed April 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/](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 April 2020.
4. [Lung cancer mortality statistics \(2016\)](#). Cancer Research UK. Accessed April 2020.
5. [Lung cancer survival statistics \(2010-11\)](#). Cancer Research UK. Accessed April 2020.