NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Pembrolizumab for treating advanced melanoma previously untreated with ipilimumab

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating advanced melanoma.

Background

Melanoma is a cancer of the skin which in its early stages is normally asymptomatic and, if detected early, before it has spread, can be curable. Melanoma can spread or metastasise to nearby lymph nodes (stage III) or to other parts of the body (stage IV). At presentation, around 1% of melanomas are in stage IV. It occurs more commonly in fair-skinned people and there is strong evidence that ultra violet exposure is causal. People with an above-average mole count, sun-sensitive skin, or a strong family history of melanoma are at greatly increased risk.

The incidence of melanoma is increasing in England with rates doubling approximately every 10-20 years. There were 11,121 people diagnosed with melanoma and 1871 related deaths in England in 2011. In the UK, melanoma is diagnosed at a mean age of around 50 years but approximately 27% of diagnoses occur in people younger than 50 years.

Early recognition of melanoma and accurate diagnosis presents the best opportunity for cure by surgical resection of the tumour. A very small minority of people with advanced disease at presentation can still have their tumours removed. People with metastatic melanoma can be treated with biological therapy, chemotherapy, radiotherapy or surgery. Some people whose disease presents with a BRAF gene mutation will receive targeted therapy. NICE technology appraisals 269 and 321 recommend vemurafenib and dabrafenib as options for treating locally advanced or metastatic BRAF V600 mutation-positive unresectable or metastatic melanoma respectively. NICE technology appraisals 319 and 268 recommend ipilimumab as an option for treating previously untreated advanced (unresectable or metastatic) melanoma and for treating advanced (unresectable or metastatic) melanoma in people who have received prior therapy respectively.

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 have a marketing authorisation in the UK for treating advanced (unresectable stage III or stage IV) melanoma. It has been studied in a clinical trial in comparison with ipilimumab in people with advanced melanoma who have not received previous therapy or who have received 1 prior therapy other than ipilimumab.

Intervention(s)	Pembrolizumab
Population(s)	People with advanced (unresectable stage III or stage IV) melanoma previously untreated with ipilimumab
Comparators	• Dacarbazine • Ipilimumab • Vemurafenib (for people with BRAF V600 mutation-positive disease) • Dabrafenib (for people with BRAF V600 mutation-positive disease)
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rate • 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 comparator technologies should 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: Technology Appraisal No. 268, December 2012, 'Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma'. Review Proposal Date November 2014. Technology Appraisal No. 269, December 2012 'Vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma'. Review Proposal Date November 2014. Technology Appraisal No. 319, July 2014, 'Ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma' Review Proposal Date June 2017. Technology Appraisal No. 321, October 2014 'Dabrafenib for treating advanced unresectable or metastatic BRAF V600 mutation-positive melanoma' Review Proposal Date October 2017. Related Guidelines: Clinical Guideline in Preparation, 'Melanoma: assessment and management of melanoma' Earliest anticipated date of publication July 2015. Related Pathways: Skin cancer overview: Melanoma, Pathway created March 2014 http://pathways.nice.org.uk/pathways/skin-cancer#content=view-node%3Anodes-melanoma Other guidance: Cancer Service Guidance CSGSTIM, May 2010, 'Improving outcomes for people with skin tumours including melanoma'.
Related National Policy	Department of Health, 2013, 'Improving outcomes: a strategy for cancer 3rd annual report' Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf Department of Health, 2009, 'Cancer commissioning guidance'