Regimen Reference Order – CUTA – tebentafusp (Cycle 1 *INPATIENT*)

Planned Course: **Once weekly (1 cycle = 21 days)**

***Note: Patients are admitted to hospital for* Cycle 1 of tebentafusp**

Indication for Use: **Uveal Melanoma**

CVAD: At Provider's Discretion

Proceed with treatment if:

- ***ANC equal to or greater than 1 x 10^9/L AND Platelets equal to or greater than 75 x 10^9/L***
- ***AST/ALT equal to or less than 3 times upper limit of normal***
- ***Total bilirubin less than or equal to 1.5 times the upper limit of normal***
- ***Systolic blood pressure greater than 100 mmHg***
- ***Creatinine clearance equal to or greater than 30 mL/min***
  - ❖ **Contact Medical Oncologist if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – CUTA – tebentafusp (Cycle 1 INPATIENT)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1 **Note: Cycle 1, Days 1, 8 and 15 must be administered as an inpatient**		
Day 1		
tebentafusp	20 mcg	IV in normal saline 100 mL over 15 minutes *Use 0.2 to 0.22 micron filter* **Alert: tebentafusp is prepared with human albumin*
Day 8		
tebentafusp	30 mcg	IV in normal saline 100 mL over 15 minutes *Use 0.2 to 0.22 micron filter* **Alert: tebentafusp is prepared with human albumin*
Day 15		
tebentafusp	68 mcg	IV in normal saline 100 mL over 15 minutes *Use 0.2 to 0.22 micron filter* **Alert: tebentafusp is prepared with human albumin*

REQUIRED MONITORING

Baseline

- EKG and then as clinically indicated
- Patient weight

All doses

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin and LDH as per Physician Orders
- Skin assessment for rash
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O2 saturation) prior to tebentafusp infusion, at 30 minutes, 60 minutes, then every 2 hours
- If cytokine release syndrome (CRS) occurs, then full vital signs every hour
- Patients must be monitored during the infusion and for **at least** 16 hours after the infusion is complete

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
cetirizine	20 mg	Orally once daily if needed for itching
acetaminophen	650 mg	Orally every 6 hours if needed for fever
metoclopramide	10 to 20 mg	Orally every 4 hours if needed for nausea or vomiting
ondansetron	8 mg	IV every 8 hours if needed

DISCHARGE INSTRUCTIONS

- Advise patient to hold anti-hypertensive medication for 24 hours prior to each tebentafusp administration

ADDITIONAL INFORMATION

- tebentafusp can cause Cytokine Release Syndrome (CRS) (fever, rigors, hypotension and hypoxemia)
- tebentafusp can cause skin rash
- If patient does not experience grade 2 or worse hypotension (requiring medical intervention) during or after the third infusion, then subsequent doses may be administered at CancerCare Manitoba (MacCharles) treatment room
- Ensure tocilizumab is in stock before starting tebentafusp administration
- Refer to Appendix A on pages 4 and 5 for toxicity management of hypotension, CRS and dermatological (rash/pruritis)

Appendix "A" Toxicity Management

Hypotension

- If systolic blood pressure is equal to or greater than 20 mmHg lower than the baseline average, repeat blood pressure 5 minutes later. If systolic blood pressure is confirmed equal to or greater than 20 mmHg lower than baseline average, inform medical oncologist to start IV fluids:
  - 250 mL NS over 15 minutes bolus followed by 1000mL NS over 3 hours
- Repeat blood pressure 30 minutes following initial bolus. If systolic blood pressure remains equal to or greater than 20 mmHg lower than baseline average:
  - Administer another bolus 250mL IV over 15 minutes
  - Contact medical oncologist on call for consideration of IV methylPREDNISolone as per below grade 2 Cytokine Release Syndrome (CRS) guideline
  - Contact medical oncologist after methylprednisolone is administered

Cytokine Release Syndrome (CRS)

Grade	Management
Grade 1: Temperature equal to or greater than 38°C, **AND** No hypotension or hypoxia	Treat for symptoms as appropriate. Monitor for escalation in cytokine release severity
Grade 2: Temperature equal to or greater than 38°C **AND** Hypotension that responds to fluids and does not require vasopressors, **OR** Oxygen requirement includes low flow nasal cannula (delivery of oxygen less than or equal to 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 Administer tocilizumab (8 mg/kg up to a maximum of 800 mg) IV every 8 hours for a maximum of 4 doses • Consider administering intravenous methylPREDNISolone 2 mg/kg/day (1 mg/kg IV every 12 hours) in patients unresponsive to tocilizumab (if symptoms do not resolve after receiving tocilizumab within 4 hours) If Grade 2 cytokine release syndrome symptoms do not rapidly improve to Grade 1 or less within 1 hour, then treat as Grade 3

Grade 3 Temperature equal to or greater than 38°C, **AND** Require a vasopressor with or without vasopressin, **OR** Require high flow nasal cannula (delivery of oxygen greater than 6L/min), face mask or non-breather mask or Venturi mask	Management as per Grade 2 and include the following measures: Administer intravenous methylPREDNISolone 2 mg/kg/day (1 mg/kg IV every 12 hours), **AND** tocilizumab (8 mg/kg up to a maximum of 800 mg) IV every 8 hours for a maximum of 4 doses Page adult ICU once first dose of tocilizumab Steroids should continue until symptoms resolve to grade 1 and then taper
Grade 4 Temperature equal to or greater than 38°C, **AND** Require multiple vasopressors (excluding vasopressin), **OR** Require oxygen by positive pressure (i.e. CPAP, BiPAP, intubation, mechanical ventilation)	Administer intravenous methylPREDNISolone 2 mg/kg/day (1 mg/kg IV every 12 hours), **AND** tocilizumab (8 mg/kg up to a maximum of 800 mg) IV every 8 hours for a maximum of 4 doses Page adult ICU once first dose of tocilizumab Steroids should continue until symptoms resolve to grade 1 and then taper

Dermatological (rash/pruritus):

Grade	Definition	Recommended treatment
1	Less than 10% BSA with or without symptoms	Symptomatic measures
2	10 to 30% BSA or intermittent pruritus	cetirizine 20mg orally daily hydrocortisone 1% cream to affected areas not responding to antihistamines
3	Greater than 30% BSA or grade 2 with substantial symptoms or constant pruritus	cetirizine 20mg orally daily hydrocortisone 1% cream to affected areas not responding to antihistamines
4	Skin sloughing greater than 30% BSA with associated symptoms	methylPREDNISolone 1mg/kg IV every 12 hours