Review proposal of 410; Talimogene laherparepvec for treating unresectable metastatic melanoma

TA410 was published in September 2016 and scheduled to be considered for review in 2019.

1. Proposal

The guidance should be transferred to the 'static guidance list'.

2. Rationale

Talimogene laherparepvec is recommended for people with melanoma for whom immunotherapy is not suitable or otherwise contraindicated. Several immunotherapies were recommended for use at the same time as the appraisal of talimogene laherparepvec and were not considered as comparators, however the committee was aware of these and took them into consideration when making its recommendations. No new evidence has been published on talimogene laherparepvec monotherapy, and there is no reason to change the recommendations. Therefore, the guidance should be transferred to the 'static guidance list.'

3. Summary of new evidence and implications for review

Has there been any change to the price of the technology(ies) since the guidance was published?

The price of the technology has not changed. The company (Amgen) have confirmed their intention to continue with the current patient access scheme.

Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?

None.

Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?

The committee noted that the cost-effectiveness results were highly uncertain because there was no direct evidence comparing talimogene laherparepvec to ipilimumab. It recognised that the company had made every reasonable effort to provide a suitable indirect comparison but judged that the evidence was insufficient to draw firm conclusions about relative efficacy. There is no new evidence available to address this uncertainty.

Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?

Appraisals of the use of new immunotherapy strategies in melanoma (pembrolizumab and nivolumab with ipilimumab) were ongoing at the same time as the appraisal of talimogene laherparepvec. These include TA357, TA384 and TA400. The committee was aware of these and acknowledged the increasing use of these technologies in clinical practice. Because the changing treatment pathway was considered by committee when making its recommendations, the availability of new technologies has no implications for the existing guidance.

Additional comments

Final results of the OPTIM trial of talimogene laherparepvec compared with granulocyte-macrophage colony-stimulating factor have been published.[1] These are consistent with the results from the primary analysis used in the appraisal and have no implications for the existing guidance.

Talimogene laherparepvec is being studied in clinical trials in combination with immunotherapies for the treatment of melanoma. These studies have no implications for the existing guidance for talimogene laherparepvec monotherapy.

The search strategy from the original ERG Report was adapted for the Cochrane Library, Medline, Medline In-Process and Embase. References from August 2015 to August 2019 were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section above. See Appendix C for further details of ongoing and unpublished studies.

4. Equality issues

No equalities issues were raised in the evidence submissions or at the Committee meeting.

Proposal paper sign off

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Contributors to this paper

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Appendix A – Information from existing guidance

1. Original remit

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

2. Current guidance

1.1 Talimogene laherparepvec is recommended, in adults, as an option for treating unresectable, regionally or distantly metastatic (Stage IIIB, IIIC or IVM1a) melanoma that has not spread to bone, brain, lung or other internal organs, only if:

- treatment with systemically administered immunotherapies is not suitable and
- the company provides talimogene laherparepvec with the discount agreed in the patient access scheme.

1.2 This guidance is not intended to affect the position of patients whose treatment with talimogene laherparepvec was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

3. Research recommendations from original guidance

N/A

Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the Technology appraisals process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to a specific date or trail.	NICE will reconsider whether a review is necessary at the specified date.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No
The guidance should be updated in an on-going clinical guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

Options	Consequence	Selected – 'Yes/No'
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider.	**Yes**
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

Appendix C – Other relevant information

Relevant Institute work

Published

Improving outcomes for people with skin tumours including melanoma (2006, updated 2010) NICE cancer service guideline (CSG8)

> Status: to be updated. The 2019 surveillance of melanoma suggested it does not reflect current service structures and is no longer fit for purpose.

Melanoma: assessment and management (2015) NICE guideline NG14

> Status: to be updated. The 2019 surveillance of melanoma highlighted the introduction of a revised 8th edition of the American Joint Committee on Cancer (AJCC) staging system for melanoma.

Melanoma (2019) NICE pathway

Skin cancer (2016) NICE quality standard 130

Technology Appraisals

Cobimetinib in combination with vemurafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma (2016) NICE technology appraisal guidance 414

Dabrafenib with trametinib for adjuvant treatment of resected BRAF V600 mutation-positive melanoma (2018) NICE technology appraisal guidance 544

Dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma (2014) NICE technology appraisal guidance 321

Encorafenib with binimetinib for unresectable or metastatic BRAF V600 mutation-positive melanoma (2019) NICE technology appraisal guidance 562

Ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma (2014) NICE technology appraisal guidance 319

Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma (2012) NICE technology appraisal guidance 268

Nivolumab for adjuvant treatment of completely resected melanoma with lymph node involvement or metastatic disease (2019) NICE technology appraisal guidance 558

Nivolumab in combination with ipilimumab for treating advanced melanoma (2016) NICE technology appraisal guidance 400

Nivolumab for treating advanced (unresectable or metastatic) melanoma (2016) NICE technology appraisal guidance 384

Pembrolizumab for adjuvant treatment of resected melanoma with high risk of recurrence (2018) NICE technology appraisal guidance 553

Pembrolizumab for advanced melanoma not previously treated with ipilimumab (2015 updated 2017) NICE technology appraisal guidance 366

Pembrolizumab for treating advanced melanoma after disease progression with ipilimumab (2015 updated 2017) NICE technology appraisal guidance 357

Trametinib in combination with dabrafenib for treating unresectable or metastatic melanoma (2016) NICE technology appraisal guidance 396

Vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma (2012 updated 2015) NICE technology appraisal guidance 269

In progress

Atezolizumab with cobimetinib for untreated BRAF wild-type metastatic melanoma [ID1470] NICE technology appraisal guidance. Publication data to be confirmed.

Nivolumab with ipilimumab for adjuvant treatment of resected advanced melanoma [ID1610] NICE technology appraisal guidance. Publication data to be confirmed.

Relatlimab with nivolumab for treating advanced malignant melanoma after immunotherapy in people over 12 [ID1612] NICE technology appraisal guidance. Publication data to be confirmed.

Details of changes to the marketing authorisation for the technology

Marketing authorisation and price considered in original appraisal

Talimogene laherparepvec has a marketing authorisation in the UK for the treatment of adults with 'unresectable melanoma that is regionally or distantly metastatic (Stage IIIB, IIIC and IVM1a) with no bone, brain, lung or other visceral disease'.

The acquisition cost of talimogene laherparepvec is £1,670 per 1 ml vial of either 1,000,000 plaque forming units (PFU) per ml or 100,000,000 PFU per ml (excluding VAT; company's submission).

The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of talimogene laherparepvec, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health

considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

Proposed marketing authorisation (for this appraisal) and current price

No changes to the current marketing authorisation. Source: SPC (March 2019)

No change to the current cost. Source: BNF (3 July 2019)

Registered and unpublished trials

No directly relevant trials identified.

Additional information

Scottish Medicines Consortium (2017) Talimogene laherparepvec (Imlygic)

References

1) Andtbacka RHI, Collichio F, Harrington J, et al. (2019) Final analyses of OPTiM: a randomized phase III trial of talimogene laherparepvec versus granulocyte-macrophage colony-stimulating factor in unresectable stage III–IV melanoma. *Journal for ImmunoTherapy of Cancer*, 7, 145.