NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Talimogene laherparepvec for treating metastatic melanoma

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of talimogene laherparepvec within its marketing authorisation for treating metastatic melanoma.

Background

Melanoma is a cancer of the skin. In its early stages, melanoma is normally asymptomatic and can often be cured by surgery (resection). However, at presentation, around 10% of melanomas have 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 increased risk.

There were 11,281 new diagnoses of melanoma and 1781 deaths registered in England in 2012. In the UK, more than one-third of people diagnosed with melanoma are aged less than 55 years. Approximately 20–73% of people with stage III melanoma (including 20–34% of people with stage IIIc) and 5–22% of those with stage IV will live longer than 5 years, with survival rates being slightly higher in women than in men.

Approximately 50% of melanomas harbour activating BRAF mutations, and over 90% of these are BRAF V600 mutations. Diagnostic tests can be used to detect the BRAF mutation, including the cobas test, generic PCR sequencing tests and other validated BRAF mutation tests.

The management of advanced melanoma is rapidly evolving, with several ongoing clinical trials, and there is uncertainty about how these treatments will be sequenced in future. Treatment for advanced, unresectable melanoma is often based upon the person's BRAF mutation status and their previous treatment history.

NICE Technology Appraisal (TA) 319 recommends ipilimumab as a treatment option for adults with previously untreated unresectable or metastatic melanoma and TA268 recommends ipilimumab as a treatment option for previously treated disease. For people with a BRAF V600 mutation, TA269 and TA321 recommend the BRAF inhibitors vemurafenib and dabrafenib as treatment options. Ipilimumab, vemurafenib and dabrafenib are only recommended if the respective companies provide the drugs at the discount agreed in the patient access schemes. Dacarbazine and supportive care may also be considered when ipilimumab or BRAF inhibitors are unsuitable or have already been tried.

The technology

Talimogene laherparepvec (Brand name unknown, Amgen) is an oncolytic immunotherapy designed to selectively replicate in tumour tissue and to initiate a systemic anti-tumour immune response. It expresses granulocyte-macrophage colony-stimulating factor (GM-CSF), a white blood cell growth factor, which can help to activate the immune system. The aim of this combination of actions is to initiate a systemic anti-tumour immune response that targets tumour cells throughout the body. It is administered by intratumoral injection.

Talimogene laherparepvec does not have a marketing authorisation in the UK for treating metastatic melanoma. It has been studied in a clinical trial compared with subcutaneously administered GM-CSF in people with unresected stage IIIb – IV melanoma.

Intervention(s)	Talimogene laherparepvec
Population(s)	Adults with advanced (unresectable or metastatic) melanoma
Comparators	• ipilimumab • vemurafenib (for people with BRAF V600 mutation positive disease) • dabrafenib (for people with BRAF V600 mutation positive disease)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • time to treatment failure • durable 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 intervention or comparator technologies will be taken into account.
Other considerations	If the evidence allows, consideration will be given to subgroups based on volume of disease and distribution of disease. 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 268, Dec 2012, 'Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma'. Static list. Technology Appraisal 269, Dec 2012, 'Vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma.' Static list. Technology Appraisal 319, Jul 2014, 'Ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma'. Review proposal date Jun 2017. Technology Appraisal 321, Oct 2014, Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma. Review proposal date Oct 2017. Ongoing appraisals: Technology Appraisal in preparation, ID661, 'Dabrafenib and trametinib for treating advanced unresectable or metastatic BRAFV600 mutation-positive melanoma'**.** Earliest anticipated date of publication Aug 2016. Technology Appraisal in preparation, ID760, 'Pembrolizumab for treating unresectable, metastatic melanoma after progression with ipilimumab'. Earliest anticipated date of publication Dec 2015. Technology Appraisal in preparation, ID801, 'Pembrolizumab for treating advanced melanoma previously untreated with ipilimumab'**.** Earliest anticipated date of publication Jan 2016. Technology Appraisal in preparation, ID815,

	'Cobimetinib in combination with vemurafenib for treating previously untreated, unresectable or metastatic BRAF V600 mutation-positive melanoma'. Earliest anticipated date of publication TBD. Technology Appraisal in preparation, ID845, 'Nivolumab for treating advanced (unresectable or metastatic) melanoma'. Earliest anticipated date of publication TBD. Related Guidelines: Clinical Guideline in preparation, 'Melanoma: assessment and management of melanoma'. Earliest anticipated date of publication July 2015. Related Interventional Procedures: Interventional procedure guidance 446, Mar 2013, 'Electrochemotherapy for metastases in the skin from tumours of non-skin origin and melanoma'. Review proposal date TBC. Interventional Procedure Guidance in preparation, 'Electrochemotherapy for the treatment of malignant melanoma (GID-IP1041)'. Earliest anticipated date of publication TBC. Related Public Health Guidance/Guidelines: Public health guidance 32, Skin cancer prevention: information, resources and environmental changes January 2011. Part review in progress; next review date Apr 2017. Related NICE Pathways: Skin cancer NICE Pathway, published July 2014Other guidance: Cancer Service Guidance CSGSTIM, May 2010, 'Improving outcomes for people with skin tumours including melanoma'.
Related National Policy	NHS England, 2013/14, NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a. NHS England, 2013/14, NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a. National Cancer Peer Review Programme, 2013, Manual for Cancer Services: Skin Measures. National Service Frameworks, Cancer Department of Health, 2013, NHS Outcomes

	Framework 2014-2015. Domains 1, 2, 4 and 5. Department of Health, 2011, Improving outcomes: a strategy for cancer Department of Health, 2009, Cancer commissioning guidance Department of Health, 2007, Cancer reform strategy