

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab for adjuvant treatment of oesophageal or gastro-oesophageal junction cancer

Draft scope

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for adjuvant treatment of resected 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. Cancers in the upper or middle part of the oesophagus are usually squamous cell carcinomas. Cancers in the lower oesophagus are usually adenocarcinomas. This includes those in the junction where the oesophagus joins the stomach<sup>1</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<sup>2</sup>.

There were an estimated 7,569 new diagnoses of oesophageal cancer in England in 2017<sup>3</sup>. It is more common in men than women, with approximately 19 new cases for every 100,000 males and 8 for every 100,000 females. Around 41% of all new cases in the UK, from 2015-2017, were diagnosed in people aged 75 and over<sup>3</sup>. Initial symptoms of disease are vague and are similar to other stomach conditions, but symptoms of advanced stages may include a lack of appetite and subsequent weight loss; fluid in the abdomen, and blood in the stool. Because of the nature of symptoms, oesophageal cancer is often diagnosed at a late stage, with around 70-80% diagnosed at stage 3 (locally advanced) or 4 (metastatic) and 20-30% diagnosed at an early stage (stage 1 or 2)<sup>3</sup>.

Over the past few years there has been a rapid increase in incidence of tumours at the junction of the oesophagus and stomach. These tend to come from changes in the lining of the oesophagus, in turn leading to adenocarcinoma of the lowest part of the oesophagus, which goes across the gastroesophageal junction.

Surgery with chemotherapy or chemoradiotherapy can be used to treat early oesophageal and gastro-oesophageal junction cancer. NICE clinical guideline (NG83) recommends that patients with localised oesophageal and gastro-oesophageal junctional adenocarcinoma may receive chemotherapy before or before and after surgery, or chemoradiotherapy before surgery. For patients with squamous cell carcinoma of the oesophagus, NICE clinical guideline (NG83) recommends radical chemoradiotherapy alone or chemoradiotherapy before surgery. The most common chemotherapy agents include fluorouracil, capecitabine, cisplatin, epirubicin and docetaxel<sup>4</sup>. In advanced oesophageal or gastro-oesophageal junction cancer,

the main aim of treatment is primarily palliative; to prevent progression, extend survival and relieve symptoms with minimal adverse effects.

**The technology**

Nivolumab (Opdivo, Bristol-Myers Squibb) is a human monoclonal antibody that targets 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 intravenously.

Nivolumab does not currently have a marketing authorisation for adjuvant treatment of oesophageal cancer in the UK. It is being studied in a clinical trial versus placebo in people with resected oesophageal or gastro-oesophageal junction cancer who have previously had treatment with chemoradiotherapy followed by surgery.

<b>Intervention(s)</b>	Nivolumab
<b>Population(s)</b>	Adults with resected oesophageal or gastro-oesophageal junction cancer.
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• Routine surveillance</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>• disease-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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>

<b>Other considerations</b>	<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>
<b>Related NICE recommendations and NICE Pathways</b>	<p>Appraisals in development:  <a href="#">Pembrolizumab with chemotherapy and surgery for treating resectable gastric or gastro-oesophageal junction cancer</a>. Proposed NICE technology appraisal [ID2696]. Publication date to be confirmed.</p> <p>Related Guidelines:  <a href="#">Oesophago-gastric cancer: assessment and management in adults</a> (2018). NICE guideline NG83. Review date: TBC</p> <p>Related Interventional Procedures:  <a href="#">Minimally invasive oesophagectomy</a> (2011) NICE interventional procedures guidance 407  <a href="#">Photodynamic therapy for early stage oesophageal cancer</a> (2006) NICE interventional procedures guidance 200</p> <p>Related Quality Standards:  <a href="#">Oesophago-gastric cancer</a> (2018) NICE quality standard 176</p> <p>Related NICE Pathways:  <a href="#">Oesophageal and gastric cancer</a> (2020) NICE pathway.</p>
<b>Related National Policy</b>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2018) <a href="#">NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View'</a></p> <p>NHS England (2019) <a href="#">Proton Beam Therapy for Oesophageal Cancer in Adults (1874)</a></p> <p>NHS England (2019) <a href="#">Clinical Commissioning Policy: 18F-fluorodeoxyglucose (FDG) positron emission tomography-computed-tomography (PET CT) as part of radical radiotherapy treatment planning for oesophageal cancer (all ages) Ref: NHS England: 170115P</a></p> <p>NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a>. Chapter 105, Specialist Cancer services (adults)</p> <p>Department of Health (2016) <a href="#">NHS Outcomes Framework 2016-2017</a>. Domains 1 and 2.</p>

### Questions for consultation

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

Which treatments are considered established clinical practice in the NHS for resected oesophageal or gastro-oesophageal cancer?

Would nivolumab only be used in people who had chemoradiotherapy and surgery, or also in people who had chemotherapy and surgery?

Would nivolumab be used in people receiving perioperative chemotherapy (i.e. chemotherapy before and after surgery)?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom nivolumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Would oesophageal and gastro-oesophageal adenocarcinoma and squamous cell carcinoma of oesophagus be expected to respond differently to nivolumab?

Where do you consider nivolumab will fit into the existing [Oesophageal and gastric cancer NICE pathway](#)?

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 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 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 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. Macmillan Cancer Support. Oesophageal Cancer. Available from: <http://www.macmillan.org.uk/information-and-support/oesophageal-gullet-cancer/understanding-cancer/types-oesophageal-cancer.html> Accessed September 2020
2. Cancer Research UK. About gastro oesophageal junction cancer. 2018. Available from: <https://www.cancerresearchuk.org/about-cancer/gastro-oesophageal-junction-cancer/about> Accessed September 2020
3. Cancer Research UK. Oesophageal Cancer Incidence Statistics. 2017. Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer/incidence#heading-Zero> Accessed September 2020
4. Cancer Research UK. Oesophageal cancer – chemotherapy treatment. Available from: <https://about-cancer.cancerresearchuk.org/about-cancer/oesophageal-cancer/treatment/chemotherapy/chemotherapy-treatment> Accessed September 2020