NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Ipilimumab in combination with dacarbazine for previously untreated unresectable malignant melanoma

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ipilimumab in combination with dacarbazine within its licensed indication for previously untreated unresectable stage III or IV malignant melanoma.

Background

Malignant 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. However, at presentation, approximately 10% of cutaneous melanomas will have metastasised. Melanoma can spread to nearby lymph nodes (stage III, advanced) or to other parts of the body (stage IV, metastatic). 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 malignant melanoma is increasing in England and Wales with rates doubling approximately every 10-20 years. There were 10,656 new diagnoses of malignant melanoma and 1,825 deaths registered in England in 2010. In the UK, melanoma is diagnosed at a mean age of around 50 years but approximately 13% of cases occur in young adults aged between 15 and 39 years old.

Early recognition of malignant 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 can still have their tumour removed. People with unresectable stage III or IV (metastatic) disease are usually managed by a specialist oncologist and first line standard care normally involves the administration of dacarbazine. Radiotherapy, immunotherapy and combination chemotherapy have also been studied in randomised clinical trials.

The technology

Ipilimumab (Bristol-Myers Squibb) is a fully human antibody that binds to cytotoxic T lymphocyte-associated antigen 4 (CTLA-4), a molecule expressed on T-cells that plays a critical role in regulating natural immune responses. Ipilimumab is designed to block the activity of CTLA-4 resulting in augmentation and prolongation of the T-cell immune response, thereby

sustaining the immune attack on cancer cells. Ipilimumab is administered intravenously. It currently has a marketing authorisation in the UK for the treatment of advanced (unresectable or metastatic) melanoma in adults who have received prior therapy. It has also been studied in combination with dacarbazine for the treatment of advanced (unresectable or metastatic) malignant melanoma in adults who have not received prior therapy. A NICE technology appraisal of ipilimumab for the treatment of advanced (unresectable or metastatic) melanoma in adults who have received prior therapy is currently on-going.

Intervention(s)	Ipilimumab (with dacarbazine)
Population(s)	People with previously untreated advanced (unresectable or metastatic) malignant melanoma
Standard comparators	• Carboplatin-based chemotherapy • Dacarbazine For people with BRAF V600 mutation-positive malignant melanoma • Vemurafenib (subject to on-going NICE appraisal)
Outcomes	The outcome measures to be considered include: • overall survival • progression free 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If evidence allows, subgroup analyses according to performance status may be considered.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal in Preparation, 'Ipilimumab for previously untreated unresectable stage III or IV malignant melanoma' Earliest anticipated date of publication tbc. Technology Appraisal in Preparation, 'Vemurafenib for the treatment of unresectable locally advanced or metastatic BRAF V600 mutation positive malignant melanoma' Earliest anticipated date of publication tbc. Related Guidelines: Clinical Guideline No. 27, June 2005, 'Referral guidelines for suspected cancer' Clinical Guideline in Preparation, 'Diagnosis and management of metastatic malignant disease of unknown primary origin' Earliest anticipated date of publication July 2011. Related Public Health Guidance: Public Health Intervention Guidance No.32, January 2011, 'Skin cancer prevention: information resources and environmental changes' Other Guidance: Cancer Service Guidance, May 2010, 'Improving outcomes for people with skin tumours including melanoma (update): the management of low-risk basal cell carcinomas in the community' Cancer Service Guidance, March 2004, 'Improving supportive and palliative care for adults with cancer'

Questions for consultation

Have the most appropriate comparators for ipilimumab in combination with dacarbazine for the treatment of previously untreated unresectable malignant melanoma been included in the scope? Are the comparators listed routinely used in clinical practice

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 ipilimumab in combination with dacarbazine 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 ipilimumab in combination with dacarbazine;

- 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 ipilimumab in combination with dacarbazine 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 malignant melanoma)?

Do you consider that the use of the ipilimumab in combination with dacarbazine 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)