**Regimen Monograph**



## A - Regimen Name

# TEBE(RAMP) Regimen

**Tebentafusp (Ramp-up)**

# TEBE Regimen

**Tebentafusp**

| | |
|---|---|
| **Disease Site** | Skin<br>Melanoma<br><br>(Uveal) |
| **Intent** | Palliative |
| **Regimen Category** | **Evidence-Informed :**<br><br>Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use. |
| **Rationale and Uses** | For the first line treatment of unresectable or metastatic uveal melanoma in positive HLA-A*02:01 genotype adult patients.<br><br>Refer to NDFP form for funding criteria. |

| | |
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| **Supplementary Public Funding** | **tebentafusp**<br>New Drug Funding Program (Tebentafusp (Outpatient) - Unresectable or Metastatic Uveal Melanoma) |

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## B - Drug Regimen

**Note**: Inpatient admission may be required for cytokine release syndrome monitoring (e.g. for the first 3 to 4 infusions). Refer to inpatient HCTFP form for funding of inpatient component. ST-QBP funding for ambulatory administration only.

**Cycle 1:**

| | | | |
|---|---|---|---|
| **tebentafusp** | 20 mcg | IV | Day 1 |
| **tebentafusp** | 30 mcg | IV | Day 8 |
| **tebentafusp** | 68 mcg | IV | Day 15 |

**Cycle 2 and onwards:**

| | | | |
|---|---|---|---|
| **tebentafusp** | 68 mcg | IV | Days 1, 8, 15 |

***Coordination with local blood bank is required prior to administration as tebentafusp requires dilution with **human albumin product** (e.g., albumin 5%).***

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## C - Cycle Frequency

**REPEAT EVERY 21 DAYS**

Until loss of clinical benefit or unacceptable toxicity

Use regimen code TEBE(RAMP) for cycle 1, then TEBE for subsequent cycles.

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Low

Also refer to CCO Antiemetic Recommendations.

**Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.

Patients must have a positive HLA-A*02:01 genotype status prior to treatment with tebentafusp.

IV fluids should be administered as necessary prior to starting tebentafusp infusion to reduce the risk of hypotension associated with cytokine release syndrome (CRS)

**Pre-medications (prophylaxis for CRS):**

If previous Grade 3 CRS, or Grade 2 CRS that did not resolve within 2-3 hours :

- Administer corticosteroid (e.g. dexamethasone 4mg or equivalent) at least 30 minutes prior to next dose.

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## E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

**Dosage with toxicity**

| Toxicity | Grade | Management/ Action |
|---|---|---|
| CRS | Grade 2* | Manage and treat symptoms as appropriate, including:<br>• IV fluids as needed for hypotension<br>• Supplemental $O_2$ and additional respiratory support as needed<br>• Increased monitoring<br><br>If symptoms do not resolve to Grade ≤1 within 2–3 hours, treat as Grade 3 |

| | | |
|---|---|---|
| | Grade 3* | Hold until CRS has resolved.<br><br>Manage symptoms as per Grade 2 and:<br><br>• Administer IV corticosteroids (e.g., 2 mg/kg/day methylprednisolone or equivalent)<br>• Consider administering tocilizumab<br><br>Resume at same dose level** |
| | Grade 4* | Discontinue.<br><br>Administer IV corticosteroids (e.g., 2 mg/kg/day methylprednisolone or equivalent)<br><br>Consider administering tocilizumab |
| Acute skin reactions | Grade 2 or 3 | Hold until < Grade 1 or baseline<br><br>Treat with systemic antihistamine and oral steroids as per local guidelines.<br><br>If no response to oral steroids, consider IV corticosteroid (e.g., 2 mg/kg/day methylprednisolone or equivalent)<br><br>Resume at same dose level** |
| | Grade 4 | Discontinue.<br><br>Administer IV corticosteroids (e.g., 2 mg/kg/day methylprednisolone or equivalent) |
| ↑ LFTs | Grade 3 or 4 | Hold***<br><br>If no improvement in 24 hours, administer IV corticosteroids<br><br>Resume at same dose level if in Grade 3 CRS also occurred**<br><br>Resume dose escalation (or same dose level if escalation complete) if Grade 3 CRS did not occur. |
| Other adverse effects | Grade 3 | Hold***<br><br>Resume at same dose level** |
| | Grade 4 | Discontinue |

*Based on ASTCT consensus grading of CRS criteria (Lee et.al 2019):
Grade 2 = temperature ≥ 38°C AND hypotension that responds to fluids and does not require vasopressors AND/OR hypoxia requiring low flow nasal cannula (delivery of oxygen ≤ 6L/min) or blow-by.
Grade 3 = temperature ≥ 38°C AND hypotension requiring a vasopressor with or without vasopressin AND/OR hypoxia requiring high flow nasal cannula (delivery of oxygen > 6L/min), face mask or non-rebreather mask or Venturi mask.
Grade 4 = temperature ≥ 38°C AND hypotension requiring multiple vasopressors (excluding vasopressin) AND/OR hypoxia requiring positive pressure (e.g. CPAP, BiPAP, intubation and mechanical ventilation)

**Do not escalate dose if severe (i.e. Grade 3) adverse reaction occurs during initial escalation. Dose escalation may resume once dose is tolerated.

***Do not restart until toxicities ≤ Grade 1 or baseline

## Hepatic Impairment

No dose adjustment is required. Elevations in ALT and AST at baseline or during treatment did not impact tebentafusp pharmacokinetics.

## Renal Impairment

| Creatinine Clearance (mL/min) | Tebentafusp Dose |
|---|---|
| ≥ 30 | No dose adjustment required |
| < 30 | No data available |

## Dosage in the Elderly

No dose adjustment is required. No overall differences in safety and efficacy were observed between patients ≥ 65 years of age compared to younger patients in the pivotal trial (in which 47% of patients were ≥ 65 years of age).

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## F - Adverse Effects

Refer to tebentafusp drug monograph(s) for additional details of adverse effects

| Very common (≥ 50%) | Common (25-49%) | Less common (10-24%) | Uncommon (< 10%), but may be severe or life-threatening |
|---|---|---|---|
| • Cytokine release syndrome (may be severe)<br>• Rash, pruritus (may be severe)<br>• Fever*<br>• Fatigue | • Nausea, vomiting*<br>• Hypo-/hyper-pigmentation<br>• Abdominal pain<br>• Edema<br>• Hypotension*<br>• Headache*<br>• Diarrhea | • ↑ LFTs, bilirubin*<br>• Musculoskeletal pain<br>• Anorexia, weight loss<br>• Constipation<br>• Cough, dyspnea<br>• Hypertension<br>• ↓$PO_4$<br>• Dizziness<br>• Paresthesia<br>• Anemia<br>• Tachycardia | • Hypoxia*<br>• QT prolongation |

*may also be associated with cytokine release syndrome

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## G - Interactions

Refer to tebentafusp drug monograph(s) for additional details

- Tebentafusp may cause transient suppression of CYP450 enzymes. Monitor and adjust doses of CYP450 substrates with narrow therapeutic index (e.g. warfarin, cyclosporine) as necessary, especially during the first 24 hours following each of the first 3 doses.
- Consider holding anti-hypertensives for 24 hours before/after tebentafusp infusion for the first 6 doses due to risk of hypotension.

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## H - Drug Administration and Special Precautions

Refer to tebentafusp drug monograph(s) for additional details

### Administration

- Tebentafusp requires dilution with sodium chloride containing **human albumin** (e.g. 5%, 20% or 25%; concentration will vary depending on availability from local blood bank) to prevent adsorption to the infusion bag.
- Dilute human albumin in 100 mL 0.9% Sodium Chloride Injection to make a final albumin concentration between 225 to 275 mcg/mL. See product monograph for more information.
- Compatible with polyolefins [e.g. polyethylene (PE) and polypropylene (PP)] or polyvinyl chloride (PVC) infusion bags.
- DO NOT use a closed system transfer device for preparation of tebentafusp infusion.
- Do not flush needle/syringe on transfer when adding the required volume of tebentafusp to the human albumin and 0.9% Sodium Chloride preparation.
- Mix gently. Do not shake.
- Administer by IV infusion over 15 to 20 minutes, through a low protein binding 0.2 micron in-line filter infusion set.
- Do not mix or administer with other drugs.
- Flush the IV line with 0.9% Sodium Chloride after each dose.
- Monitor patients for at least 16 hours following the first infusions (in the inpatient setting). If no Grade ≥ 2 hypotension, monitor for at least 30 minutes following subsequent infusions (in the ambulatory care setting).
- Store unopened vials refrigerated (2°C to 8°C) and protect from light

### Contraindications

- Patients who are hypersensitive to this drug or to any of its components.

### Warnings / Precautions

- Severe CRS has occurred with tebentafusp; ensure infusions are administered where there is immediate access to medications and equipment required to manage CRS, and that patients are euvolemic prior to initiating infusion.
- Patients with significant cardiac disease were excluded from clinical trials. Patients with pre-existing cardiovascular disorders may be at increased risk for complications associated with CRS and should be monitored.
- Caution and monitor ECG in patients with history or predisposing factors to QT interval prolongation; cases of QT interval prolongation were reported following tebentafusp treatment.
- Patients with pre-existing adrenal insufficiency on maintenance systemic corticosteroids are at an increased risk of hypotension; consider adjusting corticosteroid dose.

**Pregnancy / Lactation**

- Tebentafusp is **not recommended** for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is **not recommended** during treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Unknown

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## I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- Liver function tests (AST, ALT and total bilirubin); Baseline and as clinically indicated
- Creatinine; Baseline and as clinically indicated
- CBC; Baseline and as clinically indicated
- Clinical toxicity assessment for cytokine release syndrome (e.g. fever, hypotension, headache etc.), skin reactions, GI or cardiac effects.; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- ECG; Baseline and as clinically indicated (especially during the first 3 weeks of treatment) for patients at risk of QT prolongation.

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## J - Administrative Information

**Approximate Patient Visit**
**TEBE** 1 to 1.5 hours

**Pharmacy Workload** **(average time per visit)**
**TEBE** 86.85 minutes

**Nursing Workload** **(average time per visit)**
**TEBE** 52.50 minutes

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## K - References

Nathan P, Hassel JC, Rutkowski P, et al. Overall survival benefit with tebentafusp in metastatic uveal melanoma. N Engl J Med. 2021 Sep 23;385(13):1196-1206.

Tebentafusp drug monograph, Ontario Health (Cancer Care Ontario).

**December 2024** Added TEBE(RAMP) regimen code and modified Cycle Frequency section

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## M - Disclaimer

***Regimen Abstracts***

*A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.*

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***Regimen Monographs***

*Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.*

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