

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab with chemotherapy for treating HER2 negative advanced gastric or gastro-oesophageal junction adenocarcinoma

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating previously untreated HER2 negative advanced gastric or gastro-oesophageal junction adenocarcinoma.

Background

Gastric cancer is a malignant tumour arising from cells in the stomach. The most common type of stomach cancer is gastric or gastro-oesophageal junction¹. Gastro-oesophageal junction cancer describes cancers where the centre of the tumour is less than 5cm above or below where the oesophagus meets the stomach¹. Oesophageal cancer is a malignant tumour arising from cells lining the oesophagus. The most common histological subtype of gastric, gastro-oesophageal junction and oesophageal cancer is adenocarcinoma, with 95% of gastric cancers being adenocarcinomas^{2,3}.

Gastric cancer is more common in men than women, with approximately 3,378 cases diagnosed in men, and 1,764 cases in women in England in 2017⁴. Around half of all new cases of gastric cancer in the UK are diagnosed in people aged 75 years and over⁴. Oesophageal cancer is also more common in men than women, with approximately 5,280 cases diagnosed in men, and 2,289 cases in women in England in 2017⁵. Around 41% of all new cases of oesophageal cancer in the UK are diagnosed in people aged 75 and over⁵.

Initial symptoms of gastric or oesophageal cancer 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, vomiting blood, blood in the stool or black stool. Because of the nature of symptoms, gastric and oesophageal cancer are often diagnosed at an advanced stage, with around 17% and 29% diagnosed at stage 3 (locally advanced), and 34% and 30% diagnosed at stage 4 (metastatic) for gastric and oesophageal cancer respectively in England in 2014^{4,5}. The 5-year survival for people diagnosed with stomach cancer and oesophageal cancer between 2013 and 2017 was 21.6% and 17% respectively⁶.

The aim of treatment in advanced or metastatic gastric, gastro-oesophageal junction cancer or oesophageal adenocarcinoma is primarily palliative; to prevent progression, extend survival and relieve symptoms with minimal adverse effects. NICE technology appraisal 191 recommends capecitabine in combination with a platinum-containing agent as an option for inoperable untreated advanced gastric cancer. NICE clinical guideline 83 recommends chemotherapy combination regimens for people with gastro-oesophageal cancer who have a performance status 0 to 2 and no significant comorbidities. Chemotherapy regimens include doublet treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin or triplet

treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin plus epirubicin.

NICE technology appraisal 737 recommends pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy as an option for untreated locally advanced unresectable or metastatic carcinoma of the oesophagus or HER2-negative gastro-oesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a combined positive score (CPS) of 10 or more. NICE technology appraisal 857 recommends nivolumab with platinum- and fluoropyrimidine-based chemotherapy as an option for untreated HER2-negative, advanced or metastatic gastric, gastro-oesophageal junction or oesophageal adenocarcinoma in adults whose tumours express PD-L1 with a CPS of 5 or more.

The technology

Pembrolizumab (Keytruda, MSD) with chemotherapy does not currently have a marketing authorisation in the UK for untreated HER2-negative advanced gastric cancer. Pembrolizumab in combination with platinum- and fluoropyrimidine-based chemotherapy has a marketing authorisation in the UK for the first-line treatment of HER2 negative gastro-oesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a combined positive score equal to or greater than 10.

Pembrolizumab in combination with chemotherapy is currently being studied in clinical trials as a first-line treatment in people with locally advanced unresectable or metastatic HER2-positive gastric or gastro-oesophageal junction adenocarcinoma.

Intervention(s)	Pembrolizumab with chemotherapy
Population(s)	People with previously untreated HER2 negative advanced gastric or gastro-oesophageal junction adenocarcinoma
Subgroups	<p>If the evidence allows, the following subgroups will be considered:</p> <ul style="list-style-type: none"> • Subgroups by PD-L1 status • Subgroups by tumour location
Comparators	<ul style="list-style-type: none"> • Chemotherapy only, which includes: <ul style="list-style-type: none"> ○ doublet treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin ○ triplet treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin plus epirubicin • For people with untreated HER2-negative advanced or metastatic gastric or gastro-oesophageal junction adenocarcinoma whose tumours express PD-L1 with a CPS of 5 or more: <ul style="list-style-type: none"> ○ Nivolumab with platinum- and fluoropyrimidine-based chemotherapy

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.
Economic analysis	<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>
Other considerations	<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>
Related NICE recommendations	<p>Related technology appraisals:</p> <p>Nivolumab with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2-negative advanced gastric, gastro-oesophageal junction or oesophageal adenocarcinoma (2023). NICE technology appraisals guidance 857.</p> <p>Trifluridine–tipiracil for treating metastatic gastric cancer or gastro-oesophageal junction adenocarcinoma after 2 or more treatments (2022). NICE technology appraisals guidance 852.</p> <p>Pembrolizumab with platinum-based chemotherapy for untreated advanced oesophageal cancer (2021). NICE technology appraisals guidance 737.</p> <p>Ramucirumab for treating advanced gastric cancer or gastro-oesophageal junction adenocarcinoma previously treated with chemotherapy (2016). NICE technology appraisal guidance 378.</p> <p>Capecitabine for the treatment of advanced gastric cancer (2010). NICE technology appraisal 191.</p>

	<p>Related technology appraisals in development:</p> <p>Pembrolizumab with trastuzumab and chemotherapy for untreated HER2-positive advanced gastric or gastro-oesophageal junction cancer. NICE technology appraisal guidance [ID3742]. Publication date to be confirmed.</p> <p>Pembrolizumab with chemotherapy and surgery for treating resectable gastric or gastro-oesophageal junction cancer. NICE technology appraisal guidance [ID2696]. Publication date to be confirmed.</p> <p>Related NICE guidelines:</p> <p>Oesophago-gastric cancer: assessment and management in adults (2018). NICE guideline 83.</p> <p>Related interventional procedures:</p> <p>'Laparoscopic gastrectomy for cancer' (2008). NICE interventional procedures guidance 269.</p> <p>Related quality standards:</p> <p>Oesophago-gastric cancer (2018) NICE quality standard 176.</p>
Related National Policy	<p>The NHS Long Term Plan (2019) NHS Long Term Plan</p> <p>NHS England (2018) NHS manual for prescribed specialist services (2018/2019)</p>

Questions for consultation

Where do you consider pembrolizumab with chemotherapy will fit into the existing care pathway for HER2 negative advanced gastric or gastro-oesophageal junction adenocarcinoma?

Given that pembrolizumab with chemotherapy is already recommended for people with previously untreated HER2-negative advanced gastro-oesophageal junction adenocarcinoma with a PDL1 CPS of over 10 in NICE Technology Appraisal 737, should this appraisal be limited to people with previously untreated advanced HER2-negative gastric cancer?

Are the comparators appropriate? Are both doublet and triplet chemotherapy combinations used in clinical practice?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom pembrolizumab with chemotherapy is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Would pembrolizumab with chemotherapy be a candidate for managed access?

Do you consider that the use of pembrolizumab with chemotherapy can result in any potential 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 committee to take account of these benefits.

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 with chemotherapy 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

References

1. Cancer Research UK. [About gastro oesophageal junction cancer](#). 2022. Accessed December 2022.
2. Macmillan Cancer Support. [Types of stomach cancer](#). Accessed December 2022.
3. Cancer Research UK. [Oesophageal cancer types](#). Accessed December 2022.
4. Cancer Research UK. [Stomach cancer incidence statistics](#). Accessed December 2022.
5. Cancer Research UK. [Oesophageal cancer incidence statistics](#). 2017. Accessed December 2022.
6. Office for National Statistics (2019). [Cancer survival in England - adults diagnosed](#). Accessed December 2022.