NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Ipilimumab for previously untreated unresectable malignant melanoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ipilimumab 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, though treatment is increasingly being based upon a person's BRAF gene mutation status. 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 as monotherapy and 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
Population(s)	People with previously untreated advanced (unresectable or metastatic) malignant melanoma
Standard comparators	• 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 • 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'