BC Cancer Protocol Summary for Treatment of Relapsed and Refractory Multiple Myeloma using Teclistamab

Protocol Code	*UMYTEC*
Tumour Group	*Myeloma*
Contact Physicians	*Dr. Christopher Venner*

ELIGIBILITY:

Patients must have:

- Relapsed or refractory multiple myeloma, and
- Be refractory or intolerant to their last treatment, and
- Received at least 3 prior lines of therapy, including:
  - a proteasome inhibitor (e.g. bortezomib, carfilzomib)
  - an immunomodulatory drug (e.g. lenalidomide, pomalidomide)
  - an anti-CD38 antibody (e.g. daratumumab, isatuximab)
- Access to a treatment centre with expertise and resources to manage cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS)
- BC Cancer "Compassionate Access Program" request approval prior to treatment

Patients should have:

- Good performance status
- No signs or symptoms of active infection

Note:

- Inpatient treatment is required for at least the first 3 administrations of teclistamab (Cycle 1: Step-up dose 1, Step-up dose 2, and first treatment dose), unless there is a local plan in place for rapid assessment and intervention of suspected CRS and ICANS following outpatient administration. An adequate local plan must ensure the patient:
  - remains within the proximity of the treating facility for at least 48 hours following each dose in Cycle 1
  - is monitored daily for signs and symptoms of CRS and ICANS after administration of all Cycle 1 doses (including once daily nursing assessment)
  - is counselled on the signs and symptoms associated with CRS and ICANS and on seeking immediate medical attention should they occur at any time
- If inpatient treatment:
  - Patients to be hospitalized for the duration of Cycle 1 and for a minimum of 48 hours after Cycle 1 Day 5 treatment (first treatment dose)
  - Subsequent doses will be given in ambulatory care setting if no Grade 2 or greater reactions during and after first treatment dose

Activated: 26 Feb 2024 (as unfunded UMY0UF) Revised: 1 June 2025 (Title, protocol code, eligibility, notes, tests, supportive medications, treatment, dose modifications, precautions and references updated, exclusions added)

EXCLUSIONS:

Patient must not have:

- AL amyloidosis

TESTS:

- Baseline: CBC & Diff, creatinine, sodium, potassium, urea, total bilirubin, ALT, alkaline phosphatase, calcium, albumin, LDH, random glucose, magnesium, phosphate, ferritin, C-reactive protein, ICANS assessment, including ICE score
- Baseline (required, but results do not have to be available to proceed with first treatment; results must be checked before proceeding with cycle 2): serum protein electrophoresis ***and*** serum free light chain levels, immunoglobulin panel (IgA, IgG, IgM), HCAb, HBsAg, HBsAb, HBcoreAb, beta-2 microglobulin
- Cycle 1:
  - Prior to each dose: CBC & Diff, creatinine, sodium, potassium, calcium, magnesium, phosphate, ALT, alkaline phosphatase, total bilirubin, albumin, LDH, vital signs
  - If clinically indicated, during hospital admission: CBC & Diff, creatinine, sodium, potassium, calcium, magnesium, phosphate, ALT, alkaline phosphatase, total bilirubin, albumin, LDH, vital signs
- Cycles 2 onward*:
  - Day 1: CBC & Diff, creatinine, urea, sodium, potassium, total bilirubin, ALT, alkaline phosphatase, calcium, albumin, LDH, random glucose
  - Days 8, 15, 22 (optional if pre-cycle cytopenias, hypercalcemia, hepatic or renal dysfunction, or steroid-induced diabetes a concern. Results do not have to be available to proceed with treatment. Provider to review results, no dose modifications indicated for mid-cycle bloodwork): CBC & Diff, creatinine, sodium, potassium, total bilirubin, ALT, alkaline phosphatase, calcium, albumin, random glucose
- From cycle 3 onwards, every 4 weeks (required, but results do not have to be available to proceed with treatment): serum protein electrophoresis and serum free light chain levels
- From cycle 3 onwards, every 4 weeks (optional, results not mandatory but encouraged prior to each cycle): urine protein electrophoresis, immunoglobulin panel (IgA, IgG, IgM), beta-2 microglobulin
- If clinically indicated: phosphate, magnesium
- *If treatment restarting after treatment interruption and repeat step-up dosing required, see Cycle 1 orders

PREMEDICATIONS:

- Prior to each dose in Cycle 1, when resuming treatment after treatment interruption (if indicated, see Treatment interruptions below), and if CRS of any Grade with previous dose of teclistamab:

60 minutes prior to teclistamab:

- dexamethasone 16 mg PO/IV
- loratadine 20 mg PO (preferred) or diphenhydrAMINE 50 mg PO/IV
- acetaminophen 650 mg to 975 mg PO

SUPPORTIVE MEDICATIONS:

- **Antimicrobial Prophylaxis:**
  - Very high risk of hepatitis B reactivation. If HBsAg or HBcoreAb positive, follow hepatitis B prophylaxis as per SCHBV.
  - Prophylaxis against reactivation of varicella-zoster virus (VZV) and herpes simplex virus (HSV) is recommended prior to initiating. Patients should take valACYclovir 500 mg PO daily for the duration of the treatment
  - Pneumocystis jirovecii (PJP) prophylaxis: Cotrimoxazole 1 DS tablet PO 3 times each week (Monday, Wednesday and Friday) for a minimum of 6 months
  - Antibacterial prophylaxis: doxycycline 200 mg PO daily for 3 months. Prophylaxis may be continued at the discretion of provider. If patient unable to tolerate doxycycline 200 mg PO daily, can switch to doxycycline 100 mg PO BID. If patient unable to take doxycycline, MOXIfloxacin 400 mg PO daily or levoFLOXacin 500 mg PO daily.
  - Immunoglobulin replacement recommended if IgG level less than 5 g/L and history of infection
- **Antiemetics:**
  - Antiemetic protocol for chemotherapy with low emetogenicity (see SCNAUSEA)

TREATMENT:

- If inpatient treatment, saline lock must be inserted prior to first treatment
- Dose escalation with step-up dosing schedule mandatory at initiation of treatment and after treatment interruptions if indicated (see Treatment interruptions, below). Do not skip or modify doses. Follow schedule outlined below

Cycle 1:

- Do not administer any doses in Cycle 1 if signs or symptoms of infection regardless of Grade of infection (see Dose Modifications)

Drug	Dose		BC Cancer Administration Guideline
teclistamab	Step-up dose 1	0.06 mg/kg on Day 1	Subcutaneously** (abdomen or thigh)
	Step-up dose 2	0.3 mg/kg on Day 3*	
	First treatment dose	1.5 mg/kg on Day 5*	

* May be given 2 to 7 days after previous dose

** Administer doses greater than 2 mL as two syringes at two separate sites

- **Monitoring**: Due to the risk of treatment-related adverse events, in particular CRS, hypotension and ICANS, patients should be monitored as an inpatient during administration and for at least 48 hours following each injection for Step-up dose 1, Step-up dose 2, and the first treatment dose. A physician must be immediately available to respond to emergencies during all inpatient administrations. Consideration may be given to outpatient administration if there is a local plan in place for rapid assessment and intervention of suspected CRS and ICANS following outpatient administration. An adequate local plan must ensure the patient:
  - Remains within the proximity of the treating facility for at least 48 hours following each dose in Cycle 1
  - is monitored at minimum once daily for signs and symptoms of CRS and ICANS after administration of all Cycle 1 doses
  - is counselled on the signs and symptoms associated with CRS and ICANS and on seeking immediate medical attention should they occur at any time
- **Vital signs**: (including blood pressure, heart rate, temperature and pulse oximetry) to be measured prior to each dose in cycle 1, and as clinically indicated. If patient treated as outpatient, vital signs to be measured 15 minutes after each dose in all cycles. If patient treated as inpatient, vitals to be measured routinely per hospital policy. If there is a drop in blood pressure or clinical evidence of CRS or ICANS, notify provider immediately and continue to monitor vital signs according to SCCRS or SCICANS protocol
- Due to the risk of transient hypotension, clinicians should consider reducing or holding antihypertensive medications for 24 hours before and after the first 3

administrations of teclistamab. Appropriate management of patients, especially those with more severe hypertension, receiving medications that may cause rebound hypertension when abruptly discontinued or those who are on multiple blood pressure medications should be discussed with a cardiology consultant.
- If no Grade 2 or greater reactions during or after first treatment dose, subsequent treatment to be given in ambulatory care setting.

Cycle 2 onwards (to start 7 days after first treatment dose):

- To be administered in ambulatory care setting unless adverse reaction with previous dose(s)*

* See Treatment interruptions, below

Drug	Dose	BC Cancer Administration Guideline
teclistamab	1.5 mg/kg on Days 1, 8, 15, and 22**	Subcutaneously*** (abdomen or thigh)

** For patients who have a complete response or better for a minimum of 6 months, may consider reducing the dosing frequency to 1.5 mg/kg on Days 1 and 15

*** Administer doses greater than 2 mL as two syringes at two separate sites

Repeat every 28 days until disease progression or unacceptable toxicity.

- From Cycle 2 onward, for patients restarting with either Step-up dose 1 or Step-up dose 2 after treatment interruptions, observation and vital signs as per Cycle 1 requirements
- From Cycle 2 onward, if no treatment interruptions requiring repeat step-up dosing, patients should be observed for 15 minutes post-injection, with vital signs prior to treatment and at 15 minutes post-injection

DOSE MODIFICATIONS:

No dose reductions are recommended for teclistamab. Dose delays may be recommended as per below.

1. **Cytokine Release Syndrome (CRS):** (also see management of cytokine release syndrome protocol: SCCRS)

Grade	Management
Grade 1	• Hold until resolution • Manage per SCCRS • Give premedications prior to next dose
Grade 2 or Grade 3 (duration less than 48 hours)	• Hold until resolution • Manage per SCCRS • Give premedications prior to next dose • Admit to hospital for next dose
Grade 3 (recurrent or duration more than 48 hours) or Grade 4	• Discontinue teclistamab • Manage per SCCRS

2. **Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS):** (also see management of immune effector cell-associated neurotoxicity syndrome protocol: SCICANS)

Grade	Management
1	• Hold until resolution • Manage per SCICANS
2 or 3 (First occurrence)	• Hold until resolution • Manage per SCICANS • Admit to hospital for next dose
3 (Recurrent) or 4	• Discontinue teclistamab • Manage per per SCICANS

3. **Infections:**
    - Do not give teclistamab in patients with signs or symptoms of active infection, regardless of Grade of infection

4. Hematological: (based on pre-cycle lab work)

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Teclistamab Dose
Greater than or equal to 0.5	and	Greater than or equal to 25 without evidence of bleeding	100%
Less than 0.5*	or	Less than 25	• Call physician • Consider G-CSF support • Hold until ANC 0.5 or greater and platelets 25 or greater without bleeding • Consider transfusion support • Restart at 100%
Greater than or equal to 0.5	and	25 to 50 with bleeding	• Call physician • Hold until platelets 25 or greater without bleeding • Consider transfusion support • Restart at 100%
Febrile neutropenia	and	Greater than or equal to 25 without evidence of bleeding	• Call physician • If during Cycle 1, assess for CRS • If beyond Cycle 1, consider G-CSF support • Hold until ANC 1.0 or greater and fever resolves • Restart at 100%

* Avoid filgrastim during periods when patient at risk of CRS. Consider weekly filgrastim if clinically indicated and filgrastim is available. Filgrastim is not covered as a benefit drug by BC Cancer

5. Treatment Interruptions:

- Treatment schedule and dose may be affected
- Premedications with dexamethasone, antihistamine and acetaminophen may be required prior to next teclistamab dose when treatment resumed

Last Dose of Teclistamab Administered	Number of Days Since Last Dose Administered	Next Teclistamab Dose When Treatment Resumed
Step-up dose 1 0.06 mg/kg	7 days or less	Proceed with dose escalation: • next scheduled dose: step-up dose 2 (0.3 mg/kg). Premedications required
	More than 7 days	Restart dose escalation: • next scheduled dose: step-up dose 1 (0.06 mg/kg). Premedications required
Step-up dose 2 0.3 mg/kg	7 days or less	Proceed with dose escalation: • next scheduled dose: treatment dose (1.5 mg/kg). Premedications required
	8 to 28 days	Repeat last dose given: • next scheduled dose: step-up dose 2 (0.3 mg/kg). Premedications required
	More than 28 days	Restart dose escalation: • next scheduled dose: step-up dose 1 (0.06 mg/kg). Premedications required
Any treatment dose 1.5 mg/kg	28 days or less	Continue at same dose and schedule: • next scheduled dose: treatment dose (1.5 mg/kg). • no premedications required
	More than 28 days	Restart dose escalation: • next scheduled dose: step-up dose 1 (0.06 mg/kg). Premedications required

PRECAUTIONS:

1. **Cytokine release syndrome (CRS):** has been reported with teclistamab, typically occurring within 48 hours of dosing—most often during the Step-up doses and first treatment dose in Cycle 1. The observed symptoms include fevers, rigors, chills, hypotension (which has been severe in some patients) and hypoxemia. Other commonly reported symptoms, typically mild to moderate, include headache, facial and general edema, myalgias, nausea/vomiting and elevated liver enzymes. Late-onset CRS beyond Cycle 1 is rare. To mitigate risk, adhere to the recommended dose escalation schedule and closely monitor for CRS signs and symptoms. Patients should be admitted for the duration of Cycle 1 and for at least 48 hours after, unless a local plan is in place for outpatient delivery which ensures rapid assessment and intervention for CRS and ICANS. Patients must continue to receive teclistamab treatment at a facility equipped to manage CRS and ICANs until a full dose is delivered without incident. Outpatients showing early signs of CRS should be promptly assessed for monitoring and treatment, which may include IV fluids, corticosteroids, tocilizumab, and supportive care per SCCRS protocol. **If CRS-like symptoms occur beyond Cycle 1 following a previously tolerated full dose, alternative causes—particularly infection—should be thoroughly evaluated before attributing symptoms to CRS.**
2. **Neurologic toxicity**, including **immune effector cell-associated neurotoxicity syndrome (ICANS)** and **Guillain-Barré syndrome** can occur during treatment with teclistamab. These can be serious or life-threatening, and can be concurrent with CRS, follow the resolution of CRS, or occur in the absence of CRS. Signs and symptoms include headache, motor dysfunction (e.g., dysgraphia, dysphonia, tremor, hypokinesia and gait disturbance), peripheral neuropathy, and encephalopathy. The most frequently reported neurologic toxicity has been headache. Neurologic toxicity can occur days or weeks after the teclistamab injection and initial symptoms may be subtle. At first sign of ICANS, admit patient to hospital for further monitoring if not already admitted. Neurology consult may be required. Hold teclistamab until neurologic toxicity resolves. Symptoms are managed depending on their severity and whether they occur concurrently with CRS. Permanently discontinue teclistamab for recurrent Grade 3 and Grade 4 events. Due to the potential for ICANS and the risk of reduced consciousness, patients receiving teclistamab should avoid driving or operating heavy machinery for the duration of Cycle 1, 48 hours after the first treatment dose and until 48 hours after the third dose (first treatment dose) if re-escalation required for treatment interruption, and if experiencing neurologic symptoms. See management of immune effector cell-associated neurotoxicity protocol- SCICANS.
3. **Local injection site** and **hypersensitivity reactions** are reported during treatment with teclistamab. Local reactions include bruising, cellulitis, discomfort, erythema, hematoma, induration, inflammation, edema, pruritus, rash, and swelling. Systemic reactions have included Grade 1 pyrexia and swollen tongue,
4. **Infections** have been reported in patients treated with teclistamab. These may be severe or life-threatening. Fatalities have been reported. Fever or other evidence of infection must be assessed promptly and treated aggressively. Do not administer step-up dosing schedule if active infection.

5. **Hematologic toxicities:** Teclistamab may cause hypogammablobulinemia, neutropenia, febrile neutropenia, and thrombocytopenia. Monitor for signs of infection and bleeding.
6. **Live vaccines**: Should be discussed with most responsible physician.
7. **Hepatotoxicity** may occur with teclistamab. Elevated AST, ALT, and total bilirubin have been reported. Liver enzyme elevation may occur with or without concurrent CRS. Hold treatment for Grade 3 hepatotoxicity until Grade 1 or less, and consider discontinuation of teclistamab for Grade 4 hepatotoxicity.
8. **Drug interactions:** The initial release of cytokines associated with teclistamab treatment may suppress CYP450 enzymes. Substrates of CYP450 enzymes with a narrow therapeutic index may require dose adjustment and monitoring for toxicity if given concurrently with teclistamab. The highest risk of interaction is predicted to occur during the teclistamab dose escalation and up to 7 days after the first treatment dose, or during a CRS event.
9. **Hepatitis B Reactivation**: See SCHBV protocol for more details.
10. **Need for irradiated blood products:** Patients receiving an autotransplant require irradiated blood products from 7 days prior to collection to 3 months post transplant (6 months if total body irradiation conditioning) to eliminate the risk of potentially life-threatening transfusion-related graft-versus-host-disease. All other myeloma patients do not require irradiated blood products.
11. **Peripheral Neuropathy:** has been reported in multiple myeloma patients treated with teclistamab. In clinical trials, sensory neuropathy occurred in 16% of patients receiving teclistamab at the recommended dose. Monitor patients for signs and symptoms of neuropathy, such as numbness, tingling, or pain in the extremities. Consider dose interruption or discontinuation based on the severity of symptoms.

Call Dr. Christopher Venner or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

References:

1. Usmani SZ, Garfall AL, van de Donk NWCJ, et al. Teclistamab, a B-cell maturation antigen × CD3 bispecific antibody, in patients with relapsed or refractory multiple myeloma (MajesTEC-1): a multicentre, open-label, single-arm, phase 1 study. Lancet. 2021 Aug 21;398(10301):665-674.
2. Janssen Inc. TECVAYLI® product monograph. Toronto, Ontario; July 26, 2023
3. Raje N, Anderson K, Einsele H, et al. Monitoring, prophylaxis, and treatment of infections in patients with MM receiving bispecific antibody therapy: consensus recommendations from an expert panel. Blood Cancer J. 2023 Aug 1;13(1):116.
4. Teclistamab (Tecvayli) CADTH [Canada's Drug Agency (CDA-AMC)] Reimbursement Recommendation. Canadian Journal of Health Technologies. Apr 2024.