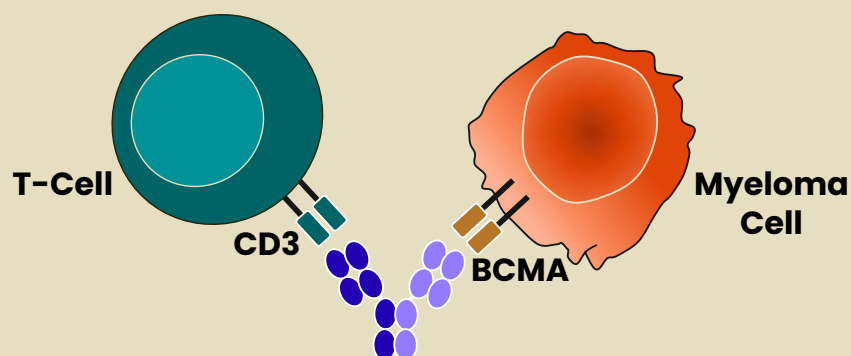


Bispecific Antibodies for Relapsed/Refractory Multiple Myeloma: Efficacy and Safety Considerations



The 4 bispecific antibodies (BsAbs) currently approved for multiple myeloma (MM) are indicated for patients with relapsed/refractory (R/R) MM after ≥ 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody¹⁻⁴

Bispecific Antibodies in R/R MM: Clinical Trials Findings⁵⁻¹⁴

Target	Agent	Trial	Prior Therapy, Median (Range)	ORR, %	mDoR, Mo	mPFS, Mo
BCMA	Elranatamab	MagnetisMM-3	5 (2-22)	61	NR	17.2
	Teclistamab	MajesTEC-1	5 (2-14)	63	24.0	11.4
	Linvoseltamab	LINKER-MM1	5 (2-16)	70	29.4	NR
GPC5D	Talquetamab	MonumenTAL-1 QWK	6 (2-14)	74	9.5	7.5
		MonumenTAL-1 Q2WK	5 (2-17)	70	17.5	11.2

mDoR, median duration of response; mPFS, median progression-free survival; NR, not reached.

Dosing and Administration of BsAbs in R/R MM¹⁻⁴



	Teclistamab	Talquetamab	Elranatamab	Linvoseltamab
Dosing/Route	Weight based/SQ	Weight based/SQ	Fixed dosing/SQ	Fixed dosing/IV
Schedule	C1: D1, D4, D7 C2: Weekly <i>Biweekly dosing after ≥ 6 mo in $\geq$ CR</i>	Weekly C1: D1, D4, D7 C2+: Weekly Biweekly C1: D1, D4, D7, D10 C2+: Biweekly	C1: D1, D4, D8 C2+: Weekly through Wk 24, then biweekly	C1: D1, D8, D15 C2+: Weekly through Wk 13, then biweekly <i>Q4W dosing if $\geq$ VGPR at or after Wk 24 and received ≥ 17 full doses</i>
Hospitalization	48 hr after all SUD	48 hr after all SUD	48 hr after 1st SUD 24 hr after 2nd SUD	24 hr after 1st and 2nd SUD

CR, complete response; SUD, step-up dose; VGPR, very good partial response.

Safety of Approved Bispecific Antibodies in R/R MM^{1-4,14-19}

Adverse Event (AE)	Teclistamab	Talquetamab	Elranatamab	Linvoseltamab
CRS occurrence 	Overall: 72% Grade 1: 50% Grade 2: 21%	Overall: 76% Grade 1: 57% Grade 2: 17%	Overall: 58% Grade 1: 44% Grade 2: 14%	Overall: 46% Grade 1: 35% Grade 2: 10%
ICANS occurrence 	Grade 1/2: 3% Grade 3/4: 0%	Grade 1/2: 3% Grade 3/4: 3%	Grade 1/2: 3% Grade 3/4: 0%	Grade 1/2: 5.4% Grade 3: 2.6%
Neutropenia 	Grade 3/4: 56%	Grade 3/4: 35%	Grade 3/4: 51%	Grade 3/4: 47%
Infection 	Grade 3/4: 35%	Grade 3/4: 17%	Grade 3/4: 31%	Grade 3/4: 38%
Skin/nail toxicity 	Not reported	62%	26%	15%
Oral toxicity 	Not reported	Overall: 80% Dysgeusia: 49% Dry mouth: 34% Dysphagia: 23% Ageusia: 18%	Not reported	Not reported

CRS, cytokine release syndrome; ICANS, immune effector cell–associated encephalopathy.

Due to the risk of CRS and neurotoxicity (including ICANS), all currently approved BsAbs for R/R MM are administered under a REMS Program. For more information, see individual prescribing information.

Managing ICANS With BsAbs²⁰



Patients taking BsAbs for R/R MM may develop neurologic toxicities, including ICANS. ICANS typically presents with

cognitive changes (confusion, inability to follow commands, attention deficits), seizures, and cerebral edema.

For more information on grading ICANS visit American Society for Transplantation and Cellular Therapy (ASTCT) Consensus Grading for CRS and Neurologic Toxicity.

Grade	Presenting Symptoms	Actions
1	ICE score 7–9	- Hold bispecific - Consider antiseizure medication
2	ICE score 3–6	- Hold bispecific - Administer dex 10 mg q6h until grade 1 - Consider antiseizure medication
3	ICE score 0–2 Seizures Raised ICP (focal edema)	- Hold bispecific - Administer dex 10 mg q6h until grade 1 - Consider antiseizure medication
4	ICE score 0 Unarousable Repetitive seizures Raised ICP with diffuse edema, etc	- Permanently discontinue bispecific - Administer dex 10 mg IV q6h until grade 1 or methylprednisolone 1000 mg daily x 3 d - Consider antiseizure medication

Managing CRS With BsAbs^{15,21}



CRS may manifest with constitutional symptoms (fever, flulike symptoms) and can progress to hypotension, hypoxia, and multiorgan failure.

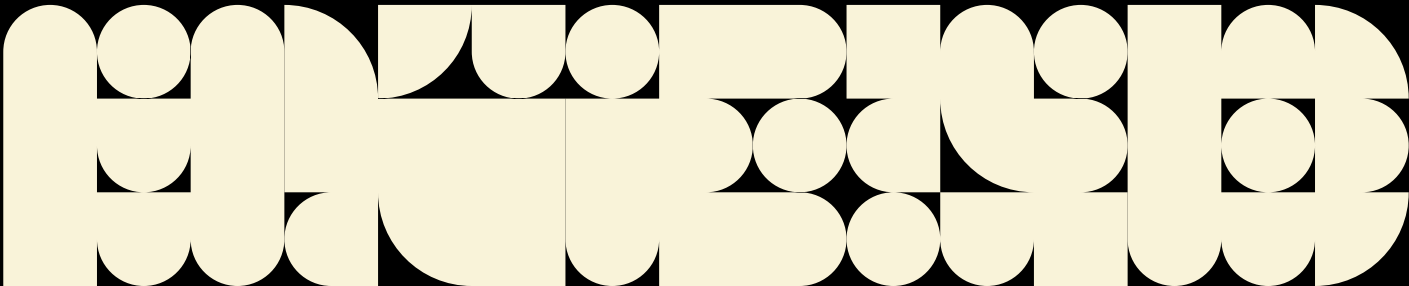
For more information on grading CRS visit [ASTCT Consensus Grading for CRS and Neurologic Toxicity](#).

CRS Grade	Per Prescribing Information	Per MonumenTAL-1 Protocol (Applies to Other BsAbs)	
		Tocilizumab	Corticosteroids
1	- Hold until CRS resolves - Administer pretreatment medications prior to next dose	May be considered	N/A
2	- Hold until CRS resolves - Administer pretreatment medications prior to next dose	- Administer 8 mg/kg IV over 1 hr - Repeat every 8 hr as needed if not responsive to IV fluids or increasing supplemental oxygen	Grade 2 Manage per guidance below if no improvement within 24 hr of tocilizumab initiation
3 <i>Duration <48 hr</i>	Patients should be hospitalized for 48 hr following next dose	Limit to a maximum of 3 doses/24 hr period; maximum total: 4 doses	Grade 3 If no improvement, begin methylprednisolone 1 mg/kg IV BID or dexamethasone equivalent (eg, 10 mg IV every 6 hr)
3 <i>Recurrent or duration ≥48 hr</i>	- Permanently discontinue - Provide supportive therapy		Grade 4 Manage as above or begin methylprednisolone 1000 mg IV QD for 3 days at discretion of the investigator
4			

Recommendations for Managing Infections With BsAbs for R/R MM²²

Patients remain susceptible to infections throughout the duration of BsAb therapy

- Use antiviral prophylaxis against HSV and VZV in all patients
- Screen for HBV reactivation risk in all patients
- Administer monthly IVIG for duration of immunoparesis and in absence of life-threatening infectious manifestations
- Use colony-stimulating factors in persons with grade ≥3 neutropenia
- Do not use prophylaxis for aspergillosis
- Use PJP prophylaxis for all patients
- Follow CDC guidelines for vaccinations



Managing GPRC5D–Associated Toxicities With Talquetamab^{23,24}

AE	Recommendation
Dysgeusia	Delay or reduce dose intensity at time of response
Oral events • Xerostomia • Periodontal disease/caries • Weight loss • Treatment of oral comorbidities	• Hydrate (eg, saliva substitutes), sugar-free chewing gum to stimulate saliva flow, SLS-free toothpastes • Regular dental review • Nutritional supplements • eg, thrush or nutritional deficiencies resulting to glossitis
Skin reactions • Prevention • Low-grade rash • Rash grade ≥ 3 or refractory to topical medications • Rash occurring C2+ or refractory to above	• Skin emollients (eg, urea 10% cream, ammonium lactate 12% cream), sunscreen • Low-potency corticosteroids for topical application, escalate to medium potency • Short durations of oral steroids (eg, prednisone) • Consult dermatologist
Nail fragility	Nail hardener, vitamin E oil/emollients

Practical Steps for Integrating BsAb Therapy in the Community Setting^{25,26}

Logistics

- Establish strong relationships between HCPs at academic and community cancer programs
- Establish clear referral pathways and protocols for the transition from inpatient to outpatient administration
- Ensure both centers can order and administer the drug and that REMS certifications are complete

Care Coordination

- Connect patients with navigators who help coordinate logistics between community cancer centers and academic institutions, if available
- Create a resource to help prepare patients to receive initial treatment at an academic center and follow-up care at a community cancer center
- Use telehealth, when possible, to provide follow-up care, symptom monitoring, and coordinate with local HCPs

AE Management

- Ensure handoff documentation includes exact dates of doses and document AEs and treatment, if applicable
- Regularly educate staff on expected side effects with BsAbs and management strategies (include written protocols and clearly defined roles/responsibilities and decide when to hospitalize patients for AEs)
- Ensure patients and caregivers understand potential toxicities of BsAb therapy including REMS requirements
- Advise patients and caregivers on when to report adverse events and to whom

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