Appendix A

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Ipilimumab for previously treated unresectable malignant melanoma

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ipilimumab within its licensed indication for previously treated unresectable stage III or IV malignant melanoma.

Background

Cutaneous melanoma is a malignant tumour 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, 10% of cutaneous melanomas will have metastasised. Melanoma can spread to nearby lymph nodes (stage III) or to other parts of the body (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 malignant melanoma is increasing in England and Wales with rates doubling approximately every 10-20 years. There were 9,695 new cases of malignant melanoma registered in England in 2008 and 1,695 related deaths in England and Wales in 2007. In the UK, melanoma is diagnosed at a mean age of around 50 years but approximately 20% of cases occur in young adults aged between 15 and 39 years old. Five-year survival rates are approximately 40-50% for stage III disease and approximately 20-30% for stage IV disease (median survival for the latter is 6 to 9 months).

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. Limited treatment options are currently available for second or subsequent line therapy.

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 no marketing authorisation in the UK. It has been studied as monotherapy in clinical trials in people aged 16 years or older who have previously been treated with systemic or immunosuppressive therapy for stage III (unresectable) or IV malignant melanoma.

Intervention(s)	Ipilimumab
Population(s)	People with previously treated unresectable stage III or IV malignant melanoma
Standard comparators	Best supportive care
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.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal in Preparation, 'Ipilimumab in combination with dacarbazine for previously untreated unresectable stage III or IV malignant melanoma' Earliest anticipated date of publication tbc. Technology Appraisal in Preparation, 'Temozolomide for advanced and metastatic melanoma' Suspended. 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

Has the most appropriate comparator for the treatment of people with previously treated unresectable stage III or IV malignant melanoma been included in the scope? Are there any other comparators which should be included?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology 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 the technology 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.