NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Final scope

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.

There are approximately 9,000 diagnoses of head and neck cancer in England 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), methotrexate or nivolumab. 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. NICE technology appraisal guidance 490 recommends nivolumab for use within the Cancer Drugs Fund as a treatment option only if the disease has progressed within 6 months of having chemotherapy.

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 recurrent or metastatic squamous cell carcinoma of the head and neck in adults who have had platinum-based therapy. It has been studied as monotherapy in a randomised controlled trial in this population, compared with methotrexate, docetaxel and cetuximab (investigator's choice).

Pembrolizumab has also been studied in trials in adults with head and neck cancer who have not had 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 had platinum-based chemotherapy
Comparators	• Retreatment with 1st line platinum-based chemotherapy (only for people whose disease has had an adequate response) • Nivolumab (for people whose disease has progressed on or within 6 months of having platinum-based chemotherapy; funded via the CDF) • Docetaxel • Paclitaxel • Methotrexate (for people who are not fit enough to have a taxane)
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 commercial schemes for the intervention or comparator technologies will be taken into account. The economic modelling for subgroups should include the costs associated with diagnostic testing for PD-L1 in people with recurrent or metastatic head and neck cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
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	**Related Technology Appraisals** Nivolumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy (2017). NICE Technology Appraisal TA490. CDF review date expected September 2019. **Appraisals in development** Pembrolizumab for untreated recurrent or metastatic squamous cell carcinoma of the head and neck. NICE technology appraisals guidance [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. Partial update in progress,

	publication date June 2018. Improving outcomes in head and neck cancers (2004). Cancer service guideline CSG6 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.

References

1. Cancer of the head and neck. Patient.co.uk. Accessed December 2017.
2. Cancer Research UK (2014) Head and neck cancer incidence statistics. Accessed December 2017.
3. National Institute for Health and Care Excellence (2016). Head and neck cancer NICE quality standard, resource impact report.
4. Macmillan cancer support (2014). The Rich Picture. People with Head and Neck cancer. Accessed December 2017.
5. Vermorken JB and Specenier P (2010) Optimal treatment for recurrent/metastatic head and neck cancer. Annals of Oncology 21: vii252–vii261.