NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Tebentafusp for treating advanced uveal melanoma
Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of tebentafusp within its marketing authorisation for treating advanced uveal melanoma.

Background

Uveal melanoma is a rare type of cancer, arising from blood-rich structures in the middle of the eye (iris, choroid or ciliary body). Uveal melanoma is biologically distinct from skin melanoma with different physiological, genetic, and epidemiologic characteristics. It is often discovered through routine optometrist eye examination. Depending on tumour location, it may not cause any symptoms until it is quite large. Symptoms include flashes of light, blurry vision, loss of vision, or floaters (spots, lines or rings moving through field of vision).[1]

Uveal melanoma has 2 distinct disease states. Stages 1 to 3 are when the tumour is contained to the eye (primary disease), and stage 4 is when it has spread to distant organs (metastatic).[1] The cancer cells often spread to the liver, but can also spread to the lungs and bones.[2]

In England in 2017 there were 481 registrations of newly diagnosed cancer of the choroid (ICD-10 code C69.3) and 59 registrations of cancer of the ciliary body (ICD-10 code C69.4).[3] The total number of newly diagnosed cancers of the eye and adnexa (surrounding tissue, ICD-10 code C69) was 701. The total number of deaths recorded under the same ICD-10 code was 119.[3] Outcomes are poor once metastatic disease occurs. The median survival from development of metastatic disease is 2 to 12 months, and 1-year survival is 10 to 15%.[4]

The aim of treatment is to prevent metastases, conserve vision and avoid pain.[2] Treatment choice depends on the location and size of the tumour. Treatments for a primary tumour include radiotherapy, phototherapy and surgery. Large tumours may require enucleation (removal of the eye). There is no well-defined standard of care for metastatic uveal melanoma in the UK, but many people have either best supportive care or dacarbazine chemotherapy. The surgical removal of liver metastases and loco-regional therapies are suitable for some people.[4]

National clinical practice guidelines state that ipilimumab can be offered for metastatic uveal melanoma following its recommendation by NICE for melanoma generically (NICE technology appraisal guidance 268, and NICE technology appraisal guidance 319).[4] Since the publication of the national guidelines, NICE has also issued the following technology appraisal guidance on immunotherapies for treating melanoma:

- pembrolizumab is recommended as an option for treating adults with advanced (unresectable or metastatic) melanoma that has not been previously treated with ipilimumab (NICE technology appraisal guidance 366), or has progressed with ipilimumab (NICE technology appraisal guidance 357)

- nivolumab is recommended, alone or in combination with ipilimumab, as an option for treating adults with advanced (unresectable or metastatic) melanoma (NICE technology appraisal guidance 384 and NICE technology appraisal guidance 400).

The technology

Tebentafusp (brand name unknown, Immunocore Ltd) is a 2-part fusion protein which enables the immune system to recognise and kill cancer cells. Tebentafusp selectively cross-links T lymphocytes to the outside of the cancer cell, which induces T lymphocyte proliferation and tumour cell death. It is administered by intravenous infusion.

Tebentafusp does not currently have a marketing authorisation in the UK for treating uveal melanoma. It has been studied in adults with advanced HLA-A*0201-positive uveal melanoma in a single-arm clinical trial, and in a randomised controlled trial compared with investigator's choice of immunotherapy (ipilimumab or pembrolizumab) or chemotherapy (dacarbazine).

Intervention(s)	Tebentafusp
Population(s)	People with advanced HLA-A*0201-positive uveal melanoma
Comparators	Established clinical management without tebentafusp
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rate (including complete response and overall response) • duration of response • 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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The use of tebentafusp is conditional on the presence of HLA-A*0201. The economic modelling should include the costs associated with diagnostic testing for HLA-A*0201 in

	people with uveal melanoma who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals. Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.
Other considerations	If the evidence allows the following subgroups will be considered: • People with uveal melanoma that is untreated in the advanced setting • People with uveal melanoma that has been previously treated in the advanced setting 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:** 'Nivolumab in combination with ipilimumab for treating advanced melanoma' (2016) NICE Technology Appraisal 400. Review date to be confirmed 'Nivolumab for treating advanced (unresectable or metastatic) melanoma' (2016) NICE Technology Appraisal 384. Review date to be confirmed 'Pembrolizumab for advanced melanoma not previously treated with ipilimumab' (2015, updated 2017) NICE Technology Appraisal 366. Review date to be confirmed 'Pembrolizumab for treating advanced melanoma after disease progression with ipilimumab' (2015, updated 2017) NICE Technology Appraisal 357. Review date to be confirmed 'Ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma' (2014) NICE Technology Appraisal 319. Review date to be confirmed 'Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma' (2012) NICE Technology Appraisal 268. Guidance on static list **Appraisals in development (including suspended appraisals):** 'Masitinib for treating malignant melanoma that has a c-Kit juxtamembrane mutation' NICE technology appraisals guidance [ID1082]. Suspended March 2020 'Atezolizumab with cobimetinib for untreated BRAF wild-type metastatic melanoma' NICE technology appraisals guidance

	[ID1470]. Suspended August 2019 'Pembrolizumab with epacadostat for untreated malignant melanoma' NICE technology appraisals guidance [ID1423]. Suspended May 2018 'Melanoma (metastatic) - paclitaxel albumin-bound nanoparticles (1st line)' NICE technology appraisals guidance [ID570]. Suspended July 2014 'Melanoma (advanced and metastatic) – temozolomide' NICE technology appraisals guidance [ID316]. Suspended February 2010 **Related guidelines:** None **Related interventional procedures:** None **Related Quality Standards:** Suspected cancer (2016) NICE quality standard 124 **Related NICE Pathways:** Managing melanoma (2020) NICE Pathway Suspected cancer recognition and referral (2018) NICE Pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) • Chapter 105: Specialist cancer services (adults) • Chapter 12: Adult specialist ophthalmology services • Chapter 79: Ocular oncology service (adults) NHS England (2018) Highly specialised services 2018. • Ocular oncology service (adults) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 to 5. NHS England (2016) 16014/P: Clinical Commissioning Policy: chemosaturation for liver metastases from ocular melanomas NHS England (2016) Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) in the treatment of oligometastatic disease. NHS England (2013) D05/PS/a: Interim Clinical Commissioning Policy Statement: stereotactic radiosurgery / radiotherapy for ocular melanoma and pituitary adenoma NHS England (2013) D01/S/e: NHS Standard Contract for national artificial eye service (all ages) NHS England (2013) D12/S(HSS)/a: 2013/14 NHS Standard

	Contract for ocular oncology service (adults and adolescents) NHS England (2013) D12/S(HSS)/b: 2013/14 NHS Standard Contract for ophthalmic pathology service (All Ages)

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for people with advanced HLA-A*0201-positive uveal melanoma? In particular:

- Should best supportive care be included as a comparator, and if so how should it be defined?
- Should chemotherapy be included as a comparator, and if so, which agents are used in clinical practice?
- Should ipilimumab be included as a comparator?
- Should pembrolizumab be included as a comparator?
- Should nivolumab (with or without ipilimumab) be included as a comparator?

Is testing for HLA-A*0201 routinely done in the NHS for uveal melanoma? What proportion of people with advanced uveal melanoma in England have HLA-A*0201-positive uveal melanoma?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom tebentafusp is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider tebentafusp will fit into the existing NICE pathway, Managing melanoma?

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 tebentafusp 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 tebentafusp 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 tebentafusp 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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).

References

1. OcuMel UK. Uveal melanoma in the eye. Accessed February 2021.

2. OcuMel UK (2015). Ocular Melanoma. Accessed February 2021.

3. Office for National Statistics. (2017) Cancer Registration Statistics, England: 2017 dataset. Accessed February 2021.

4. Nathan P, Cohen V, Coupland S et al. (2015) Uveal Melanoma UK National Guidelines. Accessed February 2021