NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab for adjuvant treatment of resected melanoma with high risk of recurrence (CDF review of TA553)

Final scope

Remit/appraisal objective

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

Background

Cutaneous melanoma is a cancer of the skin. In its early stages, melanoma is normally asymptomatic and can often be cured by surgery (resection). However, it can spread or metastasise to nearby lymph nodes or to other parts of the body. 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.

There were 12,993 new diagnoses of melanoma in 2014 and 2,080 deaths registered in England[1]. In the UK in 2012-2014, on average half of cases were diagnosed in people aged 65 and over[1].

The stage of melanoma describes how deeply it has grown into the skin, and whether it has spread. At stage I and II, there is no evidence that the tumour has spread anywhere else in the body, although there is a possibility of microscopic spread. Stage III melanoma means that the melanoma cells have spread into skin, lymph vessels, or lymph glands close to the melanoma. Stage III melanomas are considered intermediate to high risk as they more likely to spread to other distant parts of the body (stage IV melanoma) than in earlier melanoma stages. In 2012, the proportion of people in the UK diagnosed with melanoma at stage III disease was 3%[2]. Five-year survival rates are approximately 50-55% for stage III disease[3]. Advanced melanoma (stage IV) means the cancer has spread from where it started to another part of the body.

Surgery (tumour removal and wide local excision) is the main treatment for early (stage I) and medium stage (stage II and III) melanoma. Surgical removal of the nearby lymph nodes is also considered if there is evidence of microscopic spread. Early recognition of melanoma and accurate diagnosis present the best opportunities for cure. Adjuvant chemotherapy and immunotherapy following tumour removal was not widely used in UK practice. NICE has since published 3 technology appraisals in this area TA544, TA553, TA684.

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The technology

Pembrolizumab (Keytruda, MSD) 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 has a marketing authorisation in the UK for the adjuvant treatment of adults with stage III melanoma and lymph node involvement who have undergone complete resection.

Pembrolizumab also has a marketing authorisation in the UK for treating adults with unresectable or metastatic melanoma.

Intervention	Pembrolizumab
Population	People with completely resected stage III melanoma at high risk of recurrence
Comparators	Routine surveillance
Outcomes	The outcome measures to be considered include: • overall survival • recurrence-free survival • distant metastases 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 or comparator technologies will be taken into account.

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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: Dabrafenib with trametinib for adjuvant treatment of resected BRAF V600 positive malignant melanoma (2018) NICE technology appraisals guidance 544. Review date 2021. Pembrolizumab for adjuvant treatment of resected melanoma with high risk of recurrence (2018) NICE technology appraisals guidance 553. Review date 2021. Nivolumab for adjuvant treatment of completely resected melanoma with lymph node involvement or metastatic disease (2021) NICE technology appraisals guidance 684. Review date 2024. Related Guidelines: 'Melanoma: assessment and management of melanoma'. (2015) NICE guidelines NG14. Related Quality Standards: http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp 'Skin cancer' (2016) NICE quality standard QS130 Related NICE Pathways: Melanoma (2017) NICE pathway NICE pathway http://pathways.nice.org.uk/
Related National Policy	Department of Health (2016) NHS outcomes framework 2016 to 2017 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

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	NHS England (2013/14) NHS standard contract for cancer: skin (adult) A12/S/b NHS England (2013/14) NHS standard contract for cancer: chemotherapy (children, teenagers and young adults). B12/S/b NHS England Manual for Prescribed Specialised Services 2016/17. Chapter 105. Specialist cancer services (adults) https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1–5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. Cancer Research UK (2014) Skin cancer statistics. Accessed September 2017 http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/skin-cancer

2. National Cancer Intelligence Network and Cancer Research UK (2015) Routes to diagnosis by stage 2012-2013 workbook. Accessed September 2017 http://www.ncin.org.uk/publications/routes_to_diagnosis

3. Cancer Research UK (2014) Skin cancer survival statistics. Accessed September 2017 http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/skin-cancer/survival#heading-Three

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