For use at Maidstone and Tunbridge Wells NHS trust only.	
PROTOCOL CONTAINS BISPECIFIC THERAPY	
Indication	Monotherapy treatment for HLA-A*02:01-positive unresectable or metastatic uveal melanoma, as first or subsequent line of therapy in patients with a PS 0/1 and with no active brain metastases.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 21 days. Continue until disease progression or unacceptable toxicity or patient choice to stop treatment. A formal medical review as to whether treatment should continue or not will be scheduled to occur at least by the end of the first 4 weeks of treatment.
Monitoring Parameters	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • **Cardiac Monitoring:** ○ **ECG** baseline, **then before and after each dose for the first 3 weeks** of treatment, then as clinically indicated. ○ Tebentafusp treatment should be used with caution in patients with pre-existing cardiovascular disorders or a history of or predisposition to QT interval prolongation and in patients who are taking medicinal products that are known to prolong QT interval ○ **BP** baseline, before tebentafusp dose on day 1, day 8, day 15 and then at each cycle. • Monitor **FBC, LFTs** (including total blood bilirubin) and **U&Es** (including magnesium) at baseline, weekly for the first cycle and then prior to each cycle thereafter. • **CrCl** (C&G) prior to each cycle. • If neuts <1 and / or PLT <75 d/w consultant. • **Hepatic impairment:** ○ **Baseline:** No dose adjustment is recommended in mild hepatic impairment. No data in moderate or severe impairment (total bilirubin (TB) >1.5 and any AST). ○ **During treatment:** see table 1. • **Renal impairment:** No dose adjustment required in mild or moderate renal impairment (CrCl >30ml/min). No data in severe impairment, consultant decision. • **CYTOKINE RELEASE SYNDROME (CRS)and administration of tebentafusp.** ○ To minimize the risk of hypotension associated with cytokine release syndrome (CRS), ensure patients are euvolemic prior to initiating infusions. Prior to starting infusion, administer intravenous fluids based on clinical evaluation, baseline vital signs and the volume status of the patient, this should be **prescribed on the inpatient chart.** ○ Clear arrangements must be in place for the patient to be monitored as **an inpatient with overnight monitoring for signs and symptoms of CRS for 16 hours after the administration of the first 3 doses** of tebentafusp. Vital signs (e.g. blood pressure, pulse, temperature, oxygen saturation, skin check, fluid balance) should be monitored pre-dose and at a minimum of every 4 hours until resolution of symptoms. If clinically indicated, more frequent monitoring or prolongation of hospitalisation should occur. ○ Treatment and observation should be completed within normal working hours, ideally by early afternoon. ○ **If any grade 3 or 4 hypotension occurs during any of the first 3 doses, the patient must be monitored every hour for at least 4 hours in an outpatient setting for the next 3 doses.** ○ Once a 68mcg dose level is tolerated (i.e., absence of Grade >/= 2 hypotension requiring medical intervention), subsequent doses can be administered in appropriate out-patient

	ambulatory care setting. Patients must be observed for a minimum of 30 minutes following each infusion. ○ For patients with pre-existing adrenal insufficiency on maintenance systemic corticosteroids, consider adjusting the corticosteroid dose to manage the risk of hypotension. ○ Healthcare professionals must be familiar with the grading of cytokine release syndrome (CRS), the required monitoring and management and the indications for use of tocilizumab, and have all undergone training in these clinical issues Tocilizumab should be immediately available if required for the treatment of CRS. ○ All patients must be counselled on the risk, signs and symptoms of CRS and advised to contact their healthcare team immediately if they experience signs and symptoms of CRS. ○ If CRS is suspected follow Trust guidelines and SPC guidance. ○ For Grade 2 CRS that is persistent (lasting 2-3 hours) or recurrent (occurrence of >/= Grade 2 CRS with more than one dose), administer corticosteroid premedication (e.g. dexamethasone 4 mg or equivalent) at least 30 minutes prior to next dose. ○ For grade 3 CRS, withhold tebentafusp until Grade </= 1. At next treatment, resume at same dose level (i.e. do not escalate) after appropriate risk versus benefit assessment and monitor patient accordingly. Once dose level is tolerated, resume pre-planned dosing schedule. For Grade 3 CRS, administer corticosteroid premedication (e.g. dexamethasone 4 mg or equivalent) at least 30 minutes prior to next dose. ○ For Grade 4 CRS, permanently discontinue tebentafusp. ○ Supportive medication should be prescribed as required (e.g. chlorphenamine, paracetamol, hydrocortisone). Please prescribe on inpatient chart as required. • **Management of adverse reactions and dose adjustments: (see table 1)** ○ **QTcF:** If QTcF exceeds 500 msec or increases by >/=60 msec from baseline, tebentafusp treatment should be withheld. Treatment should be resumed once QTcF interval improves to <500 msec or is <60 msec from baseline value. Depending on persistence and severity of the cardiac event and any associated CRS, tebentafusp treatment should be withheld or discontinued. ○ **Acute Skin reactions:** Acute skin reactions mainly included rash, pruritus, erythema and cutaneous oedema, usually occurring within the first 3 doses of treatment. Acute skin reactions can be managed with antihistamine and topical corticosteroids. Consider systemic steroids for persistent or severe symptoms, see **table 1** for recommended management and dose modification. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ No formal drug interaction studies have been performed with tebentafusp. ○ Initiation of treatment causes transient release of cytokines that may suppress CYP450 enzymes. The highest drug-drug interaction risk is during the first 24 hours of the first three doses in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index. In these patients, monitor for toxicity (e.g., warfarin) or drug concentrations (e.g. ciclosporin). Adjust the dose of the concomitant drug as needed. • **Pregnancy and contraception:** Women of childbearing potential should use effective contraception during treatment with tebentafusp and for at least 1 week after last dose of tebentafusp. • The patient should be provided with the appropriate KIMMTRAK ® (tebentafusp) – Patient Guide
References	SPC accessed online 11.05.2026 CDF list V1.344 accessed online 11.05.2026

NB for funding information, refer to CDF and NICE Drugs Funding List

Table 1 Recommended Management and Dose Modifications for tebentafusp

Adverse Reactions	Severity of Adverse Reaction	Management
Acute skin reactions	Grade 2 or 3	Use local skin management and systemic antihistamine regimen. Topical corticosteroid treatment can be considered for symptomatic rash that does not respond to anti-pruritic regimen. Consider systemic steroids for persistent or severe symptoms. Withhold until Grade ≤ 1 Resume at same dose level (i.e., do not escalate if Grade 3 skin reactions occurred during initial dose escalation; resume escalation once dosage is tolerated)
	Grade 4	Permanently discontinue Administer intravenous corticosteroid (e.g., 2 mg/kg/day methylprednisolone or equivalent)
Elevated liver enzymes	Grade 3 or 4	Withhold until ≤ Grade 1 or baseline. Resume at same dose level if the elevated liver enzymes occur in the setting of Grade 3 CRS; resume escalation if next administration is tolerated. If the elevated liver enzymes occur outside the setting of Grade 3 CRS resume escalation if the current dose is less than 68 mcg, or resume at same dose level if dose escalation has completed Administer intravenous corticosteroids if no improvement within 24 hours
Other clinically relevant adverse reactions	Grade 3	Withhold until ≤ Grade 1 or baseline Resume at same dose level (i.e., do not escalate if other Grade 3 adverse reaction occurred during initial dose escalation; resume escalation once dosage is tolerated)
	Grade 4	Permanently discontinue

Cycle 1 only step up dosing schedule: 21 day cycle, day 1, 8 and 15 to be administered as inpatient.

Day	Drug	Dose	Route	Infusion Duration	Administration
	FLUIDS: to be administered prior to tebentafusp infusion as per clinical evaluation and volume status				
1	**TEBENTAFUSP**	**20mcg**	IV	15-20mins	In 100ml sodium chloride 0.9% containing human albumin (to make a final human albumin concentration between 225 mcg/mL and 275 mcg/ml). Administer via in-line 0.22micron filter. Flush line with 0.9% sodium chloride after use. Use a dedicated line.
8	**TEBENTAFUSP**	**30mcg**	IV	15-20mins	In 100ml sodium chloride 0.9% containing human albumin (to make a final human albumin concentration between 225 mcg/mL and 275 mcg/ml). Administer via in-line 0.22micron filter. Flush line with 0.9% sodium chloride after use. Use a dedicated line.
15	**TEBENTAFUSP**	**68mcg**	IV	15-20mins	In 100ml sodium chloride 0.9% containing human albumin (to make a final human albumin concentration between 225 mcg/mL and 275 mcg/ml). Administer via in-line 0.22micron filter. Flush line with 0.9% sodium chloride after use. Use a dedicated line.
	Patient to be monitored as an inpatient with overnight monitoring for signs and symptoms of CRS for 16 hours after the administration of the **first 3 doses** see notes above for further detail.				
TTO	Drug	Dose	Route	Directions	
Day 1	Aquamax		topical	Apply as directed. Supply on cycle 1 and then only as required.	
	Cetraben		topical	Apply as directed. Supply on cycle 1 and then only as required.	
	Hydroxyzine	25mg	PO	TDS PRN	

Cycle 2 onwards repeat every 21 days.

Day	Drug	Dose	Route	Infusion Duration	Administration
	FLUIDS: to be administered prior to tebentafusp infusion as per clinical evaluation and volume status				
1, 8, and 15	**TEBENTAFUSP**	**68mcg**	IV	15-20mins	In 100ml sodium chloride 0.9% containing human albumin (to make a final human albumin concentration between 225 mcg/mL and 275 mcg/ml). Administer via in-line 0.22micron filter. Flush line with 0.9% sodium chloride after use. Use a dedicated line.
	Patients should be observed for infusion-related reactions and hypersensitivity reactions for 30 minutes following administration of terbentafusp.				
TTO	Drug	Dose	Route	Directions	
Day 1	Aquamax		topical	Apply as directed. Supply on cycle 1 and then only as required.	
	Cetraben		topical	Apply as directed. Supply on cycle 1 and then only as required.	
	Hydroxyzine	25mg	PO	TDS PRN	