Regimen Monograph

A - Regimen Name

TECL(RAMP) Regimen

Teclistamab (Ramp-up)

TECL Regimen

Teclistamab

Disease Site	Hematologic Multiple Myeloma
Intent	Palliative
Regimen Category	**Evidence-Informed :** 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	Treatment of relapsed or refractory myeloma in patients who have received previous therapies including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody

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B - Drug Regimen

Step-up Dose 1:

teclistamab	0.06 mg /kg	Subcut	One-time dose*

(This drug is not publicly funded. Universal compassionate access program is available.)

Then, wait 2 to 7 days and give Step-up Dose 2:

teclistamab	0.3 mg /kg	Subcut	One-time dose*

(This drug is not publicly funded. Universal compassionate access program is available.)

Wait 2 to 7 days, then:

teclistamab	1.5 mg /kg	Subcut	Once weekly*

(This drug is not publicly funded. Universal compassionate access program is available.)

*Refer to the dose banding tables in the product monograph to determine the total dose for step-up and treatment doses.

Inpatient admission may be required for cytokine release syndrome (CRS) monitoring (e.g. during step-up and first treatment doses).

Note: ST-QBP funding for ambulatory administration only

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C - Cycle Frequency

REPEAT ONCE WEEKLY

Until disease progression or unacceptable toxicity

Use regimen code TECL(RAMP) for the step-up doses and the first treatment dose, followed by TECL for subsequent doses

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

- Also refer to CCO Antiemetic Summary.

Pre-medications (prophylaxis for CRS):

Give 1 to 3 hours prior to each step-up dose and first treatment dose*:

- Corticosteroid (oral or IV dexamethasone, 16 mg)
- Antihistamine (oral or IV diphenhydramine, 50 mg or equivalent)
- Antipyretic (oral or IV acetaminophen, 650 mg to 1000 mg or equivalent)

*May be required prior to other doses (e.g. repeat doses due to delays during the step-up schedule, or if patient experienced CRS with prior teclistamab dose).

Other Supportive care:

- Consider prophylaxis against Pneumocystis jirovecii pneumonia (PJP) and herpes virus infections.
- Consider other antimicrobial prophylaxis as per local guidelines.
- Teclistamab should be administered to adequately hydrated patients.

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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

Dose reductions are not recommended.

Dose may be delayed due to toxicity; dose upon resuming treatment will depend on duration of delay and last administered dose (Table 3).

Table 1 - CRS and ICANS Toxicity Management

Recommendations below are based on the pivotal trial. Refer to Crombie et al. and Rodriguez-Otero et al. for alternative CRS and ICANS management guidelines.

Toxicity	Grade[a]	Management / Action	Next dose
CRS	Grade 1	Hold until CRS has resolved. Manage and treat symptoms as appropriate: • Consider tocilizumab.	Administer pre-treatment medication prior to dose. Resume dose as recommended in Table 3.
	Grade 2	Hold until CRS has resolved. Manage and treat symptoms as appropriate: • IV tocilizumab as per institutional guidelines • If no improvement within 24hr of starting tocilizumab, administer IV methylprednisolone 1 mg/kg BID or equivalent. • Continue corticosteroids until ≤ Grade 1, then taper over 3 days.	Administer pre-treatment medications prior to dose. Resume dose as recommended in Table 3. Monitor patient daily for 48 hours following dose.
	Grade 3 (<48hr duration)	Hold until CRS has resolved. Manage and treat symptoms as appropriate: • IV tocilizumab as per institutional guidelines • If no improvement, administer IV methylprednisolone 1 mg/kg BID or equivalent. • Continue corticosteroids until ≤ Grade 1, then taper over 3 days.	Administer pre-treatment medications prior to dose. Resume dose as recommended in Table 3. Monitor patient daily for 48 hours following dose.
	Grade 3 (>48hr duration or recurrent)	Stop teclistamab. Manage and treat symptoms as appropriate:	Permanently discontinue.

		• IV tocilizumab as per institutional guidelines • Corticosteroids as above	
	Grade 4	Stop teclistamab Manage and treat symptoms as appropriate: • IV tocilizumab as per institutional guidelines • Corticosteroids as per Grade 3, OR • Methylprednisolone IV 1000 mg/ day x 3 days • If no improvement or worsens, consider alternate immunosuppressants, as per institutional guidelines.	Permanently discontinue.
ICANS	Grade 1	Hold until ICANS has resolved. Manage and treat symptoms as appropriate[b]: • Monitor neurologic symptoms; consider neurology consultation. • Consider seizure prophylaxis (e.g. levetiracetam).	Resume dose as recommended in Table 3.
	Grade 2, or Grade 3 (1st occurrence)	Hold until ICANS has resolved. Manage and treat symptoms as appropriate[b]: • IV dexamethasone 10mg q6h, or equivalent • Continue dexamethasone (or equivalent) until ≤ Grade 1, then taper. • Consider neurology consultation and other specialists as needed. • Consider seizure prophylaxis (e.g. levetiracetam).	Resume dose as recommended in Table 3. Monitor patient daily for 48 hours following dose.

	Grade 3 (recurrent)	Stop teclistamab. Manage and treat symptoms as appropriate[b]: • IV dexamethasone 10mg q6h, or equivalent • Continue dexamethasone (or equivalent) until ≤ Grade 1, then taper. • Consider neurology consultation and other specialists as needed. • Consider seizure prophylaxis (e.g. levetiracetam).	Permanently discontinue.
	Grade 4	Stop teclistamab. Manage and treat symptoms as appropriate[b]: • IV dexamethasone 10mg q6h, or equivalent • Continue dexamethasone (or equivalent) until ≤ Grade 1, then taper. OR • Consider IV methylprednisolone IV 1000 mg/ day x 3 days; if improves, manage as above. • Consider neurology consultation and other specialists as needed. • Consider seizure prophylaxis (e.g. levetiracetam).	Permanently discontinue.

[a] Grade based on American Society for Transplantation and Cellular Therapy (ASTCT) consensus grading (Lee et al 2019).

[b] Anticytokine therapy is recommended if ICANS occurs concurrently with CRS. Refer to MajesTEC-1 study protocol, or local institutional guidelines for management if concurrent CRS.

Table 2 - Hematologic and Other Non-hematologic Toxicities

Toxicity	Severity	Action
Infection	Any Grade (during step-up dosing schedule)	Hold* until infection has resolved (i.e. no active infection).
	Grade 3 (after step-up dosing schedule)	Hold* until infection improves to Grade ≤ 1.
	Grade 4 (after step-up dosing schedule)	Hold* until infection improves to Grade ≤ 1, OR Consider discontinue.
PML	Any Grade	Hold and investigate. Discontinue if confirmed.
Neurotoxicity (excluding ICANS)	Grade 1	Hold* until symptoms resolve or stabilize.
	Grade 2, or Grade 3 (first occurrence)	Hold* until symptoms improve to Grade ≤ 1. Provide supportive therapy.
	Grade 3 (recurrent), or Grade 4	Discontinue. Provide supportive therapy.
Neutropenia	ANC < 0.5 × 10^9/L	Hold* until ANC ≥ 0.5 × 10^9/L.
	Febrile neutropenia	Hold* until ANC ≥ 1 × 10^9/L and fever has resolved.
Thrombocytopenia	Platelets < 25 ×10^9/L	Hold* until platelets > 25 × 10^9/L and no evidence of bleeding.
	Platelets 25 - 50 × 10^9/L with bleeding	Hold* until platelets > 25 × 10^9/L and no evidence of bleeding.
Anemia	Hb < 80 g/L	Hold* until Hb ≥ 80 g/L.
Other non-hematological adverse effects	Grade 3	Hold* until adverse effect improves to Grade ≤ 1.
	Grade 4	Hold* until adverse effect improves to Grade ≤ 1, OR Consider discontinue.

*Resume at dose described in Table 3.

Table 3 - Recommended Dose After Dose Delay

Last Administered Dose (mg/kg)	Duration of Delay	Action
Step-up Dose 1 (0.06)	≤ 7 days	Resume at 0.3 mg/kg and continue step-up dosing schedule.
	> 7 days	Resume at 0.06 mg/kg and continue step-up dosing schedule.
Step-up Dose 2 (0.3)	≤ 7 days	Resume at 1.5 mg/kg and continue once weekly.
	8 - 28 days	Resume at 0.3 mg/kg and continue step-up dosing schedule.
	> 28 days	Resume at 0.06 mg/kg and continue step-up dosing schedule.
Any Treatment Dose (1.5)	≤ 28 days	Resume at 1.5 mg/kg and continue once weekly.
	> 28 days	Resume at 0.06 mg/kg and continue step-up dosing schedule.

Hepatic Impairment

Severity	Bilirubin		AST	Teclistamab Dose
Mild	≤ ULN	AND	> ULN	No dose adjustment.
	> 1 to 1.5 x ULN	AND	any	No dose adjustment.
Moderate or Severe	> 1.5 x ULN	AND	any	No data.

Renal Impairment

Severity	Creatinine Clearance (mL/min)	Teclistamab Dose
Mild or Moderate	≥ 30	No dose adjustment.
Severe	< 30	Limited data.

Dosage in the Elderly

No dose adjustment is required. In the pivotal trial (MajesTEC-1), 48% and 15% of patients were 65 and 75 years of age or older, respectively. No overall differences in safety or effectiveness were observed between these patients and younger patients.

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F - Adverse Effects

Refer to teclistamab 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
• Fever, chills • Cytokine release syndrome (may be severe) • Myelosuppression ± infection, bleeding (may be severe) • Musculoskeletal pain	• Fatigue • Injection site reaction • Diarrhea • Nausea, vomiting • Headache	• Cough, dyspnea • Constipation • Hypoxia • Motor dysfunction (e.g. hypokinesia, dysphonia, dysgraphia, tremor) • Peripheral neuropathy • Edema • Anorexia • Hypogammaglobulinemia • Nephrotoxicity	• ICANS • Encephalopathy • Guillain-Barré syndrome • PML • Hypersensitivity • Opportunistic or new/reactivated viral infections

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G - Interactions

Refer to teclistamab drug monograph(s) for additional details.

- Teclistamab 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 step-up dosing schedule, up to 7 days after the first treatment dose, or during a CRS event.

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H - Drug Administration and Special Precautions

Refer to teclistamab drug monograph(s) for additional details.

Administration

- Teclistamab should be administered by **subcutaneous injection only.** Do not administer IV.
- Vials are available in 2 different concentrations (10 mg/mL and 90 mg/mL). Ensure correct vial size is selected for preparation; do not combine. Refer to the product monograph for details on preparation.
- Allow vial to come to room temperature over 15 minutes; do not warm.
- Gently swirl vial to mix. Do not shake.
- Withdraw required volume into syringe. Injection volume should not exceed 2 mL; divide doses requiring > 2 mL into multiple syringes.
- Injection into the abdomen is preferred, but may be injected into thigh.
- Do not inject into areas where skin is red, bruised, scarred, tattooed or not intact.
- If multiple injections are required, injection sites should be at least 2 cm apart.
- Monitor patients for 48 hours after administration of all doses within the step-up dosing schedule for signs or symptoms of CRS or ICANS.
- 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 and ICANS have occurred with teclistamab; ensure step-up schedule is followed and infusions are administered where there is immediate access to medications and equipment required to manage CRS and ICANS.
- ICANS has been reported with teclistamab; caution in patients with a history of stroke, seizure or neurological conditions.
- Patients should avoid driving or operating heavy machinery during and for 48 hours after step-up dosing schedule, or if any new neurological symptoms present due to the risk of a depressed level of consciousness from ICANS.
- Patients with active infection should not receive teclistamab step-up dosing schedule.
- Vaccination with live virus vaccines is not recommended for at least 4 weeks prior to, during and for at least 4 weeks after treatment with teclistamab. The risk of vaccine-associated infection may be increased or immune response to vaccines may be reduced.
- Patients with conditions such as autoimmune disease or thyroiditis, Type 1 diabetes, allogenic stem cell transplant (within 6 months), CNS or meningeal involvement were excluded from clinical trials; assess benefit-risk of teclistamab treatment in these patients.

Pregnancy / Lactation

- This regimen is not recommended for use in pregnancy. Human IgG is known to cross the placenta after the first trimester of pregnancy and teclistamab has the potential to be transmitted to the fetus.
    - 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.
- Consider assessment of immunoglobulin levels in newborns of patients treated with teclistamab.
- Breastfeeding is not recommended during this 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

- CBC; Baseline and before each dose; more frequently if clinically indicated
- Clinical toxicity assessment for CRS and ICANS; At each visit and for 48 hours after all doses in step-up dosing schedule
- LFTs, bilirubin; Baseline and as clinically indicated
- Renal function tests; Baseline and as clinically indicated
- CRP, ferritin; Baseline and as clinically indicated
- Coagulation tests (e.g. aPTT, INR, PT, fibrinogen); Baseline and as clinically indicated
- Immunoglobulin levels; As clinically indicated
- Clinical toxicity assessment for infection, injection-site reactions, neurotoxicity, pulmonary and cardiac toxicity.; At each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit
TECL 1.5 hours

Pharmacy Workload **(average time per visit)**
TECL 17.000 minutes

Nursing Workload **(average time per visit)**
TECL 44.833 minutes

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K - References

Crombie JL, Graff T, Falchi L, et al. Consensus recommendations on the management of toxicity associated with CD3×CD20 bispecific antibody therapy. *Blood* 2024; 143 (16): 1565–1575.

Lee W, Santomasso BD, Locke FL, et al. ASTCT consensus grading for cytokine release Syndrome and neurologic toxicity associated with immune effector cells. Biol Blood Marrow Transplant. 2019;25:625-38.

Moreau P, Garfall AL, van de Donk NWCJ, et al. Teclistamab in relapsed or refractory multiple myeloma. N Engl J Med 2022 Aug 11;387(6):495-505.

Rodriguez-Otero P, Usmani S, Cohen AD, et al. International Myeloma Working Group. International Myeloma Working Group immunotherapy committee consensus guidelines and recommendations for optimal use of T-cell-engaging bispecific antibodies in multiple myeloma. Lancet Oncol. 2024 May;25(5):e205-e216

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

November 2024 Updated units in Dosage with Toxicity 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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