# Appeal Appendix 1: EAG modelling

The Evidence Assessment Group (EAG) provided modelling results for their preferred scenarios (Table 1 below).

Following the first committee meeting and issuing of the ACD in June 2022, Immunocore provided the file: ‘*NICE\_ID1441\_Addendum 2\_updated B3\_ACIC*’ and an accompanying updated cost-effectiveness model in September 2022. The EAG provided a report on this in July 2023.

The below details are a copy of the EAG document ‘*ID1441 tebentafusp EAG response to addendum 2*’ - results provided in file: ‘*6a. ID1441 Tebentafusp EAG response to CS Addendum 2 Results v0.1 23.06.23 [ACIC].*’

## *‘‘1. Cost-effectiveness results*

*Given the EAG comments provided on CS addendum 2, the EAG preferred using used the generalised gamma distribution and the log-logistic distribution (producing an ICER range) for OS and the generalised gamma distribution for both PFS and TTD (same distribution for both treatments for all three outcomes). Notably, the EAG could not produce the EAG consistent with the original EAG basecase as some functionality the EAG initially implemented in the economic model, e.g. monthly BSC costs per cycle in the PD health state, was not implemented in the updated company’s model (this adjustment did increase the ICER by roughly ; original ERG report Table 6.2). The EAG analyses are provided in Table 1.****’’****[sic]*

## *Table 1: Deterministic ERG base-case (without the fixing violation for post* progression health state costs)

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| --- | --- | --- | --- | --- | --- |
| **Technologies** | **Total costs (£)** | **Total QALYs** | **Incremental costs (£)** | **Incremental QALYs** | **ICER (£/QALY)** |
| **Original EAG base-case 1 (Extrapolation of OS – generalised gamma)** |
| Tebentafusp |  |  |  |  |  |
| IC |  |  |  |  |  |
| **Original EAG base-case 2 (Extrapolation of OS – log logistic)** |
| Tebentafusp |  |  |  |  |  |
| IC |  |  |  |  |  |
| **Updated EAG base-case 1 (Extrapolation of OS – generalised gamma) – without the fixing violation for post progression health state costs** |
| Tebentafusp |  |  |  |  |  |
| Pembrolizumab |  |  |  |  |  |
| **Updated EAG base-case 2 (Extrapolation of OS – log logistic) – without the fixing violation for post progression health state costs** |
| Tebentafusp |  |  |  |  |  |
| Pembrolizumab |  |  |  |  |  |

CS = company submission; ERG = Evidence Review Group; ICER = incremental cost effectiveness ratio; IC = investigator’s choice; OS = overall survival; PFS = progression-free survival; QALY = quality adjusted life years; TTD = time to treatment discontinuation

**Company response**

In discussing the ICERs and stating their preference for the EAGs scenarios, the Committee’s preference has resulted in a situation where a price that would be cost-effective for tebentafusp is simply not feasible. This is due to the fact that the Committee has been unable to land on a set of preferred assumptions that result in a reasonably certain ICER and which could be made acceptable with a simple change to the price. Nevertheless, and as stated above, the Committee preferred the EAG’s preferred assumptions to those of the company and these produced very high ICERs even when the company provided a PAS price of per vial ( % of the list price).

In the absence of the EAG calculating a cost-effective price for tebentafusp according to their preferred scenarios (above), the company replicated the EAG’s scenarios. According to the EAG scenarios in Table 1, factoring in the increase in the ICER by roughly to account for monthly BSC costs per cycle in the PD health state and applying an assumption for the discount of pembrolizumab of %, the price for tebentafusp would need to be

per vial to reach an ICER less than £50,000. The cost of tebentafusp per patient would be and is significantly below cost of providing tebentafusp in England, Wales and

Northern Ireland. Clearly, this is not a viable option for the company. It simply does not add up, is illogical and is a result of the committee’s conclusions that are fundamentally wrong.

# Appeal Appendix 2: Tebentafusp evidence for NICE HST criteria

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| --- | --- |
| **The condition is very rare defined by 1:50,000 in****England** | The Office of National Statistics data for total incidence population of uveal melanoma (UM) is 540 in England (diagnostic codes C69.3 and C69.4) (1). The incidence numbers for primary UM are therefore equivalent to >0.5 per 50,000.Approximately 50% of these patients will develop advanced uveal melanoma (0.25 per 50,000). |
| **Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications** | UM is a rare disease, from a total incidence of 540 patients per year, around half will go on to develop advanced (metastatic or unresectable) UM (Kolandjian et al. 2013). Of these 270 metastatic patients, 47% will be HLA-A\*02\*01 positive. Of these 127 HLA-A\*02\*01 positive metastatic UM patients, clinical experts deem only 102 patients will be clinically eligible for tebentafusp.The target population in this ultra-rare condition is expected to be very small at around 100 patients per year and will remain at this level over time. Tebentafusp is only effective in patients with the MHC HLA allele HLA-A\*02:01 allele, which is present in ~47% of the population. Consequently, there is no risk that treatment could be extended to all of the metastatic UM population. |
| **The very rare condition****significantly shortens life or severely impairs its****quality** | UM is an ultra-rare, highly malignant, and life-limiting disease that initially affects the vascular layers of the eye. UM is distinct from other types of melanoma in its molecular pathology and physiology and an area of significant clinical unmet need.Up to half of all patients with UM go on to develop metastatic disease (2). Following diagnosis of metastatic disease, the prognosis is poor with a 1-year survival rate of only ~50%. In 90% of patients the first metastatic site is the liver and eventual liver failure is the predominant cause of death from the disease (3-6).Evidence, although sparse, suggests that patients with metastatic UM have a greater frequency of mental-health disorders, including anxiety and depression, as well as poorer QoL. A study by Nshimiyimana et al in 2018 demonstrated that, among 65 metastatic UM patients completing the Hospital Anxiety and Depression Scale andthe World Health Organization brief QoL instruments, |

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| --- | --- |
|  | 30.8% (n=20) had at least borderline anxiety, 13.8% (n=9) had at least borderline depression, and 32.3% (n=21) had a decrease in QoL (7).Advanced UM therefore both significantly shortens life and impairs its quality. |
| **No satisfactory treatment options exist, or, if it does the technology is likely to be of significant****additional benefit to those affected** | Tebentafusp is a first in class and highly specialised treatment representing the first significant development in advanced UM treatment and the only treatment specifically targeted to advanced UM. Patient prognosis and outcomes have not improved in nearly 40 years (8).Recent therapeutic advances in cutaneous melanoma have been assessed in UM patients, but such therapies have not shown a statistically significant improvement in outcomes or demonstrated a substantial benefit to patients with UM (2, 9).The current UK clinical guidelines recommend clinicians consider offering tebentafusp to HLA-A\*02:01 positive fit patients with metastatic disease pending availability (2). |

Appeal Appendix 3: Outcome of second TSOP meeting on HST routing

25th October 2021



References

1. ONS. Cancer registration statistics, England 2017 dataset ons.gov.uk: Office of National Statistics; 2019 [Available from: [hiips://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/d](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancerregistrationstatisticscancerregistrationstatisticsengland) [atasets/cancerregistrationstatisticscancerregistrationstatisticsengland](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancerregistrationstatisticscancerregistrationstatisticsengland).
2. Yang J, Manson DK, Marr BP, Carvajal RD. Treatment of uveal melanoma: where are we now? Therapeutic advances in medical oncology. 2018;10:1758834018757175.
3. Kuk D, Shoushtari AN, Barker CA, Panageas KS, Munhoz RR, Momtaz P, et al. Prognosis of Mucosal, Uveal, Acral, Nonacral Cutaneous, and Unknown Primary Melanoma From the Time of First Metastasis. The oncologist. 2016;21(7):848-54.
4. Damato BE, Dukes J, Goodall H, Carvajal RD. Tebentafusp: T cell redirection for the treatment of metastatic uveal melanoma. Cancers. 2019;11(7).
5. Nathan P, Coupland S, Lewis R, Modi S, Rashid S, Sacco J, et al. Uveal Melanoma Guidelines UK: Uveal Melanoma Guideline Development Group; 2022 [Available from: [hiips://melanomafocus.org/for-professionals/rare-melanoma-guidelines-and-consultations/uveal-](https://melanomafocus.org/for-professionals/rare-melanoma-guidelines-and-consultations/uveal-melanoma-guidelines/) [melanoma-guidelines/](https://melanomafocus.org/for-professionals/rare-melanoma-guidelines-and-consultations/uveal-melanoma-guidelines/).
6. Rantala ES, Hernberg M, Kivelä TT. Overall survival after treatment for metastatic uveal melanoma: a systematic review and meta-analysis. Melanoma research. 2019;29(6):561-8.
7. Nshimiyimana R, Guzetta CE, Brown MM, Zhou Q, Johnson JM, Sato T, et al. Pilot study of anxiety, depression, and quality of life in patients with the diagnosis of metastatic uveal melanoma. Supportive Care in Cancer. 2018;26 (Supplement 3):S393.
8. Frenkel S, Rosenne H, Briscoe D, Hendler K, Bereket R, Molcho M, et al. Long-term uveal melanoma survivors: measuring their quality of life. Acta Ophthalmol. 2018;96(4):e421-e6.
9. Khoja L, Atenafu EG, Suciu S, Leyvraz S, Sato T, Marshall E, et al. Meta-analysis in metastatic uveal melanoma to determine progression free and overall survival benchmarks: an international rare cancers initiative (IRCI) ocular melanoma study. Ann Oncol. 2019;30(8):1370-80.