NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Avelumab for treating non-small-cell lung cancer after platinum-based chemotherapy

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of avelumab within its marketing authorisation for treating non-small-cell lung cancer after platinum-based chemotherapy.

Background

Lung cancer falls into two main histological categories: non-small-cell lung cancers (NSCLC), which account for 88% of all lung cancers[1], and small-cell lung cancers. NSCLC may be grouped by tumour histology into squamous cell carcinoma, adenocarcinoma and large-cell carcinoma, with the latter 2 being collectively referred to as 'non-squamous' lung cancer. Cancer cells expressing an immunologic marker called programmed cell death 1 ligand (PD-L1) are believed to suppress certain immune responses and cause increased tumor aggressiveness.

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). Around a third of people with lung cancer survive for more than 1 year after diagnosis[1], however this is reduced to a fifth of people diagnosed at stage IV[2]. In 2015, approximately 31,700 people were diagnosed with NSCLC in England, of whom 74% had stage III or stage IV disease.[3]

About one-third of patients with NSCLC have disease which is suitable for potentially curative surgical resection. However, 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 EGFR-TK, ALK or PD-L1 status, histology (squamous or non-squamous) and previous treatment experience.

NICE recommends platinum-based chemotherapy as a first-line treatment for people with stage III or IV NSCLC and good performance status (NICE CG121). For people with locally advanced or metastatic NSCLC whose disease has progressed after chemotherapy, NICE recommends docetaxel monotherapy (CG121), nintedanib plus docetaxel (for adenocarcinoma; TA347) and pembrolizumab (PD-L1 positive; TA428). Through the Cancer Drugs Fund, nivolumab is also available as a treatment option for people with locally advanced or metastatic PD-L1 positive non-squamous NSCLC, whose disease has progressed after chemotherapy (TA484).

The technology

Avelumab (Bavenico, Merck) is an anti-PD-L1 monoclonal antibody with a dual mechanism of action. It aims to bind and block the inhibitory signalling through PD-1/PD-L1 resulting in the activation of T-cells and cell-mediated immune responses against tumour cells or pathogens. Avelumab is administered by IV infusion.

Avelumab does not currently have a marketing authorisation in the UK for the treatment of NSCLC after platinum-based chemotherapy. It is being studied in a clinical trial versus docetaxel, in people with locally advanced, metastatic or recurrent PD-L1 positive NSCLC after failure of a platinum-based doublet.

Intervention(s)	Avelumab
Population(s)	People with locally advanced, metastatic or recurrent PD-L1 positive NSCLC whose disease has progressed after treatment with platinum-based chemotherapy
Comparators	• Docetaxel monotherapy • Nintedanib with docetaxel (for people with NSCLC of adenocarcinoma histology) • Pembrolizumab (for people with locally advanced or metastatic PD-L1 positive NSCLC) • Atezolizumab (subject to NICE guidance) • Best supportive care.
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. If appropriate, the appraisal should include consideration of the costs and implications of additional testing for biological markers, but will not make recommendations on specific diagnostic tests or devices. 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 of any patient access schemes for the intervention or comparator technologies will be taken into account.
Other considerations	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**: Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non−small−cell lung cancer (2015). NICE Technology Appraisal 347. Review date: July 2018. Nivolumab for previously treated non-squamous non-small-cell lung cancer (2017). NICE Technology Appraisal 484. Expected review date: June 2019. Nivolumab for previously treated squamous non-small-cell lung cancer (2017). NICE Technology Appraisal 483. Expected review date: June 2019.Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy (2017). NICE Technology Appraisal 428. Review date: January 2019. Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer (2016). NICE Technology Appraisal 403. Review date: August 2019. **Suspended appraisals:** Vandetanib for the second and subsequent line treatment of non-small cell lung cancer after previous platinum containing chemotherapy (suspended

	appraisal). NICE Technology Appraisal [ID46]. Publication date to be confirmed. **Appraisals in development:** Atezolizumab for treating non-small-cell lung cancer after platinum-based chemotherapy NICE technology appraisal guidance [ID970] Publication date to be confirmed. **Related Guidelines:** Lung cancer (2011). NICE guideline CG121. Expected update publication date: March 2019 **Related Quality Standards:** Lung cancer **(**2012). NICE quality standard 17. **Related NICE Pathways:** Lung cancer (2018). NICE Pathway.
Related National Policy	**National Service Frameworks** Cancer **Department of Health** Department of Health (2013) NHS Outcomes Framework 2014–2015 Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf **NHS England** NHS England (2014) Manual for Prescribed Specialised Services 2013/14. Chapter 105: Specialist cancer services (adults) http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf

Questions for consultation

Is the expected use of avelumab for treating locally advanced, metastatic or recurrent NSCLC after platinum-based chemotherapy restricted to PD-L1 positive NSCLC?

Have all relevant comparators for avelumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for non-small-cell lung cancer after platinum-based chemotherapy?

How should best supportive care be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom avelumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider avelumab will fit into the existing lung cancer NICE pathway?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which avelumab will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider avelumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of avelumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is avelumab likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References.

1. Royal College of Physicians (2017) National Lung Cancer Audit Report 2016 (for the audit period 2015). Accessed October 2017
2. Cancer Research UK (2017) Lung cancer survival statistics (2014 data). Accessed March 2018.
3. Health and Social Care Information Centre (2017) National Lung Cancer Audit annual report 2016 (for the audit period 2015)

