NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab before surgery (neoadjuvant) then with radiotherapy after surgery (adjuvant) for newly diagnosed, resectable, locally advanced, squamous cell head and neck cancer ID6477

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab before surgery (neoadjuvant) then with radiotherapy (with or without cisplatin) after surgery (adjuvant) for untreated, resectable, locally advanced, squamous cell head and neck cancer.

Background

Head and neck cancer is a heterogenous group of malignant tumours that arise in the head and neck at the following sites: skin and lip, oral cavity, oropharynx, larynx, hypopharynx, nasopharynx, salivary glands, nasal cavity and paranasal sinuses, and external auditory meatus and middle ear. The most common histological type of head and neck cancer is squamous cell carcinoma (approximately 90%)[1], particularly that affecting the oral cavity, oropharynx and larynx. Although the local metastases of head and neck cancer occur frequently (usually spreading through the lymphatic system in the neck), distant metastases are less common.

In 2022, there were approximately 11,417 cases of head and neck cancer diagnosed in England.[2] The development of head and neck cancer is associated with tobacco, alcohol and other environmental and dietary factors. Survival depends on several factors, mainly the origin of the cancer and the stage of the disease at diagnosis. In 2020, there were 2,669 deaths from head and neck cancer in England.[3]

Treatment options for untreated squamous head and neck cancer vary according to the specific sites involved and the stage of diagnosis as recommended by NICE guidance NG36. These treatments can include surgical resection, post operative radiotherapy with or without chemotherapy, or neoadjuvant treatment prior to surgery followed by radiotherapy with or without chemotherapy. NICE technology appraisal guidance 145 recommends cetuximab in combination with radiotherapy for locally advanced squamous cell carcinoma where platinum-based chemotherapy is contraindicated. For people with recurrent or metastatic disease NICE technology appraisal 473 recommends cetuximab in combination with platinum-based chemotherapy only if the cancer has started in the oral cavity. NICE technology appraisal 661 recommends pembrolizumab for metastatic or unresectable squamous cell head and neck cancer. NICE technology appraisal 736 recommends nivolumab as a treatment option for adults whose disease has progressed on platinum-based chemotherapy.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) does not currently have a marketing authorisation in the UK for untreated, locally advanced, squamous cell head and neck cancer. Pembrolizumab before surgery (neoadjuvant) then with

radiotherapy (with or without cisplatin) after surgery (adjuvant) is being studied in a randomised controlled trial in adults with untreated, newly diagnosed, resectable, locally advanced, squamous cell head and neck cancer.

Intervention(s)	Pembrolizumab before surgery (neoadjuvant) then with radiotherapy (with or without cisplatin) after surgery (adjuvant)
Population(s)	Adults with untreated, newly diagnosed, resectable, locally advanced squamous cell head and neck cancer
Subgroups	If the evidence allows subgroups will be considered based on: • Whether pembrolizumab is used before and after surgery • PD-L1 tumour proportion score

Comparators	For neoadjuvant (before surgery) or adjuvant (after surgery) head and neck cancer:
	• Established clinical management without pembrolizumab including but not limited to:
	  ○ Platinum-based chemotherapy regimens
	  ○ Radiotherapy with or without chemotherapy
	  ○ Best supportive care
	For locally advanced head and neck cancer:
	• Cetuximab in combination with radiotherapy

Outcomes	The outcome measures to be considered include: • overall survival • event-free survival • progression-free survival • disease-free survival • response times • 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 availability and cost of biosimilar and generic products should 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	**Related technology appraisals:** Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck (2008) NICE technology appraisal guidance 145 Cetuximab for treating recurrent or metastatic squamous cell cancer of the head and neck (2017) NICE technology appraisal guidance 473 Pembrolizumab for untreated metastatic or unresectable recurrent head and neck squamous cell carcinoma (2020) NICE technology appraisal guidance 661 Nivolumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy (2021) NICE technology appraisal guidance 736 **Related NICE guidelines:** Cancer of the upper aerodigestive tract: assessment and management in people aged over 16 and over (2018) guideline NG36 **Related quality standards:** Head and neck cancer (2017) NICE quality standard 146
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan

	NHS England (2023) Manual for prescribed specialist services (2023/2024)

Questions for consultation

Would pembrolizumab be given as both neoadjuvant and adjuvant treatment?

Are there situations where pembrolizumab would be given either only as neoadjuvant or only as an adjuvant treatment?

Are there any clinical features post-surgery that may make patients less likely to benefit from adjuvant treatment?

Where do you consider pembrolizumab will fit into the existing care pathway for head and neck cancer?

Are the subgroups suggested 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?

Are the comparators suggested appropriate?

Please select from the following, will pembrolizumab be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would pembrolizumab be a candidate for managed access?

Do you consider that the use of pembrolizumab can result in any potential 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 committee to take account of these benefits.

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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Vigneswaran N, Williams MD. Epidemiological trends in head and neck cancer and aids in diagnosis. (2014) Oral Maxillofacial Surgery Clin North

2. Cancer Registration Statistics (2022) Cancer registration statistics, England 2020. Accessed February 2025

3. NHS England (2022). Cancer mortality statistics, England 2020. Accessed February 2025