NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Pembrolizumab for treating advanced melanoma in people previously untreated with ipilimumab

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its licensed indication for treating advanced melanoma in people previously untreated with ipilimumab.

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. First-line treatment normally involves the administration of dacarbazine. Some people whose disease presents with a BRAF gene mutation will receive targeted therapy. NICE technology appraisal 269 recommends vemurafenib as an option for treating locally advanced or metastatic BRAF V600 mutation-positive unresectable or metastatic melanoma. NICE technology appraisal 268 recommends ipilimumab as an option for treating advanced (unresectable or metastatic) melanoma in people who have received prior therapy.

The technology

Pembrolizumab (Brand name unknown, Merck Sharp & Dohme) is a humanised, anti-programmed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and 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 in people previously untreated with ipilimumab. 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 who have not received previous treatment or who have received 1 prior therapy other than ipilimumab.
Comparators	• dacarbazine (or temozolomide for people with brain metastases) • ipilimumab • vemurafenib (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 in Preparation, 'Ipilimumab for previously untreated unresectable stage III or IV malignant melanoma' Earliest anticipated date of publication July 2014. Technology Appraisal in Preparation, 'Dabrafenib for treating advanced unresectable or metastatic BRAF V600 mutation-positive melanoma' Earliest anticipated date of publication TBC. Technology Appraisal in Preparation, 'Paclitaxel formulated as albumin-bound nanoparticles for the first-line treatment of metastatic melanoma'. Earliest anticipated date of publication May 2015. 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, 2011, 'Improving outcomes: a strategy for cancer' Department of Health, 2009, 'Cancer commissioning guidance'

Questions for consultation

Have all relevant comparators for pembrolizumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for advanced melanoma in people previously untreated with ipilimumab? Is dacarbazine used at this point in the treatment pathway?

Are there any subgroups of people in whom pembrolizumab is expected to be more clinically effective and cost effective?

Where do you consider pembrolizumab will fit into the existing NICE pathway Skin cancer overview: 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.

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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)