NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab for previously treated oesophageal or gastro-oesophageal junction cancer

Draft scope

Draft 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[1]. Oesophageal cancer is the 13th most common cancer in the UK, with an estimated 9,211 new diagnoses in the UK each year, accounting for approximately 3% of all cases[2]. 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[2]. 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)[2].

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[3]. It is more common in men than women, with approximately 3,500 cases diagnosed in men, and 1,800 cases in women in England in 2014[4].

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. There is currently no standard treatment for previously treated advanced oesophageal or GOJ cancer in the UK.

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. Taxane (docetaxel or paclitaxel) monotherapy may be an option or combination therapy may be given once again. 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.

Intervention(s)	Pembrolizumab
Population(s)	People with previously treated oesophageal or gastro-oesophageal junction cancer.
Comparators	• Chemotherapy (such as paclitaxel, docetaxel, or irinotecan monotherapy) • best supportive care (including but not limited to antiemetics, blood transfusions, oesophageal stents)
Outcomes	The outcome measures to be considered include: • overall survival • objective response rate • progression-free survival • 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 will be taken into account.

Other considerations	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:** Ramucirumab for treating advanced gastric cancer or gastro–oesophageal junction adenocarcinoma previously treated with chemotherapy (2016) NICE technology appraisal guidance 378. Next review date January 2019. Trastuzumab for the treatment of HER2-positive metastatic gastric cancer (2010) NICE technology appraisal guidance 208. Guidance on static list. **Appraisals in development (including suspended appraisals)** Nivolumab for previously treated gastric or gastro-oesophageal junction cancer. NICE technology appraisals guidance [ID1118]. Publication expected August 2018. Pembrolizumab for gastric or gastroesophageal junction adenocarcinoma NICE technology appraisal guidance [ID1305]. Publication expected: TBC Avelumab for treating gastric or gastro-oesophageal junction cancer after 2 therapies NICE technology appraisal guidance [ID1289]. Publication expected: TBC Nivolumab for previously treated oesophageal cancer NICE technology appraisal guidance [ID1249]. Publication expected: TBC Pembrolizumab for previously treated metastatic gastric or gastro-oesophageal junction cancer NICE technology appraisal guidance [ID1168]. Appraisal suspended Pertuzumab for untreated metastatic HER2-positive gastric or gastro-oesophageal junction cancer NICE technology appraisal guidance [ID1096]. Appraisal suspended **Related Guidelines:**

	Oesophago-gastric cancer: assessment and management in adults (2018). NICE guideline NG83. Review date January 2020. Barrett's oesophagus: ablative therapy (2010). NICE guideline CG106.Review date: TBC **Related Interventional Procedures:** Laparoscopic gastrectomy for cancer (2008). NICE interventional procedures guidance 269. **Related NICE Pathways:** Oesophageal and gastric cancer overview (2018) NICE pathway
Related National Policy	NHS England (2017) Next steps on the five year forward view NHS England (2014) NHS Five year forward view NHS England (2017/18) Manual for Prescribed Specialised Services. Chapter 105 Specialist cancer services (adults) NHS England (2013) NHS Standard contract for cancer: Oesophageal and gastric (adult) section B part 1- service specification REF: B11/S/a Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domain 1.

Questions for consultation

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

Which treatments are considered to be established clinical practice in the NHS for previously treated oesophageal or gastro-oesophageal junction cancer?

- Which chemotherapies are used?
- How is BSC defined and what treatments are used?

Are the outcomes listed appropriate?

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

Where do you consider pembrolizumab will fit into the existing NICE pathway on 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 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 pembrolizumab 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 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. 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). Cancer Research UK. Accessed December 2016

4. Stomach cancer statistics. Cancer Research UK. Accessed December 2016.

