Clinical Guidance: Use of Bispecific T-cell Engagers (TCEs) in the Management of Relapsed/ Refractory Multiple Myeloma

CITE
Canadian Institute for the Transfer of KnowledgE

Do	• **Monitor patients for signs and symptoms** of infection prior to and during treatment with TCEs and manage appropriately.[1] • **Collect baseline serostatus and history** for cytomegalovirus (CMV), human immunodeficiency virus (HIV) and hepatitis B/C virus (HBV, HCV) prior to TCE treatment.[1-5] • Use acyclovir or valacyclovir prophylaxis to **prevent herpes simplex and varicella zoster** for duration of therapy, in addition to pre-treatment recombinant vaccination series, where feasible.[1,2,5] • Start ***Pneumocystis jirovecii* pneumonia prophylaxis** for patients on TCE therapy.[2] • **Administer pre-treatment medications** (acetaminophen, dexamethasone, and an antihistamine) 1 hour prior to step-up doses to reduce the risk of cytokine release syndrome (CRS).[6] • **Monitor immunoglobulin (Ig) levels** and administer Ig replacement subcutaneously or intravenously for patients with **hypogammaglobulinemia**.[2]
Stop	• Do not initiate TCE therapy in patients with **active infection**.[1,6,7]
Consider	• Consider use of **antifungal monitoring** in patients with a history of fungal infections, prolonged neutropenia, or prolonged high-dose corticosteroid use.[1,2] • Consider use of **antibiotic prophylaxis** in patients with high risk of infection.[1] • Consider **prophylactic colony-stimulating factor** in patients with documented ⩾grade 3 neutropenia.[2]

Background

Multiple myeloma is an aggressive cancer characterized by the proliferation of abnormal clonal plasma cells, typically affecting adult patients ⩾65 years old. Complications include anemia, bone damage, increased susceptibility to infections, and progressive immune and kidney dysfunction.[8-10]

Almost all patients with multiple myeloma eventually relapse, with the time interval of sustained remission decreasing with each line of therapy.[11] In the relapsed/refractory setting (RRMM), multiple myeloma is associated with a poor prognosis. After failure of three classes of therapies (proteasome inhibitors, immunomodulatory agents, and anti-CD38 monoclonal antibodies), patients on subsequent treatment regimens show a median overall survival of 9.3 months.[8] Moreover, some patients do not achieve a durable, or any, response to treatment, further demonstrating a need for effective therapeutic options in the RRMM population.[9]

Use of Bispecific T-cell Engagers in the Management of RRMM

Bispecific T-cell engagers (TCE), including chimeric antigen receptor (CAR)-T-cell immunotherapies and bispecific antibody therapies, have improved survival of patients with RRMM.[14] CAR T-cell therapy involves modifying T-cells extracted from a patient's own blood, which are then injected back into the patient as a one-time treatment.[15] Bispecific antibody therapy engages both the patient's own cytotoxic T-cells and myeloma cells, and patients are typically treated to progression or toxicity.[15] TCEs are designed to bind to a T-cell epitope and an extracellular tumour antigen (such as B-cell maturation antigen [BCMA] or GPRC5D), releasing cytotoxic granules and stimulating cytotoxic T-cell activity, leading to tumour cell death.[15,16]

mSMART guidelines recommend use of BCMA-directed therapies in patients who are triple-class refractory, i.e., refractory to proteasome inhibitors (bortezomib, carfilzomib), immunomodulatory agents (lenalidomide, pomalidomide), and anti-CD38 monoclonal antibody therapies (daratumumab, isatuximab).[12]

Currently approved under *Notice of Compliance with Conditions based on promising evidence of clinical effectiveness*, available TCEs in Canada include:

- Elrexfio™ (elranatamab): anti-BCMA-CD3 bispecific antibody[7]
- Tecvayli™ (teclistamab): anti-BCMA-CD3 bispecific antibody[6]
- Talvey™ (talquetamab): anti-GPRC5D-CD3 bispecific antibody[16] *(recently approved)*

TCE Patient Profile

- Treatment of RRMM should be tailored to the individual, considering patients':[12,13]
  - Previous treatment tolerance
  - Trajectory of myeloma marker
  - Cytogenetic risk profile
  - Frailty
  - Patient preference
  - Comorbidities, including amyloidosis, cardiac disease, renal insufficiency
- TCEs are indicated as monotherapy for patients who have failed ⩾3 lines of therapy[6,7]
- Contraindications include hypersensitivity to the medication or its components[6,7]

Authors: Mohammed Aljama, MD, FRCPC (Chair); Shreyash Dalmia, MD, FRCPC; Mohammad S. Ebraheem, MD, FRCPC; Chris Hillis, MD, FRCPC

Last Updated 11/2025

Clinical Guidance: Use of Bispecific T-cell Engagers (TCE) in the Management of Relapsed/ Refractory Multiple Myeloma

CITE
Canadian Institute for the Transfer of Knowledge

TCE Treatment Administration

Initiate TCE treatment with step-up dosing schedule according to product monograph to reduce the risk of CRS. Do not initiate TCE treatment in patients with active infection.[6,7]

Administration routes and schedules

Dose may be weight based or fixed, depending on the product, and administered by subcutaneous injection in the abdomen/thigh. See product monograph for specific dosing and injection volumes. Patients should be treated until progression or unacceptable toxicity.[6,7]

Dosing schedule	Dose	elranatamab (Elrexfio™)[7]	teclistamab (Tecvayli™)[6]
Step-up dosing schedule Include pre-treatment medications 1 hour prior	**Step-up dose 1**	12 mg on week 1, day 1	0.06 mg/kg single dose on week 1, day 1
		A minimum of 2 days should be maintained between *step-up dose 1* (12 mg) and *step-up dose 2* (32 mg)	*Step-up dose 2* may be given between 2 to 7 days after *step-up dose 1*
	Step-up dose 2	32 mg on week 1, day 4	0.3 mg/kg single dose on week 1, day 3
		A minimum of 3 days should be maintained between *step-up dose 2* (32 mg) and the first *treatment* (76 mg) dose	First *treatment dose* (1.5 mg/kg) may be given between 2 to 7 days after *step-up dose 2*
	Treatment dose	76 mg, week 2, day 1	1.5 mg/kg single dose on week 1, day 5
Weekly dosing schedule	**Treatment dose**	Week 3-24: day 1, 76 mg once weekly	1.5 mg/kg, week 2, day 5, then once weekly
	Minimum gap	6 days	5 days
Extended dosing schedule	**Treatment dose**	*For patients who have achieved and maintained ⩾partial response for 2 months:* Week 25 onward: day 1, 76 mg biweekly *For patients who have maintained a response following ⩾24 weeks of biweekly dosing* Week 49 onward: day 1, 76 mg once every four weeks	*For patients who have achieved and maintained a stringent complete response for ⩽6 months:* 1.5 mg/kg, week 2, day 5, then biweekly

Recommendations for restarting therapy after dosage delay

If a dose is missed, administer the dose as soon as possible, and adjust the dosing schedule to maintain the dosing interval. Consider administering pre-medication prior to step-up dose 1 and 2 when restarting therapy.[6,7]

Last dose given	elranatamab (Elrexfio™)	teclistamab (Tecvayli™)	Restart at dose
Step-up dose 1: Elrexfio™ = 12 mg Tecvayli™ = 0.06 mg/kg	⩽14 days[a]	⩽7 days	**Step-up dose 2**
	>14 days	>7 days	**Step-up dose 1**
Step-up dose 2 Elrexfio™ = 32 mg Tecvayli™ = 0.3 mg/kg	0-14 days	0-7 days	**Full treatment dose**
	15–28 days[a]	8–28 days	**Step-up dose 2**
	>28 days	>28 days	**Step-up dose 1**
Full treatment dose Elrexfio™ = 72 mg Tecvayli™ = 1.5 mg/kg	⩽42 days[b]	⩽28 days[b,c]	**Full treatment dose**
	43–84 days[a]		**Step-up dose 2**
	>84 days	>28 days	**Step-up dose 1**

[a]If tolerated, increase to full treatment dose (76 mg) 4 days later [b]Do not administer pre-treatment medications [c]Resume at full treatment dose (1.5 mg/kg), and schedule (once weekly or every 2 weeks)

Dosing considerations and potential adjustments

Dose reductions are only recommended in patients with CRS concerns, in which case, reduce the dose by one level, or as per product monograph. Dose delays may be required to manage toxicities related to TCE therapy.[6,7]

Authors: Mohammed Aljama, MD, FRCPC (Chair); Shreyash Dalmia, MD, FRCPC; Mohammad S. Ebraheem, MD, FRCPC; Chris Hillis, MD, FRCPC

Last Updated 11/2025

Clinical Guidance: Use of Bispecific T-cell Engagers (TCE) in the Management of Relapsed/ Refractory Multiple Myeloma

CITE
Canadian Institute for the Transfer of KnowledgE

Monitoring, Prophylaxis, and Management of Infectious Complications

Multiple myeloma patients are at a much higher risk of infections than the general population due to the cumulative effect of disease, treatment, and host-related factors, particularly in the RRMM setting.[2,17] In addition, TCEs are associated with an increased risk of infection compared to conventional multiple myeloma treatments, including new or reactivated viral infections (e.g., HBV) along with a risk of opportunistic infections.[2,6,7] Adverse events attributable to TCEs include CRS, peripheral neuropathy, hypogammaglobulinemia, immune effector cell-associated neurotoxicity syndrome (ICANS), cytopenias, and infections.[1,2,17]

As severe, life-threatening, or fatal infections have been reported in patients receiving TCEs, monitoring for signs and symptoms of infection prior to and during treatment with TCEs is strongly recommended. Prophylaxis should be administered for patients where applicable. Consider collecting baseline CMV history and serostatus (IgG/IgM) with serial CMV DNA monitoring if reactivation is noted, and HBV (surface antigen, core antibody, surface antibody), HCV, and HIV serostatus prior to TCE treatment initiation.[1-5] TCE dosing should be maintained during prophylaxis but can be temporarily discontinued until infection resolution during treatment.[2]

Risk factors

Hypogammaglobulinemia: Prolonged hypogammaglobulinemia is associated with TCE therapy, which increases infection risk.[1-3,5]

- In patients with hypogammaglobulinemia/history of recurrent infections, consider monthly monitoring for Ig levels during Ig treatments.[2]
- Administer Q1M intravenous immunoglobulin (IVIg) treatment in patients at risk and without life-threatening infectious manifestations for the duration of TCE treatment until Ig levels are ⩾400 mg/dL.[2]
- Dose reduction in TCE is not required for patients with hypogammaglobulinemia on Ig replacement.[2]

Neutropenia: Consider antibacterial or antifungal prophylaxis with prolonged neutropenia (absolute neutrophil count ⩽100 cells per µL for ⩾7 days). **In patients with documented ⩾grade 3 neutropenia, it is recommended to use colony-stimulating factors.**[2]

Recommendations to reduce risk of infections[1-5]

Infection type	Population	Screening	Prophylaxis	Monitoring	Treatment
Bacterial	All	No	Vaccinate for pneumonia	No	Broad-spectrum antibiotics; use targeted therapy as per guidelines
	High risk of or history of recurrent bacterial infections and/or prolonged neutropenia	No	Yes (levofloxacin)	No	
Viral	All	No	Vaccinate annually for COVID-19	No	As per guidelines
Herpes simplex or varicella zoster	All	No	Yes (acyclovir or valacyclovir), vaccinate	No	As per guidelines
CMV	All	Yes	No	Monitor using CMV DNA copies if infection risk is suspected	Oral valganciclovir, IV ganciclovir, or foscarnet; consult with Infectious Diseases for guidance on treatment thresholds
HBV	All	Yes (core, surface antigen /antibodies)	Yes (as per standard guidelines)	No	As per guidelines
HCV	All	Yes (anti-HCV antibodies)	No	No	As per guidelines
HIV	In younger patients and in areas with a high prevalence of HIV	Yes	No	No	Consult with Infectious Diseases
Influenza	All	No	Vaccinate annually for influenza	Test if suspected	Oseltamivir
Fungal	All	No	No	Monitor for signs of infection, especially if *aspergillosis* is suspected	Consult with Infectious Diseases
	Recurrent fungal infections, prolonged neutropenia, or >2 weeks high-dose corticosteroid use	Yes	No		
P. jirovecii infection	All	No	Yes (trimethoprim-sulfamethoxazole, dapsone, atovaquone, or inhaled pentamidine)	If suspected	As per guidelines

Authors: Mohammed Aljama, MD, FRCPC (Chair); Shreyash Dalmia, MD, FRCPC; Mohammad S. Ebraheem, MD, FRCPC; Chris Hillis, MD, FRCPC

Last Updated 11/2025

Clinical Guidance: Use of Bispecific T-cell Engagers (TCE) in the Management of Relapsed/ Refractory Multiple Myeloma

CITE
Canadian Institute for the Transfer of KnowledgE

Practical Management of Treatment-related Toxicities

Adverse events associated with TCE therapy

Major adverse events of TCEs include anemia, prolonged cytopenias, immunosuppression, and frequent infections. Serious, life-threatening, or fatal reactions can occur in patients receiving TCEs, including CRS, neurotoxicity, and ICANS.[6,7,18]

Grading and management of CRS

CRS is a common manifestation associated with TCE therapy and is most commonly grade 1-2 and controllable.[19] CRS should be identified based on its clinical presentation, and other causes of fever, hypoxia, and hypotension should be evaluated and treated. Due to the high risk of infection, broad-spectrum antibiotics are often initiated to rule out active infection.[19]

Manage CRS according to the product monograph or recommendations below and consider further management per current practice guidelines. Administer supportive therapy for CRS, which may include intensive care for severe or life-threatening CRS, as well as antipyretic agents, intravenous fluid support, vasopressors, anti-IL-6 or anti-IL-6 receptor medications (i.e., tocilizumab), corticosteroids, or supplemental oxygen. Consider laboratory testing to monitor for disseminated intravascular coagulation and hematology parameters, as well as pulmonary, cardiac, renal, and hepatic function.[6,7]

Recommendations for Management of CRS

CRS Grade	Supportive Care	TCE	Tocilizumab	Corticosteroids
Grade 1	• Antipyretics • IV fluids • Use of vasopressors • Investigate for infection and start broad spectrum antibiotics	Withhold TCE until CRS resolves	Consider use	Continue corticosteroids use until the event is Grade 1 or less, then taper over 3 days
Grade 2			• Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg) • Repeat Q8H as needed, if not responsive to IV fluids or increasing supplemental oxygen • Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses	If no improvement within 24 hours: • Methylprednisolone 1 mg/kg IV BID OR • Equivalent dexamethasone (e.g., 10 mg IV Q6H) **OR**
Grade 3				• Methylprednisolone 1 mg/kg IV BID OR • Equivalent dexamethasone (e.g., 10 mg IV Q6H) **OR**
Grade 4				• Methylprednisolone: ○ 1 mg/kg IV BID **OR** ○ 1000 mg IV OD Q3D, per physician discretion **OR** • Equivalent dexamethasone (e.g., 10 mg IV Q6H) **OR** • If no improvement or if condition worsens, consider alternate immunosuppressants

Management of neurologic toxicity, including ICANS

Serious or life-threatening neurologic toxicities, including encephalopathy and ICANS, can occur following treatment. While relatively rare, ICANS should be managed according to the recommendations below and consider further management per current practice guidelines.[19] The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. If concurrent CRS, manage as per table above.[6,7,20,21]

Incidence of adverse events

Adverse event	Therapy	Incidence	Median time to onset from last dose (range)	Median duration (range)
CRS	elranatamab[7]	Any grade: 57.9% Grade 3+: 0.5%	2 days (1–9 days)	2 days (1–19 days)
	teclistamab[6]	Any grade: 72% Grade 3 +: 0.6%	2 days (1-6)	2 days (1-9)
ICANs	elranatamab[7]	Any grade: 3.3%, all grade 1 or 2	3 (1-4 days)	2 (1-18 days)
	teclistamab[6]	Any grade: 3%, all grade 1 or 2	4 days (2-8 days)	3 days (1-20 days)

Authors: Mohammed Aljama, MD, FRCPC (Chair); Shreyash Dalmia, MD, FRCPC; Mohammad S. Ebraheem, MD, FRCPC; Chris Hillis, MD, FRCPC

Last Updated 11/2025

Clinical Guidance: Use of Bispecific T-cell Engagers (TCE) in the Management of Relapsed/ Refractory Multiple Myeloma

CITE
Canadian Institute for the Transfer of KnowledgE

Recommendations for management of ICANS

ICANS Grade	Supportive Care	TCE	Corticosteroids	
Grade 1	• **Rule out other causes** of neurologic symptoms • Consider non-sedating, anti-seizure medicines for **seizure prophylaxis** • Monitor neurologic symptoms and consider and **consider specialist consultation** • **Provide supportive therapy,** which may include intensive care, for severe or life-threatening neurologic toxicities	Withhold TCE until ICANS resolves	Continue dexamethasone use until resolution to Grade 1 or less, then taper	
			If concurrent CRS	***If no concurrent CRS***
Grade 2			If no improvement after starting tocilizumab, consider dexamethasone if not already taking other corticosteroids	Administer dexamethasone 10 mg IV Q6H
Grade 3		If repeated, consider discontinuing TCE	Administer dexamethasone 10 mg Q6H	
Grade 4		Consider discontinuing TCE	Administer dexamethasone 10 mg Q6H OR Methylprednisolone 1000 mg QD for ⩾2 days	

References:

1. Raje NS, Anaissie E, Kumar SK, et al. Consensus guidelines and recommendations for infection prevention in multiple myeloma: a report from the International Myeloma Working Group. *Lancet Haematol.* 2022;9(2):e143-e161. doi:10.1016/S2352-3026(21)00283-0
2. 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;13(1):1-17. doi:10.1038/s41408-023-00879-7
3. Mohan M, Chakraborty R, Bal S, et al. Recommendations on prevention of infections during chimeric antigen receptor T-cell and bispecific antibody therapy in multiple myeloma. *Br J Haematol.* 2023;203(5):736-746. doi:10.1111/bjh.18909
4. De Groot JJB, Webb MJ, Raubenheimer JE, Struwig MC, Louw VJ. Concomitant HIV infection in newly diagnosed multiple myeloma patients is hard to recognise and should be tested for routinely in areas of high endemicity. *South Afr Med J Suid-Afr Tydskr Vir Geneeskd.* 2017;107(9):781-787. doi:10.7196/SAMJ.2017.v107i9.12360
5. Reynolds G, Cliff ERS, Mohyuddin GR, et al. Infections following bispecific antibodies in myeloma: a systematic review and meta-analysis. *Blood Adv.* 2023;7(19):5898-5903. doi:10.1182/bloodadvances.2023010539
6. Janssen Inc. TECVAYLI (teclistamab injection) product monograph. Published online June 26, 2025. Accessed November 13, 2025. https://www.janssenlabels.com/ca/content/labelling/TECVAYLI/tecvayli_cpm.pdf
7. Pfizer Canada ULC. ELREXFIO™ (elranatamab injection) product monograph. Published online October 3, 2025. Accessed November 13, 2025. https://www.pfizer.ca/en/our-products/elrexfio-elranatamab-injection
8. Parrondo RD, Ailawadhi S, Cerchione C. Bispecific antibodies for the treatment of relapsed/refractory multiple myeloma: updates and future perspectives. *Front Oncol.* 2024;14. doi:10.3389/fonc.2024.1394048
9. Torre A de la. Evolving role of novel therapies in myeloma: T-cell engagers and antibody-drug conjugates. *Can Hematol Today.* Published online June 7, 2023:16-19. doi:10.58931/cht.2023.2233
10. Laubach JP. Multiple myeloma: UptoDate. *Up to Date.* February 27, 2024. Accessed May 3, 2024. https://www.uptodate.com/contents/multiple-myeloma-initial-treatment
11. Rajkumar SV. Multiple myeloma: 2022 update on diagnosis, risk stratification, and management. *Am J Hematol.* 2022;97(8):1086-1107. doi:10.1002/ajh.26590
12. mSMART. Treatment Guidelines - Multiple Myeloma. Published online February 2023. Accessed April 24, 2024. https://www.msmart.org/s/mSMART-RelapsedMM_V7_Feb2023.pdf
13. Mikhael J, Ismaila N, Cheung MC, et al. Treatment of Multiple Myeloma: ASCO and CCO Joint Clinical Practice Guideline. *J Clin Oncol.* 2019;37(14):1228-1263. doi:10.1200/JCO.18.02096
14. Tanenbaum B, Miett T, Patel SA. The emerging therapeutic landscape of relapsed/refractory multiple myeloma. *Ann Hematol.* 2023;102(1):1-11. doi:10.1007/s00277-022-05058-5
15. Definition of CAR T-cell therapy - NCI Dictionary of Cancer Terms - NCI. February 2, 2011. Accessed May 6, 2024. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy
16. Janssen Inc. TALVEY (talquetamab injection). Published online April 30, 2024. Accessed September 17, 2024. https://www.janssen.com/canada/sites/www_janssen_com_canada/files/prod_files/live/talvey_cpm.pdf
17. Ahmed A, Killeen RB. Relapsed and Refractory Multiple Myeloma. In: StatPearls. StatPearls Publishing; 2024. Accessed April 24, 2024. http://www.ncbi.nlm.nih.gov/books/NBK592405/
18. Dima D, Ullah F, Mazzoni S, et al. Management of Relapsed–Refractory Multiple Myeloma in the Era of Advanced Therapies: Evidence-Based Recommendations for Routine Clinical Practice. *Cancers.* 2023;15(7):2160. doi:10.3390/cancers15072160
19. Raje NS, Cohen AD, Patel KK, Donk NWCJ van de, Richter J, San-Miguel J. Practical Aspects of Immunotherapy: A Report from the 20th International Myeloma Society (IMS) Annual Meeting. *Clin Lymphoma Myeloma Leuk.* 2024;0(0). doi:10.1016/j.clml.2024.03.005
20. Lee DW, 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(4):625-638. doi:10.1016/j.bbmt.2018.12.758
21. Lesokhin AM, Tomasson MH, Arnulf B, et al. Elranatamab in relapsed or refractory multiple myeloma: phase 2 MagnetisMM-3 trial results. *Nat Med.* 2023;29(9):2259-2267. doi:10.1038/s41591-023-02528-9

Authors: Mohammed Aljama, MD, FRCPC (Chair); Shreyash Dalmia, MD, FRCPC; Mohammad S. Ebraheem, MD, FRCPC; Chris Hillis, MD, FRCPC

Last Updated 11/2025