NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated unresectable advanced malignant pleural mesothelioma ID4044

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pembrolizumab with pemetrexed and platinum-based chemotherapy within its marketing authorisation for untreated unresectable advanced malignant pleural mesothelioma.

Background

Malignant pleural mesothelioma is a cancer affecting the membranes lining the outer surface of the lungs and the inside of the chest wall (the pleura). It is a highly aggressive tumour; the majority of people with this condition present and are diagnosed in the advanced stages of the disease and most have a poor prognosis. Pleural mesothelioma can be divided into 3 histologic subtypes, epithelioid, sarcomatoid and a combination of epithelioid and sarcomatoid known as biphasic.

Malignant pleural mesothelioma accounts for approximately 96% of all mesothelioma diagnoses.[1] Most cases are linked to exposure to asbestos in the workplace. People typically present with the condition 20 to 50 years after exposure, and over half of all diagnoses are in people aged 75 and older.[1] Between 2016 and 2018 approximately 6,950 people were diagnosed with pleural mesothelioma in UK (approximately 2,300 per year) and 83% of diagnoses were in men.[1]

The aim of treatment is to prolong life expectancy, reduce tumour size and improve symptoms. NICE technology appraisal guidance 818 recommends nivolumab with ipilimumab as an option in adults with untreated unresectable malignant pleural mesothelioma if they have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. NICE technology appraisal guidance 135 recommends pemetrexed with cisplatin as a treatment option for people with untreated malignant pleural mesothelioma for whom surgical resection is inappropriate. British Thoracic Society guidelines recommend carboplatin in combination with pemetrexed where cisplatin is contraindicated or has adverse risk For people who are not fit enough to receive chemotherapy, best supportive care is used to control disease symptoms. There is no current standard for best supportive care in pleural mesothelioma.

The technology

Pembrolizumab (Keytruda, Merck Sharp and Dohme) with pemetrexed and platinum-based chemotherapy does not currently have a marketing authorisation in the UK for untreated unresectable advanced malignant pleural mesothelioma. It has been studied in a phase II/III clinical trial in which pembrolizumab with pemetrexed and cisplatin was compared with two treatments (pembrolizumab alone, and pemetrexed with cisplatin) in people with unresectable advanced and or metastatic malignant pleural mesothelioma.

Intervention(s)	Pembrolizumab with pemetrexed and platinum-based chemotherapy
Population(s)	Adults with untreated unresectable advanced malignant pleural mesothelioma
Subgroups	If the evidence allows the following subgroups will be considered: • histologic subtype (epithelioid, sarcomatoid, biphasic) • level of programmed death-ligand 1 (PD-L1) expression.
Comparators	• Nivolumab with ipilimumab • Pemetrexed with cisplatin • Pemetrexed with carboplatin (for people for whom treatment with cisplatin is unsuitable)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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 and cost of biosimilar and generic products should be taken into account. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies 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	**Related technology appraisals:** Nivolumab with ipilimumab for untreated unresectable malignant pleural mesothelioma (2022) NICE technology appraisal guidance 818. Pemetrexed for the treatment of malignant pleural mesothelioma (2008) NICE technology appraisal guidance 135. **Related technology appraisals in development:** Pegargiminase with pemetrexed and cisplatin for untreated advanced malignant pleural mesothelioma. NICE technology appraisal guidance [ID1575]. Publication date to be confirmed
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2013) 2013/14 NHS Standard contract for cancer: malignant mesothelioma (adult) Ref: B10/S/a NHS England (2023) Prescribed specialist services manual. Chapter 105 NHS England (2022) Specialised Services Quality Dashboard (SSQD) metric definitions for malignant mesothelioma

Questions for consultation

Where do you consider pembrolizumab with pemetrexed and platinum-based chemotherapy will fit into the existing care pathway for untreated unresectable advanced malignant pleural mesothelioma?

In practice, would pembrolizumab with pemetrexed be offered with any platinum-based chemotherapies other than cisplatin?

Would pembrolizumab with pemetrexed and platinum-based chemotherapy be a candidate for managed access?

Do you consider that the use of pembrolizumab with pemetrexed and platinum-based 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 pemetrexed and platinum-based 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. (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).

However, NICE is considering if it is appropriate to evaluate this technology through its cost comparison evaluation process. Please provide 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).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?

- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.

- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

References

1. Royal College of Physicians (2020). National Mesothelioma Audit.