NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab with ipilimumab for untreated recurrent or metastatic squamous cell cancer of the head and neck cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab with ipilimumab within its marketing authorisation for untreated recurrent or metastatic squamous cell cancer of the head and neck.

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]. Approximately 60% of patients present with locally advanced disease at diagnosis. In most of these patients, the disease reoccurs, with approximately 20 to 30% developing distant metastases[3]. 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. NICE technology appraisal guidance 473 recommends cetuximab in combination with platinum-based chemotherapy as a treatment option only if the cancer started in the oral cavity. NICE technology appraisal guidance 490 recommends nivolumab as a treatment option within the Cancer Drugs Fund for adults whose disease has progressed on platinum-based chemotherapy[a].

[a] Products recommended for use in the Cancer Drugs Fund after 1 April 2016 should not be considered as comparators, or appropriately included in a treatment sequence, in subsequent

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a humanised monoclonal antibody that targets and blocks a receptor on the surface of lymphocytes known as PD-1. This receptor is part of the immune checkpoint pathway, and blocking its activity may promote an anti-tumour immune response. Nivolumab is administered by intravenous infusion.

Ipilimumab (Yervoy, Bristol-Myers Squibb) is a fully human antibody that binds to and blocks the activity of cytotoxic T lymphocyte-associated antigen 4 (CTLA-4), thereby sustaining the immune attack on cancer cells. It is administered intravenously.

Nivolumab with ipilimumab does not currently have a marketing authorisation in the UK for untreated recurrent or metastatic squamous cell carcinoma of the head and neck. It has been studied in clinical trials in people with untreated recurrent or metastatic squamous cell carcinoma of the head and neck whose disease is suitable for platinum-based chemotherapy. It was compared with cetuximab in combination with cisplatin or carboplatin and fluorouracil and nivolumab monotherapy.

Intervention(s)	Nivolumab with ipilimumab
Population(s)	Adults with recurrent or metastatic squamous cell carcinoma of the head and neck previously untreated in the recurrent or metastatic setting and for whom platinum-based chemotherapy is an option
Comparators	• Platinum-based chemotherapy regimens • Cetuximab with platinum-based chemotherapy (only if the cancer started in the oral cavity)
Outcomes	The outcome measures to be considered include: • overall survival • progressions-free survival • response rate • adverse effects of treatment • health-related quality of life.

relevant appraisals. https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisal-guidance/cancer-drugs-fund/CDF-comparator-position-statement.pdf

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 arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The economic modelling for subgroups should include the costs associated with diagnostic testing for PD-L1 status 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 tumour expression of PD-L1 status for oropharyngeal cancer will be considered. The availability and cost of biosimilar products should be taken into account. 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 squamous cell carcinoma of the head and neck after platinum-based chemotherapy (2017) NICE technology appraisal 490. Review date November 2020. Cetuximab for treating recurrent or metastatic squamous cell cancer of the head and neck (2017) NICE technology appraisal 473. Review date August 2020. **Terminated appraisals:** Pembrolizumab for treating recurrent or metastatic

	squamous cell carcinoma of the head and neck after platinum-based chemotherapy. NICE technology appraisals guidance ID1066. **Appraisals in development (including suspended appraisals):** Pembrolizumab for untreated recurrent or metastatic squamous cell carcinoma of the head and neck. NICE technology appraisals guidance ID1140. Publication expected February 2020. Head and neck cancer - contusugene ladenovec. NICE technology appraisals guidance [ID76]. Publication date to be confirmed. **Related Guidelines:** Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over (2016, updated 2018). NICE guideline 36. 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 146. **Related NICE Pathways:** Upper aerodigestive tract cancer NICE pathway (2017, updated 2019).
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan. NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Specialist cancer services (adults) 105 (page 274). Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2, 3 and 5.

Questions for consultation

Is the population included in the scope defined appropriately?

Is diagnostic testing for PD-L1 expression routinely available in NHS practice in England for head and neck cancer?

Have all relevant comparators for pembrolizumab been included in the scope? Which treatments are considered to be established clinical practice in the

NHS for treating recurrent or metastatic squamous cell head and neck cancer?

Are the outcomes listed appropriate?

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

Where do you consider nivolumab with ipilimumab will fit into the existing NICE pathway, upper aerodigestive tract 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 nivolumab with ipilimumab 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 nivolumab with ipilimumab 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 nivolumab with ipilimumab 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 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 April 2019.
2. Cancer Research UK (2014) Head and neck cancer incidence statistics. Accessed December 2017.
3. Vermorken JB and Specenier P (2010) Optimal treatment for recurrent/metastatic head and neck cancer. Annals of Oncology 21: vii252–vii261.

