NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy.

Background

Head and neck cancers include cancers of the mouth (oral cavity), throat and upper gullet (oropharynx, nasopharynx and hypopharynx), voice box (larynx) and nasal sinuses. The most common type of head and neck cancer is squamous cell carcinoma (approximately 90%)[1]. Although local metastases of head and neck cancer occur frequently (usually spreading through the lymphatic system in the neck), distant metastases are less common.

The annual incidence of head and neck cancer in England is estimated to be 0.024% and 0.010% for males and females (2014 data)[2], respectively, equating to approximately 9,000 new diagnoses each year[2-4]. Approximately 60% of patients present with locally advanced disease at diagnosis. In most of these patients, the disease reoccurs, with approximately 20–30% developing distant metastases[5]. Survival depends on several factors, mainly the origin of the cancer and the stage of the disease at diagnosis.

Treatment options for squamous head and neck cancer vary according to the specific sites involved. In some people with recurrent disease, the tumour is treated with surgery or radiotherapy with curative intent. In people with metastatic disease or who have previously received radiotherapy, palliative chemotherapy is normally given to control the disease and improve quality of life. Platinum-based chemotherapy is commonly used for recurrent or metastatic head and neck cancer. There is no established pathway of care when platinum-based therapy is not clinically appropriate. For disease that has progressed during or after platinum-based therapy, the treatments used in clinical practice in England include taxane-based chemotherapies (such as docetaxel and, less commonly, paclitaxel) or methotrexate. Methotrexate is normally reserved for people whose disease has a poor performance status and who are not fit enough to have a taxane, or as subsequent therapy for people who have had a single-agent taxane.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised monoclonal antibody that acts on the 'programmed death 1' protein (PD‑1).

The PD‑1 protein is part of the immune checkpoint pathway, and blocking its activity may promote an anti-tumour immune response. It is administered intravenously.

Pembrolizumab does not currently have a marketing authorisation in the UK for treating adults with recurrent or metastatic squamous cell carcinoma of the head and neck who have received platinum-based therapy. It has been studied in a randomised controlled trial in this population, compared with methotrexate, docetaxel and cetuximab.

Pembrolizumab has also been studied in trials in adults with head and neck cancer who have not received treatment in the metastatic setting. This population will be considered in a separate NICE technology appraisal of pembrolizumab.

Intervention(s)	Pembrolizumab
Population(s)	Adults with recurrent or metastatic squamous cell carcinoma of the head and neck who have received platinum-based chemotherapy
Comparators	• docetaxel • paclitaxel • methotrexate (for people who are not fit enough to have a taxane) • nivolumab (subject to ongoing NICE appraisal)
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. 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	If the evidence allows, subgroups based on the tumour expression of PD-L1 will be considered. 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	**Appraisals in development** Nivolumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy. NICE technology appraisals guidance [ID971]. Publication expected August 2017. Pembrolizumab for untreated recurrent or metastatic squamous cell carcinoma of the head and neck. Proposed NICE technology appraisal [ID1140]. Publication date to be confirmed. **Related Guidelines** Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over (2016). NICE guideline NG36 Review date TBC. Improving outcomes in head and neck cancers (2004). Cancer service guideline NCG6 Review date June 2020. **Related Quality Standards** Head and neck cancer (2017). NICE quality standard QS146. **Related NICE Pathways** Head and neck cancer NICE pathway

Related National Policy	**NHS England** NHS England (2016) Manual for prescribed specialised services 16/17. Specialist cancer services (adults) 105 (page 228) **National Service Frameworks** Cancer **Other policies** Department of Health, NHS Outcomes Framework 2016-2017, April 2016. Domains 2, 4 and 5.

Questions for consultation

Is diagnostic testing for PD-L1 expression routinely available in NHS practice in England?

Have all relevant comparators for pembrolizumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for recurrent or metastatic head and neck cancer after platinum-based chemotherapy?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom pembrolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider pembrolizumab will fit into the existing NICE pathway for head and neck 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 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 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 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. We welcome comments on the appropriateness and suitability of the cost comparison methodology to this topic.

- Is the new technology 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. Cancer of the head and neck. Patient.co.uk [accessed May 2017].

2. National Institute for Health and Care Excellence (2016). Head and neck cancer NICE quality standard. Draft for consultation.

3. Macmillan cancer support (2014). The Rich Picture. People with Head and Neck cancer [accessed May 2017].

4. http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oral-cancer/incidence#heading-Zero

5. Vermorken JB and Specenier P (2010) Optimal treatment for recurrent/metastatic head and neck cancer. Annals of Oncology 21: vii252–vii261.