

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

**Pembrolizumab for previously treated oesophageal or gastro-oesophageal junction cancer**

**Final scope**

**Remit/appraisal objective**

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for previously treated oesophageal or gastro-oesophageal junction cancer.

**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. Together, these account for over 95% of oesophageal cancer cases<sup>1</sup>. Oesophageal cancer is the 13<sup>th</sup> most common cancer in the UK, with an estimated 9,000 new diagnoses in the UK each year, accounting for approximately 3% of all cases<sup>2</sup>. It is more common in men than women, with approximately 19 new cases for every 100,000 males and 9 for every 100,000 females. Around 80% of all new cases are diagnosed in people aged over 60 years<sup>2</sup>. Because of the nature of symptoms, oesophageal cancer is often diagnosed at an advanced stage, with around 70-80% diagnosed at stage 3 (locally advanced) or 4 (metastatic)<sup>2</sup>.

Gastro-oesophageal junction (GOJ) cancer describes cancers where the centre of the tumour is less than 5cm above or below where the oesophagus meets the stomach. The most common type of stomach cancer is gastric or GOJ adenocarcinoma, which affects about 95% of people with the disease<sup>3</sup>. It is more common in men than women, with approximately 13.6 new cases for every 100,000 males and 7.2 for every 100,000 females in UK in 2015<sup>4</sup>.

Surgery with or without radiotherapy can be used to treat early oesophageal and GOJ cancer. Chemotherapy is sometimes used when surgery with or without radiotherapy is not effective.

The aim of treatment in advanced oesophageal and GOJ cancer is primarily to prevent progression, extend survival and relieve symptoms with minimal adverse effects. There is no standard treatment for previously treated advanced oesophageal and GOJ cancer. Best supportive care is commonly used at this stage. Chemotherapy may also be an option. NICE technology appraisal 378 does not recommend ramucirumab for treating advanced gastric cancer or GOJ adenocarcinoma previously treated with chemotherapy.

**The technology**

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised monoclonal anti-programmed cell death-1 (PD-1) antibody (IgG4/kappa isotype with a stabilising sequence alteration in the Fc region) produced in Chinese hamster ovary cells by recombinant DNA technology. It is administered intravenously.

Pembrolizumab does not have a marketing authorisation in the UK for oesophageal or GOJ cancer. It is being studied in a clinical trial compared with paclitaxel, docetaxel or irinotecan monotherapy in people with advanced or metastatic adenocarcinoma or squamous cell carcinoma of the oesophagus or Siewert type I adenocarcinoma of the GOJ that has progressed after first-line standard therapy.

<b>Intervention(s)</b>	Pembrolizumab
<b>Population(s)</b>	People with previously treated oesophageal or gastro-oesophageal junction cancer
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• Chemotherapy (such as paclitaxel, docetaxel, or irinotecan monotherapy)</li> <li>• Best supportive care (including but not limited to antiemetics, blood transfusions, oesophageal stents)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• objective response rate</li> <li>• progression-free survival</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 will be taken into account.</p>

<p><b>Other considerations</b></p>	<p>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.</p>
<p><b>Related NICE recommendations and NICE Pathways</b></p>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">Ramucirumab for treating advanced gastric cancer or gastro-oesophageal junction adenocarcinoma previously treated with chemotherapy</a> (2016) NICE technology appraisal guidance 378. Next review date January 2019.</p> <p><a href="#">Trastuzumab for the treatment of HER2-positive metastatic gastric cancer</a> (2010) NICE technology appraisal guidance 208. Guidance on static list.</p> <p><b>Appraisals in development (including suspended appraisals)</b></p> <p><a href="#">Nivolumab for previously treated gastric or gastro-oesophageal junction cancer</a>. NICE technology appraisals guidance [ID1118]. Publication expected: TBC.</p> <p><a href="#">Pembrolizumab for gastric or gastroesophageal junction adenocarcinoma</a> NICE technology appraisal guidance [ID1305]. Publication expected: TBC</p> <p><a href="#">Avelumab for treating gastric or gastro-oesophageal junction cancer after 2 therapies</a> NICE technology appraisal guidance [ID1289]. Publication expected: TBC</p> <p><a href="#">Nivolumab for previously treated oesophageal cancer</a> NICE technology appraisal guidance [ID1249]. Publication expected: January 2020</p> <p><a href="#">Pembrolizumab for previously treated metastatic gastric or gastro-oesophageal junction cancer</a> NICE technology appraisal guidance [ID1168]. Publication expected: TBC</p> <p><a href="#">Pertuzumab for untreated metastatic HER2-positive gastric or gastro-oesophageal junction cancer</a> NICE technology appraisal guidance [ID1096]. Appraisal suspended</p> <p><b>Related Guidelines:</b></p>

	<p><a href="#">Oesophago-gastric cancer: assessment and management in adults</a> (2018). NICE guideline NG83. Review date January 2020.</p> <p><a href="#">Barrett's oesophagus: ablative therapy (2010)</a>. NICE guideline CG106. Review date: TBC</p> <p><b>Related Interventional Procedures:</b></p> <p><a href="#">Laparoscopic gastrectomy for cancer</a> (2008). NICE interventional procedures guidance 269.</p> <p><b>Related NICE Pathways:</b></p> <p><a href="#">Oesophageal and gastric cancer overview</a> (2018) NICE pathway</p>
<b>Related National Policy</b>	<p><a href="#">NHS Long term plan (2019)</a></p> <p>NHS England (2017/18) <a href="#">Manual for Prescribed Specialised Services</a>. Chapter 105 Specialist cancer services (adults)</p> <p>NHS England (2013) <a href="#">NHS Standard contract for cancer: Oesophageal and gastric (adult) section B part 1- service specification</a> REF: B11/S/a</p> <p>Department of Health, <a href="#">NHS Outcomes Framework 2016-2017</a> (published 2016): Domain 1.</p>

## References

1. Macmillan Cancer Support. Oesophageal Cancer. 2015 [cited 2018 03.04.]; Available from: <http://www.macmillan.org.uk/information-and-support/oesophageal-gullet-cancer/understanding-cancer/types-oesophageal-cancer.html>
2. Cancer Research UK. Oesophageal Cancer Incidence Statistics. 2015 (reviewed 2018) [cited 2018.02.18]; Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/incidence#heading-Zero>
3. Types of stomach cancer (2016). [Macmillan Cancer Support](#). Accessed January 2019
4. Cancer Research UK. Stomach cancer incidence statistics. 2015 (reviewed 2019) [cited 2019.01.10]; Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/stomach-cancer/incidence>