# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Proposed Health Technology Appraisal

## Ipilimumab for the adjuvant treatment of completely resected high risk stage III or IV melanoma

## Draft scope (pre-referral)

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ipilimumab within its licensed indication for the adjuvant treatment of completely resected high risk stage III or IV melanoma.

### Background

Cutaneous 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. 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 increased risk.

The incidence of melanoma is increasing in England with rates doubling approximately every 10-20 years. There were 10,656 new diagnoses of melanoma in 2010 and 1871 deaths registered in England in 2011. In the UK, melanoma is diagnosed at a mean age of around 50 years but approximately 27% of cases occur in people aged under 50 years. The stage of a melanoma describes how deeply it has grown into the skin, and whether it has spread. Stage I means the tumour is either thinner than 2 mm, or less than 1 mm thick but has broken the surface of the skin (ulcerated). Stage II melanomas are thicker than 2 mm or thicker than 1 mm and ulcerated. At stage I and II, the tumour will have not spread anywhere else in the body. Most stage I and II melanomas can be cured. Stage III melanoma means that the melanoma cells have spread into skin, lymph vessels, or lymph glands close to the melanoma. Stage III melanomas are considered intermediate to high risk as they more likely to spread to other parts of the body than in earlier melanoma stages. Between 2006 and 2010, the proportion of people in the UK diagnosed with melanoma at stage III disease was 11.1%. Five-year survival rates are approximately 50-55% for stage III disease. Advanced melanoma (stage IV) means the cancer has spread from where it started to another part of the body.

Surgery (tumour removal and wide local excision) is the main treatment for early (stage I) and medium stage (stage II and III) melanoma. Early recognition of melanoma and accurate diagnosis present the best opportunities for cure. Adjuvant chemotherapy and immunotherapy following tumour removal is not currently standard UK practice.

## The technology

Ipilimumab (Yervoy, Bristol-Myers Squibb) is a fully human antibody that binds to cytotoxic T lymphocyte-associated antigen 4 (CTLA-4). Ipilimumab blocks the inhibitory signal of CTLA-4 resulting in T-cell activation, proliferation, and lymphocyte infiltration into tumours which leads to tumour cell death. Ipilimumab is administered intravenously.

Ipilimumab does not hold a UK marketing authorisation for the adjuvant treatment of melanoma. It has been studied in a clinical trial compared with placebo as adjuvant therapy in adults with high risk stage III melanoma that has been completely removed by surgery. It is also being studied in a clinical trial compared with high-dose interferon alfa-2b in adults with completely resected stage III or IV (with distant skin, subcutaneous, lymph node or lung metastases only) melanoma.

Ipilimumab has a UK marketing authorisation for the treatment of advanced (unresectable or metastatic) melanoma in adults who have received prior therapy.

| | |
|---|---|
| **Intervention(s)** | Ipilimumab as adjuvant therapy |
| **Population(s)** | People with high risk stage III or IV melanoma that has been completely removed by surgery |
| **Comparators** | Adjuvant therapy without ipilimumab |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• disease free survival<br>• distant metastases free survival<br>• response rate<br>• adverse effects of treatment<br>• 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.<br><br>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.<br><br>Costs will be considered from an NHS and Personal Social Services perspective.<br><br>The availability of any patient access schemes for the intervention should be taken into account. |
| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. |
| **Related NICE recommendations and NICE Pathways** | Related Technology Appraisals:<br><br>Technology Appraisal No. 268, December 2012. 'Ipilimumab for treating people with previously treated advanced (unresectable or metastatic) melanoma. Review date: November 2014.<br><br>Technology Appraisal in preparation, 'Ipilimumab for previously untreated unresectable stage III or IV malignant melanoma'. Earliest anticipated publication date June 2014.<br><br>Related Clinical guidelines:<br><br>Clinical Guideline in Preparation, 'Melanoma: assessment and management of melanoma'. Earliest anticipated date of publication TBC. |
| **Related National Policy** | None. |

**Questions for consultation**

Have all relevant comparators for ipilimumab been included in the scope?

- Are there any adjuvant treatments considered to be established clinical practice in the NHS following complete resection of a high risk stage III or IV melanoma?
- Should interferon be included as a comparator?

Is ipilimumab likely be used as adjuvant therapy in UK clinical practice following complete resection of stage IV melanoma? If so, what would the relevant comparators be for this subgroup?

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. For example, is ipilimumab likely to be more clinically or cost effective in subgroups of people defined by performance status?

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 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 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.

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)