TEBENTAFUSP (Kimmtrak)

INDICATION (ICD10) C69

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (TEB1)

1. Tebentafusp monotherapy for adult patients with human leukocyte antigen (HLA) LA A*02:01 positive unresectable or metastatic uveal melanoma, does not have symptomatic or untreated brain metastases. PS 0 or 1. (TA1027)

REGIMEN

Cycle 1

Day 1
Sodium chloride 0.9% 500-1000ml IV infusion over 30-60 minutes
TEBENTAFUSP 20mcg in 100ml human serum albumin in sodium chloride 0.9% IV infusion over 15 minutes
Sodium chloride 0.9%1000ml IV infusion over 3-5 hours

Day 8
Sodium chloride 0.9% 500-1000ml IV infusion over 30-60 minutes
TEBENTAFUSP 30mcg in 100ml human serum albumin in sodium chloride 0.9% IV infusion over 15 minutes
Sodium chloride 0.9%1000ml IV infusion over 3-5 hours

Day 15
Sodium chloride 0.9% 500-1000ml IV infusion over 30-60 minutes
TEBENTAFUSP 68mcg in 100ml human serum albumin in sodium chloride 0.9% IV infusion over 15 minutes
Sodium chloride 0.9%1000ml IV infusion over 3-5 hours

Day 22
Sodium chloride 0.9% 500-1000ml IV infusion over 30-60 minutes
TEBENTAFUSP 68mcg in 100ml human serum albumin in sodium chloride 0.9% IV infusion over 15 minutes

Cycle 2 onwards

Days 1, 8, 15 and 22 Sodium chloride 0.9% 500-1000ml IV infusion over 30-60 minutes
TEBENTAFUSP 68mcg in 100ml human serum albumin in sodium chloride 0.9% IV infusion over 15 minutes

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression.
A formal medical review as to how tebentafusp is being tolerated and whether treatment with tebentafusp should continue or not will be scheduled to occur at least by the end of the first 4 weeks of treatment.

ANTI-EMETICS

Low emetic risk

CONCURRENT MEDICATION REQUIRED

Tebentafusp	To minimise the risk of hypotension associated with cytokine release syndrome (CRS), administer intravenous fluids prior to starting tebentafusp, based on clinical evaluation and the volume status of the patient. Patients should not receive any pre-medications before the first infusion of tebentafusp, except for patients with history of adrenal insufficiency managed with physiologic replacement doses of corticosteroid and select exceptions: Patients with pre-existing adrenal insufficiency managed with replacement dose corticosteroid should receive prophylactic stress dose corticosteroid prior to tebentafusp dosing for a minimum of 4 weekly doses. Stress dose prophylaxis with doses following the first 4 doses will be at the discretion of the prescriber. Due to the risk of hypotension, all patients receiving anti-hypertensive medications must discontinue all anti-hypertensive therapy for 24 hours prior to dosing and for 24 hours after dosing for the first 4 doses of tebentafusp. Tocilizumab needs to be available for immediate access if required to manage CRS for the first 3 doses of tebentafusp.

ADMINISTRATION

Tebentafusp	Ensure tebentafusp infusion is completed within 4 hours of being removed from the fridge. First three doses should be administered in a hospital setting with overnight monitoring for signs and symptoms of CRS for at least 16 hours. Vital signs including BP, temperature, pulse, O_2 sats, fluid balance, skin checks 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. Subsequent infusions - observe patients for 1 hour following 4th dose (day 22), (unless grade 3 or grade 4 hypotension with previous cycle in which case observe for 4 hours), and then a minimum of 30 minutes following each subsequent infusions.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Tebentafusp –neutral

Use a sterile, non-pyrogenic, low protein binding 0.2micron in-line filter infusion set.

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E, Mg^{++} and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Serum creatinine - GFR each dose
Blood pressure – baseline and every 4 hours. (If any grade 3 or 4 hypotension occurs during any of the first 3 infusions, the patient will be monitored every hour for the next 4 hours in an outpatient setting for the next 3 infusions).
Vital signs eg temperature, pulse, O_2 sats, fluid balance, skin checks – baseline and every 4 hours
ECG - pre-dose and post dose for the first three doses, then as clinically indicated

MAIN TOXICITES AND ADVERSE REACTIONS

Tebentafusp	Cytokine release syndrome (CRS). Hypotension - if any grade 3 or 4 hypotension occurs during any of the first 3 infusions, the patient will be monitored every hour for the next 4 hours in an outpatient setting for the next 3 infusions.

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Tebentafusp	Ciclosporin Warfarin

DOSE MODIFICATIONS

Tebentafusp

Cytokine release syndrome (CRS)

Grade 1 Temperature ≥38°C No hypotension or hypoxia	Treat for symptoms as appropriate. Monitor for escalation in CRS severity.
Grade 2 Temperature ≥38°C Hypotension that responds to fluids and does not require vasopressors. Oxygen requirement includes low flow nasal cannula (delivery of oxygen ≤6L/min) or blow-by	Symptom management as per grade 1 in addition to the following measures. Administer bolus intravenous fluids as needed for hypotension Manage oxygen requirement with supplemental oxygen and additional respiratory support as needed. Increase monitoring to determine resolution or escalation in severity. If grade 2 CRS symptoms do not rapidly improve to grade ≤1 within 2-3 hours, then treat as grade 3. 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 (eg dexamethasone 4mg or equivalent) at least 30 minutes prior to next dose.
Grade 3 Temperature ≥38°C Require a vasopressor with or without vasopressin. Require high flow nasal cannula (delivery of oxygen >6L/min), face mask or non-rebreather mask or Venturi mask	Management per grade 2 and include the following measures: Administer high-dose intravenous corticosteroid (eg 2mg/kg/day methylprednisolone or equivalent). Increase monitoring to determine resolution or escalation in severity. Consider administering tocilizumab. Withhold tebentafusp until grade≤1. At next treatment, resume Tebentafusp at same dose level (ie do not escalate) after appropriate risk versus benefit assessment and monitor patient accordingly. Once dose level is tolerated, can resume pre-planned dosing schedule. For grade 3 CRS, administer corticosteroid premedication (eg dexamethasone 4mg or equivalent) at least 30 minutes prior to next dose.
Grade 4 Temperature ≥38°C Require multiple vasopressors. Requiring positive pressure (e.g. CPAP, BiPAP, intubation and mechanical ventilation).	Permanently discontinue tebentafusp. Administer intravenous corticosteroid (eg 2mg/kg/day methylprednisolone or equivalent).

Acute skin reactions grade 2 or 3	Use local skin management and systemic antihistamine regimen eg initial dose chlorphenamine IV and then hydroxyzine prn. Topical corticosteroid treatment can be considered for symptomatic rash that does not respond to anti-pruritic regimen eg betnovate ointment body or hydrocortisone1% face and topical emollients. Consider systemic steroids for persistent or severe symptoms eg hydrocortisone 100mg IV. Withhold tebentafusp until grade ≤1. Resume tebentafusp at same dose level (ie do not escalate if grade 3 skin reactions occurred during initial dose escalation; resume escalation once dosage is tolerated).
Acute skin reactions grade 4	Permanently discontinue tebentafusp. Administer intravenous corticosteroid (eg 2mg/kg/day methylprednisolone or equivalent).
Elevated liver enzymes grade 3 or 4	Withhold tebentafusp until ≤grade 1 or baseline. Resume tebentafusp 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 68mcg 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 tebentafusp until ≤grade 1 or baseline. Resume tebentafusp at same dose level (ie do not escalate if other grade 3 adverse reaction occurred during initial dose escalation; resume escalation once dosage is tolerated).
Other clinically relevant adverse reactions grade 4	Permanently discontinue tebentafusp.

Hepatic impairment
Tebentafusp
No dose adjustment is recommended for patients with mild hepatic impairment.
Tebentafusp has not been studied in patients with moderate or severe hepatic impairment at baseline.

Renal impairment
Tebentafusp
Based on pharmacokinetic analyses, dose adjustment is not necessary in patients with mild to moderate renal impairment.
Patients with severe renal impairment have not been evaluated and should be treated with caution. No dose recommendations can be made for patients with severe renal impairment because of the lack of pharmacokinetic data.

REFERENCES
1. SPC