

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

**Pembrolizumab with platinum-based chemotherapy for untreated advanced oesophageal cancer**

**Draft scope**

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of pembrolizumab with platinum-based chemotherapy within its marketing authorisation for unresectable locally advanced or metastatic oesophageal cancer that has not been previously treated.

**Background**

Oesophageal cancer is a malignant tumour arising from cells lining the oesophagus (gullet), which is the muscular tube through which food passes from the throat to the stomach. The two main types of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. In the upper and middle part of the oesophagus, cancers tend to be squamous cell carcinomas, which develop from cells that make up the inner lining of the oesophagus. Cancers in the lower part tend to adenocarcinomas, which usually develop in gland cells.<sup>1</sup> The most common symptoms are difficulty swallowing, food regurgitation, nausea or vomiting, unexplained weight loss and persistent indigestion or cough.<sup>2</sup>

Oesophageal cancer is more common in men than women. In 2017, there were 2,289 new diagnoses in women and 5,280 in men (a total of 7,569 new cases) in England.<sup>3</sup> The risk of developing oesophageal cancer increases with age. Around 40% of all new cases in UK are diagnosed in people aged over 75.<sup>4</sup> Because of the nature of symptoms, oesophageal cancer is often diagnosed at an advanced stage. On average 70-80% are diagnosed at stage 3 (locally advanced) or 4 (metastatic).<sup>5</sup> For adults diagnosed between 2013 and 2017 in England, the 1-year survival rate for people with oesophageal cancer is around 47% and 5-year survival rate is 17%.<sup>6</sup>

Clinical guideline NG83 recommends palliative combination platinum-based chemotherapy (doublet or triplet treatment) for people with locally advanced or metastatic cancer. Similarly, chemotherapy, local tumour treatment (including stenting or palliative radiotherapy) or best supportive care is recommended for people with non-metastatic oesophageal cancer that is not suitable for surgery and cannot be encompassed within a radiotherapy field.

**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 untreated advanced oesophageal cancer. It has been studied in a randomised clinical trial, in combination with cisplatin and fluorouracil versus cisplatin plus

fluorouracil in people with previously untreated locally advanced unresectable, or metastatic oesophageal cancer.

<b>Intervention(s)</b>	Pembrolizumab with platinum-based chemotherapy
<b>Population(s)</b>	Adults with unresectable locally advanced or metastatic oesophageal cancer
<b>Comparators</b>	Platinum-based chemotherapy including doublet (cisplatin or oxaliplatin with fluorouracil or capecitabine) and triplet treatments (cisplatin or oxaliplatin with fluorouracil or capecitabine plus epirubicin)
<b>Outcomes</b>	The outcome measures to be considered include: <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rate</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.</p>
<b>Other considerations</b>	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.
<b>Related NICE recommendations and NICE Pathways</b>	<p><b>Related Technology Appraisals:</b></p> <p>None</p> <p><b>Appraisals in development (including suspended appraisals):</b></p> <p><a href="#">Nivolumab with cisplatin and fluorouracil for untreated advanced oesophageal squamous cell carcinoma. [ID2712]</a></p>

	<p>Proposed NICE technology appraisal guidance. Publication date to be confirmed.</p> <p><a href="#">Pembrolizumab with trastuzumab and chemotherapy for untreated HER2-positive advanced gastric or gastro-oesophageal junction cancer</a> [ID3742] Proposed NICE technology appraisal guidance. Publication date to be confirmed.</p> <p><a href="#">Pembrolizumab for gastric or gastroesophageal junction adenocarcinoma</a> [ID1305] Proposed NICE technology appraisal guidance. Publication date to be confirmed.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">Oesophago-gastric cancer: assessment and management in adults</a> (2018). NICE guideline 83 Review date: not published.</p> <p><b>Related Interventional Procedures:</b></p> <p><a href="#">Endoscopic submucosal dissection of oesophageal dysplasia and neoplasia</a> (2010) NICE interventional procedures guidance 355</p> <p><a href="#">Palliative photodynamic therapy for advanced oesophageal cancer</a> (2007) NICE interventional procedures guidance 206</p> <p><b>Related Quality Standards:</b></p> <p><a href="#">Oesophago-gastric cancer</a> (2018) NICE quality standard 176</p> <p><b>Related NICE Pathways:</b></p> <p><a href="#">Oesophageal and gastric cancer</a> (last updated 2018) NICE Pathway</p>
<p><b>Related National Policy</b></p>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a> NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a> Chapter 2A</p> <p>Department of Health (2014) <a href="#">The national cancer strategy: 4<sup>th</sup> annual report</a> Chapters 4 and 5</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 4 and 5 <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a></p>

**Questions for consultation**

Is it appropriate to include people with gastroesophageal junction cancer in the scope?

- Is oesophageal cancer clinically distinct to gastroesophageal junction cancer?

Have all relevant comparators for pembrolizumab with platinum-based chemotherapy been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for untreated unresectable locally advanced, or metastatic oesophageal cancer?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom pembrolizumab with platinum-based chemotherapy is expected to be more clinically effective and cost effective or other groups that should be examined separately?

- If evidence allows, should squamous cell carcinoma, adenocarcinoma and adenosquamous cell carcinoma be considered separately?

Where do you consider pembrolizumab with platinum-based chemotherapy will fit into the existing NICE pathway, [oesophageal and gastric 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, fluoropyrimidines and cisplatin are 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 with platinum-based chemotherapy 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 with platinum-based chemotherapy 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

Draft scope for the appraisal of pembrolizumab with platinum-based chemotherapy for untreated advanced oesophageal cancer

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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. Macmillan cancer support (2020) [Signs and symptoms of oesophageal cancer](#). Accessed April 2020
2. Macmillan cancer support (2020) [What is oesophageal cancer?](#) Accessed April 2020
3. Office for National Statistics (2019) [Cancer registration statistics, England, 2017](#). Accessed April 2020.
4. Cancer Research UK (2019) [Oesophageal cancer incidence statistics](#). Accessed April 2020.
5. NCRAS (2019) [Stage breakdown by CCG 2017](#). Accessed April 2020.
6. Office for National Statistics (2019) [Cancer survival in England - adults diagnosed](#) Accessed April 2020.