NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab for adjuvant treatment of resected stage III and IV melanoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating resected stage III and IV melanoma.

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 are 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]. Advanced melanoma (stage IV) means the cancer has spread from where it started to another part of the body. Five-year survival rates are approximately 50-55% for stage III disease and 20-30% for stage IV disease[3].

Surgery (tumour removal and wide local excision) is the main treatment for early (stage I) and medium stage (stage II and III) melanoma. Only a small proportion of advanced (stage IV) melanoma can be completely removed by surgery[4]. 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 are not widely used in UK practice. People who have had surgery to remove stage III or IV tumours are at high risk of relapse and death; for example, 5-year relapse-free survival is 28-44% for stage III melanoma[5].

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The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) 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.

Nivolumab does not currently have a marketing authorisation in the UK for treating people with resected melanoma. It is being studied in a clinical trial compared with ipilimumab in people with completely resected stage IIIb/C or Stage IV melanoma. Nivolumab has a marketing authorisation in the UK for treating adults with unresectable or metastatic melanoma, alone or in combination with ipilimumab.

Intervention	Nivolumab
Population	People with completely resected stage III or IV melanoma
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: None Related Technology Appraisals in development (including suspended appraisals) 'Dabrafenib with trametinib for adjuvant treatment of resected BRAF V600 positive malignant melanoma' NICE technology appraisals guidance [ID1226]. Expected publication date December 2018. 'Pembrolizumab for adjuvant treatment of melanoma with high risk of recurrence' NICE technology appraisals guidance [ID1266]. Publication date to be confirmed 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

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4. Stage IV melanoma: completely resectable patients are scarce. Wevers and Hoekstra. Ann Surg Oncol. 2013 Jul;20(7):2352-6

5. Stage-specific survival and recurrence in patients with cutaneous malignant melanoma in Europe – a systematic review of the literature. Svedman et al. Clinical Epidemiology. 2016; 8:109-22.

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