NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Tebentafusp for treating advanced (unresectable or metastatic) uveal melanoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of tebentafusp within its marketing authorisation for treating advanced (unresectable or metastatic) HLA-A*0201-positive 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] Around 47% of uveal melanoma is human leukocyte antigen (HLA)-A*0201 positive.[4] Outcomes are poor once metastatic disease occurs. The median survival from development of metastatic disease is around 13 months,[5] and 1-year survival is around 50%.[6]

People with advanced (unresectable or metastatic) uveal melanoma are usually offered immunotherapy, although the evidence for these is based on cutaneous melanoma. NICE has recommended the following immunotherapies for use in melanoma: ipilimumab (NICE technology appraisal guidance 268 and NICE technology appraisal guidance 319), pembrolizumab (NICE technology appraisal guidance 357 and NICE technology appraisal guidance 366) and nivolumab alone (NICE technology appraisal guidance 384) or with ipilimumab (NICE technology appraisal guidance 400). People for whom immunotherapy is not suitable may have dacarbazine chemotherapy or best supportive care.

The technology

Tebentafusp (KIMMTRAK, 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 previously treated metastatic 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) in people who have had no previous systemic therapy for metastatic disease.

Intervention(s)	Tebentafusp
Population(s)	Adults with advanced (unresectable or metastatic) HLA-A*0201-positive uveal melanoma
Comparators	• Immunotherapies (pembrolizumab, ipilimumab, nivolumab [alone or in combination with ipilimumab]) • Chemotherapy (dacarbazine) • Best supportive care may be an additional comparator for people who have had previous treatment
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rate • 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.
Other considerations	If the evidence allows, consideration will be given to the clinical and cost effectiveness of tebentafusp at different lines of therapy. 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)

References

1. OcuMel UK. Uveal melanoma in the eye. Accessed August 2021.
2. OcuMel UK (2015). Ocular Melanoma. Accessed August 2021.

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

4. The Allele Frequencies Database (2021). Accessed August 2021

5. Kuk D, Shoushtari A, Barker C et al. (2016). Prognosis of Mucosal, Uveal, Acral, Nonacral, Cutaneous, and Unknown Primary Melanoma from the Time of First Metastasis. Oncologist, 21(7): 848-854

6. Damata B, Dukes J, Goodall H et al. (2019). Tebentafusp: T Cell Redirection for the Treatment of Metastatic Uveal Melanoma. Cancers, 11(7): 971