Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Pembrolizumab with etoposide and a platinum-based compound for untreated extensive-stage small-cell lung cancer ID1509

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab with etoposide and a platinum-based compound within its marketing authorisation for untreated extensive-stage small-cell lung cancer.

Background

Lung cancer falls into 2 main histological categories: non-small-cell lung cancers and small-cell lung cancers. Small-cell lung cancer (SCLC) is a type of lung cancer that grows rapidly and spreads quickly to other parts of the body. SCLC can be classified as limited disease (cancer has not spread beyond one lung or nearby lymph nodes) or extensive-stage disease (the cancer has spread beyond one lung)[1]. Common symptoms of SCLC include weight loss, malaise, bone pain, breathlessness and haemoptysis.

In 2017 there were 38,888 cases of lung cancer registered in England[2]. Around 12% of lung cancer cases are SCLC[1]. The prognosis for patients with SCLC is poor, with a 5-year survival rate of 10%[3]. An estimated 66% of people with extensive-stage SCLC receive chemotherapy[4].

The aims of treatment for extensive-stage disease are to prolong survival and improve quality of life. NICE guideline 122 recommends that all patients with untreated extensive-stage SCLC who are fit enough should be offered platinum-based combination chemotherapy, for a maximum of six cycles. The disease response and drug toxicity should be assessed before each cycle. In clinical practice, treatment may be with etoposide in combination with a platinum therapy, or where etoposide is contraindicated, irinotecan in combination with cisplatin or gemcitabine in combination with carboplatin (in patients with poor prognosis)[5]. Thoracic radiotherapy can be offered after chemotherapy if there has been a complete response at distant sites and at least a good partial response within the thorax.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised monoclonal 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.

It does not currently have a marketing authorisation in the UK for untreated extensive-stage small-cell lung cancer. It is being studied in a clinical trial with

chemotherapy (etoposide and either cisplatin or carboplatin) for untreated extensive-stage small-cell lung cancer.

Intervention(s)	Pembrolizumab with etoposide and a platinum-based compound
Population(s)	People with untreated extensive-stage small-cell lung cancer
Comparators	Platinum-based combination chemotherapy regimens.
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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 commercial arrangements for the intervention or comparator and subsequent treatment technologies will be taken into account.
Other considerations	If the evidence allows, subgroups by level of PD-L1 expression may be considered (above or below 1%). 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.

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Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Topotecan for the treatment of relapsed small-cell lung cancer (2009). NICE technology appraisal 184. Placed on the static list in 2013. **Appraisals in development:** Atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer. NICE technology appraisals guidance [ID1504]. Publication expected February 2020. **Related Guidelines:** Lung cancer: diagnosis and management (2019). NICE guideline 122. **Related Interventional Procedures:** Microwave ablation for treating primary lung cancer and metastases in the lung (2013). NICE interventional procedures guidance 469. **Related Quality Standards:** Lung cancer in adults (2012). NICE quality standard 17. **Related NICE Pathways:** Lung cancer (2018) NICE Pathway
Related National Policy	**NHS England:** NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 18: Adult thoracic surgery services and chapter 105: Specialist cancer services (adults). NHS England (2017/19) Standard contract for cancer: chemotherapy (adult) **Department of Health and Social Care:** Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2.

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Questions for consultation

Have all relevant comparators for pembrolizumab with etoposide and a platinum-based compound been included in the scope? Which treatments are considered to be established clinical practice in the NHS for untreated extensive-stage small-cell lung cancer?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom pembrolizumab with etoposide and a platinum-based compound is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider pembrolizumab with etoposide and a platinum-based compound will fit into the existing NICE Pathway, Lung cancer?

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 pembrolizumab with etoposide and a platinum-based compound 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 pembrolizumab with etoposide and a platinum-based compound 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 pembrolizumab with etoposide and a platinum-based compound 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.

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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).

References

1. Cancer Research UK, Lung cancer: Stages, types and grades (Accessed November 2019)

2. Office for National Statistics (2018) Cancer Registration Statistics, England 2016 (Accessed November 2019)

3. Alvarado-Luna G, Morales-Espinosa D. Treatment for small cell lung cancer, where are we now?—a review. Transl Lung Cancer Res 2016;5(1):26-38

4. Khakwani A, Rich AL, Tata LJ et al. Small-Cell Lung Cancer in England: Trends in Survival and Chemotherapy Using the National Lung Cancer Audit. PLOS ONE. 2014. 9 (2) e89426

5. European Society for Medical Oncology. (2013). Small-cell lung cancer: ESMO Clinical Practice Guidelines. (Accessed October 2018)