**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Appraisal**

# Pembrolizumab for adjuvant treatment of resected stage 2 melanoma with high risk of recurrence [ID3908]

**Draft scope**

## Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for the adjuvant treatment of resected stage 2 melanoma with high risk of recurrence.

## Background

Cutaneous melanoma is a cancer of the skin. In its early stages (0-2), melanoma has not spread so it can often be cured by surgery (resection). Most melanomas occur in people with pale skin. The risk factors are skin that tends to burn in the sun, having many moles, intermittent sun exposure and sunburn.

In England in 2017, there were 13,740 registrations of newly diagnosed cases of malignant melanoma of skin.[1] Of those diagnosed, around 91% are diagnosed with stage 1 or 2 melanoma.[2] England and Wales recorded 2,106 deaths from malignant melanoma of skin in 2017.[3]

The stage of melanoma describes how deeply it has grown into the skin, and whether it has spread. At stage 1 and 2, there is no evidence that the tumour has spread anywhere else in the body, although there is a possibility of microscopic spread. Stage 2 melanomas can be split into three types: 2A (between 1-2mm thick with ulceration or 2-4mm without ulceration), 2B (2-4mm thick with ulceration or thicker than 4mm without ulceration) and 2C (thicker than 4mm with ulceration).[4] Stage 2B and 2C melanomas are considered to be intermediate to high risk of recurrence because the tumour is thicker and deeper in the skin, which makes it difficult to remove all cancerous cells. Disease recurrence after surgery is experienced by 43% of people with stage 2B and 60% of stage 2C melanoma.[5] 5-year survival with stage 2B and 2C is similar to a more advanced melanoma (3B); 87, 82 and 83% respectively.[6]

Surgery (tumour removal and wide local excision) is the main treatment for stage 1 (clinical margin of at least 1cm) and stage 2 (clinical margin of at least 2cm) melanoma. Sentinel lymph node biopsy may be offered to determine if any cancer has spread to the lymph nodes (stage 3) and surgical removal of the near lymph nodes is considered. People with stage 2B and 2C melanoma who have had complete surgical resection are considered to be at high risk of recurrence and are offered routine surveillance for signs of recurrence. Early recognition of melanoma and accurate diagnosis present the best opportunities for cure.

## The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, anti-programmed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Pembrolizumab does not currently have a marketing authorisation in the UK for the adjuvant treatment of resected stage 2B or 2C melanoma. It has been studied in a clinical trial compared to a placebo in people with high risk of recurrence aged 12 years and older with complete resection of stage 2B or 2C cutaneous melanoma.

Pembrolizumab has a marketing authorisation in the UK for the treatment of advanced (unresectable or metastatic) melanoma in adults (TA366, TA357) and the adjuvant treatment of adults with Stage 3 melanoma and lymph node involvement who have undergone complete resection (TA533).

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| **Intervention(s)** | Pembrolizumab |
| **Population(s)** | People aged 12 years and older with stage 2B or 2C cutaneous melanoma who have undergone complete resection (at high risk of recurrence). |
| **Comparators** | Routine surveillance |
| **Outcomes** | The outcome measures to be considered include:<br>• Overall survival<br>• Recurrence-free survival<br>• Distant metastasis-free survival<br>• Adverse effects of treatment<br>• 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.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement 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:<br>Pembrolizumab for adjuvant treatment of resected melanoma |

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| | with high risk of recurrence (2018) NICE technology appraisal guidance 553. Review date 2021.<br><br>Appraisals in development:<br><br>Pembrolizumab for adjuvant treatment of resected melanoma with high risk of recurrence. NICE technology appraisals guidance [ID3776, review of TA553]. Publication expected January 2022.<br><br>Related Guidelines:<br><br>Melanoma: assessment and management (2015) NICE guideline NG14. Review date 2022.<br><br>Sunlight exposure: risks and benefits (2016) NICE guideline NG34.<br><br>Improving outcomes for people with skin tumours including melanoma (2006 updated 2010) NICE guideline CSG8.<br><br>Related Public Health Guidance/Guidelines:<br><br>Skin Cancer Prevention (2011, updated 2016). Public health guideline PH32.<br><br>Related Quality Standards:<br><br>Skin cancer (2016). NICE quality standard QS130.<br><br>Related NICE Pathways:<br><br>Melanoma (2020) Nice pathway. |
| **Related National Policy** | The NHS Long Term Plan, 2019. NHS Long Term Plan.<br><br>Department of Health (2016) NHS outcomes framework 2016 to 2017.<br><br>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020.<br><br>Department of Health (2014) The national cancer strategy: 4th annual report.<br><br>Department of Health (2011) Improving outcomes: a strategy for cancer.<br><br>Department of Health (2009) Cancer commissioning guidance.<br><br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019): 105 - Specialist cancer |

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| | services (adults) and 106 – Specialist cancer services for children and young people.<br><br>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains NHS Outcomes Framework 2016-2017: Domains 1-5. |

**Questions for consultation**

Are there any adjuvant treatments considered to be established clinical practice in the NHS for adjuvant treatment following complete resection of stage 2 melanoma?

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, Melanoma?

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. Office for National Statistics (2019). Cancer registration statistics, England 2017 dataset. Assessed July 2021.

2. National Cancer Registration and Analysis Service. (2016) Routes to diagnosis of cancer by stage 2012-2013 workbook (link is external). London: NCRAS. Accessed August 2021.

3. Office for National Statistics (2018). Death registrations summary tables - England and Wales 2017 dataset. Assessed July 2021.

4. Cancer Research UK (2020) Melanoma - stage 2. Accessed July 2021.

5. Berger AC, Ollila DW, Christopher A, et al. (2017) Patient symptoms are the most frequent indicators of recurrence in patients with American Joint Committee on Cancer stage II melanoma. Journal of the American College of Surgeons. 224(4), 652-659. Accessed July 2021.

6. Gershenwald JE, Scolyer RA, Hess KR et al. (2017) Melanoma staging: evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA Cancer Journal for Clinicians. 67(6), 472–492. Accessed July 2021.