NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab with ipilimumab for treating squamous cell carcinoma of the head and neck

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab with ipilimumab within its marketing authorisation for treating squamous cell carcinoma 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 [2-4]. 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. Platinum-based chemotherapy is commonly used for recurrent or metastatic head and neck cancer. NICE technology appraisal 473 recommends cetuximab with platinum-based chemotherapy as a treatment option for recurrent or metastatic squamous cell cancer of the head and neck in adults only if the cancer started in the oral cavity.There is no established pathway of care when platinum-based therapy is not clinically appropriate. NICE technology appraisal 145 recommends cetuximab in combination with radiotherapy as a treatment option for locally advanced squamous cell cancer of the head and neck in people whose Karnofsky performance-status score is 90% or greater and for whom all forms of platinum-based chemotherapy are contraindicated.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb Pharmaceuticals Ltd) 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 IV 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 in combination with ipilimumab does not currently have a marketing authorisation in the UK for squamous cell carcinoma of the head and neck. It has been studied in a randomised controlled trial compared with cetuximab plus cisplatin/carboplatin plus fluorouracil as first line therapy in adults with recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) that is not amenable to curative therapy.

Intervention(s)	Nivolumab in combination with ipilimumab
Population(s)	Adults with recurrent or metastatic squamous cell carcinoma of the head and neck that is not amenable to curative therapy
Comparators	• cetuximab in combination with platinum-based chemotherapy (for cancers that started in the oral cavity) • platinum-based chemotherapy regimens
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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 tumour expression of PD-L1 status 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:** Cetuximab for treating recurrent or metastatic squamous cell cancer of the head and neck (2017) NICE technology appraisal guidance TA473. Review date August 2020. Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck (2008) NICE technology appraisal guidance TA145. Guidance on static list. **Appraisals in development (including suspended appraisals):** Cancer of the upper aereodigestive tract: assessment and management in people aged 16 and over (2016) NICE guidance 36 [being updated] Pembrolizumab for untreated recurrent or metastatic squamous cell carcinoma of the head and neck [ID1140] NICE technology appraisal guidance. Publication date TBC

	Related Guidelines: Improving outcomes in head and neck cancers (2004) NICE guideline CSG6 **Related Interventional Procedures:** Thoracoscopic excision of mediastinal parathyroid tumours (2007) NICE interventional procedures guidance 247 Interstitial photodynamic therapy for malignant parotid tumours (2008) NICE interventional procedures guidance 259 **Related Quality Standards:** Head and neck cancer (2017) NICE quality standard 146 Suspected cancer (2016) NICE quality standard 124 **Related NICE Pathways:** Upper aerodigestive tract cancer (2017) NICE pathway
Related National Policy	**NHS England** NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Specialist cancer services (adults) 105 (page 234) NHS England. National Programmes of care and clinical reference groups. B03. Specialised Cancer Surgery. Cancer: Head and Neck (Adult) (accessed 14 06 2018) **National Service Frameworks** Cancer **Other policies** Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 2, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

How is nivolumab with ipilimumab expected to be used in clinical practice?

- Would it be used as an alternative to platinum-containing regimens or when platinum-containing regimens are not appropriate?
- Which treatments are considered curative for squamous cell carcinoma of the head and neck?

Have all relevant comparators for nivolumab with ipilimumab been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for head and neck cancer not amenable to curative therapy?
- Should best supportive care be included as a comparator?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other 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).

References

1. Cancer of the head and neck. Patient.co.uk. Accessed June 2018.

2. Cancer Research UK (2014) Head and neck cancer incidence statistics. Accessed June 2018.

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 June 2018.

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

