

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Proposed Health Technology Appraisal**

**Talimogene laherparepvec for treating metastatic melanoma**

**Draft scope (Pre-referral)**

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of talimogene laherparepvec (T-VEC) within its marketing authorisation for treating metastatic melanoma.

**Background**

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. Melanoma can spread or metastasise to nearby lymph nodes (stage III) or to other parts of the body (stage IV). At presentation, around 1% of melanomas are in 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 melanoma is increasing in England with rates doubling approximately every 10-20 years. There were 11,121 people diagnosed with melanoma and 1871 related deaths in England in 2011. In the UK, melanoma is diagnosed at a mean age of around 50 years but approximately 27% of diagnoses occur in people younger than 50 years.

Early recognition of 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 at presentation can still have their tumours removed. People with metastatic melanoma can be treated with biological therapy, chemotherapy, radiotherapy or surgery. Some people whose disease presents with a BRAF gene mutation will receive targeted therapy. NICE technology appraisals 269 and 321 recommend vemurafenib and dabrafenib as options for treating locally advanced or metastatic BRAF V600 mutation-positive unresectable or metastatic melanoma. NICE technology appraisals 319 and 268 recommend ipilimumab as an option for treating previously untreated and previously treated advanced (unresectable or metastatic) melanoma respectively.

**The technology**

Talimogene laherparepvec, T-VEC (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.

T-VEC 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.

<b>Intervention(s)</b>	Talimogene laherparepvec (T-VEC)
<b>Population(s)</b>	Adults with stage IIIb – IV melanoma
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• dacarbazine</li> <li>• ipilimumab</li> <li>• vemurafenib (for people with BRAF V600 mutation positive disease)</li> <li>• dabrafenib (for people with BRAF V600 mutation positive disease)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rate</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>
<b>Other considerations</b>	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.
<b>Related NICE recommendations and NICE pathways</b>	<p>Related Technology Appraisals:</p> <p>Technology Appraisal No. 268, December 2012, 'Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma'. Review Proposal Date November 2014.</p> <p>Technology Appraisal No. 269, December 2012 'Vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma'. Review Proposal Date November 2014.</p> <p>Technology Appraisal No. 319, July 2014, 'Ipilimumab for previously untreated unresectable stage III or IV malignant melanoma' Review Proposal Date June 2017.</p> <p>Technology Appraisal No. 321, October 2014 'Dabrafenib for treating advanced unresectable or metastatic BRAF V600 mutation-positive melanoma' Review Proposal Date October 2017.</p> <p>Related Guidelines:</p> <p>Clinical Guideline in Preparation, 'Melanoma: assessment and management of melanoma' Earliest anticipated date of publication July 2015.</p> <p>Related Pathways: Skin cancer overview: Melanoma, Pathway created March 2014</p> <p><a href="http://pathways.nice.org.uk/pathways/skin-cancer#content=view-node%3Anodes-melanoma">http://pathways.nice.org.uk/pathways/skin-cancer#content=view-node%3Anodes-melanoma</a></p> <p>Other guidance:</p> <p>Cancer Service Guidance CSGSTIM, May 2010, 'Improving outcomes for people with skin tumours including melanoma'.</p>
<b>Related National Policy</b>	<p>Department of Health, 2013, <a href="#">'Improving outcomes: a strategy for cancer 3rd annual report'</a></p> <p>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 2, 4 and 5. <a href="https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf">https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf</a></p> <p>Department of Health, 2009, <a href="#">'Cancer commissioning guidance'</a></p>

### Questions for consultation

Have all relevant comparators for T-VEC been included in the scope? Which treatments are considered to be established clinical practice in the NHS for metastatic melanoma? Are systemic therapies listed in the comparators section in the scope appropriate comparators for T-VEC? Is best supportive care considered an appropriate comparator for T-VEC? If so, how should best supportive care be defined?

Are there any subgroups of people in whom T-VEC is expected to be more clinically effective and cost effective?

Where do you consider T-VEC will fit into the existing NICE pathway [Skin cancer overview: melanoma](#)?

Are there any health service resources that need to be put in place in order to make T-VEC available in the NHS?

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 T-VEC 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 T-VEC 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 T-VEC 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/article/pmg19/chapter/1-Introduction>)