Management of Patients With Relapsed/Refractory Multiple Myeloma Treated With Talquetamab: Highlights From Pharmacists' Perspectives

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Abstract

Talquetamab is a first-in-class G protein–coupled receptor family C group 5 member D (GPRC5D) and CD3-targeting bispecific antibody with > 71% overall response in patients with relapsed or refractory multiple myeloma who have progressed on three other drug classes. GPRC5D is highly expressed on myeloma cells, along with some expression in normal hair follicles, skin, and tongue. Its unique expression on these normal tissues results in a distinct pattern of adverse events (AEs), as observed in the phase I/II MonumenTAL-1 trial. GPRC5D-related AEs included oral side effects (e.g., dysgeusia, dysphagia, xerostomia) and dermatologic toxicities (e.g., skin, nail). These AEs can be managed by dose modifications, emollients, and/or topical or oral corticosteroids. Cytokine release syndrome and immune effector cell–associated neurotoxicity syndrome were consistent with the T-cell redirection mechanism of talquetamab and can be managed consistent with other trials of T-cell redirection therapies. Infection rates were mostly grades 1 or 2, and grade ≥ 3 infection rates were lower than B-cell maturation antigen–targeting bispecific antibodies; infections were treated with anti-infective agents. Adverse events were manageable and led to few treatment discontinuations. This review reports on talquetamab safety in MonumenTAL-1, with an additional pharmacy focus on strategies related to drug dispensing and clinical management.

Multiple myeloma (MM) is a malignant plasma cell disorder with an estimated 188,000 cases worldwide according to Global Cancer Observatory statistics (International Agency for Research on Cancer & World Health Organization, 2022). In the United States alone, MM accounts for ~2% of cancer diagnoses and > 2% of cancer deaths (Padala et al., 2021). The treatment landscape of MM has changed dramatically over the last decade, particularly with the development of novel therapies such as anti-CD38 antibodies, bispecific antibodies, and chimeric antigen receptor T-cell therapies (Rajkumar, 2020; Tanenbaum et al., 2023). Patient outcomes have improved with the advancement of treatment options (Kumar et al., 2014); however, almost all patients relapse and may become refractory to treatment, with choice of therapy dependent on several patient-related factors (Mateos et al., 2022; Rajkumar, 2020). Novel therapies, with alternate and distinct mechanisms of action, are therefore useful to treat relapsed or refractory MM (RRMM; Berdeja et al., 2021; Moreau et al., 2022; Munshi et al., 2021).

Talquetamab (Talvey) is a first-in-class, bispecific antibody that targets both G protein–coupled receptor family C group 5 member D (GPRC5D) on myeloma cells and CD3-expressing T cells (Chari et al., 2022). GPRC5D is highly expressed on myeloma cells and has little to no expression on normal B cells (Verkleij et al., 2021). Talquetamab redirects T cells to mediate killing of GPRC5D-expressing myeloma cells (Chari et al., 2022). In August 2023, the US Food and Drug Administration (FDA) approved talquetamab for adult patients with RRMM who received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody (European Medicines Agency, 2024; Janssen Biotech Inc., 2023a).

Talquetamab is currently being evaluated as monotherapy in the phase I/II MonumenTAL-1 clinical study (NCT03399799/NCT04634552) for the treatment of RRMM (Chari et al., 2024), as well as in combination with other therapies (Cohen et al., 2023; Dholaria et al., 2023). MonumenTAL-1 is a first-in-human trial of talquetamab for patients with RRMM (Chari et al., 2022), given via subcutaneous (SC) injection. Two dosing regimens were identified in the trial: 0.4 mg/kg weekly (QW) and 0.8 mg/kg every other week (Q2W). Results showed an overall response rate of 72% to 74% between the two cohorts (Chari et al., 2024).

This review reports on the safety of talquetamab in MonumenTAL-1, with a focus on strategies for pharmacists, nurse practitioners, physician assistants, and other health-care team members who participate in selection, optimization, and implementation of MM treatment and associated supportive care regimens, as well as education on clinical management of talquetamab adverse events (AEs).

PATHOPHYSIOLOGY

GPRC5D expression in normal tissue was shown on immune cells of the plasma cell phenotype, hair follicles, and filiform papillae of the tongue (Chari et al., 2024; Goldsmith et al., 2021; Smith et al., 2019). This distinctive expression profile may contribute to unique AEs observed with talquetamab. The mechanism by which GPRC5D causes skin AEs remains unclear because GPRC5D expression is restricted to hair follicles and eccrine sweat glands (Chari et al., 2024; Inoue et al., 2004; Smith et al., 2019). Skin and nail AEs observed during MonumenTAL-1 included rashes, pruritus, and onycholysis, among others. In the oral cavity, GPRC5D expression is limited to the filiform papillae of the tongue, which do not contain residential/interstitial plasma cells or taste receptors (Chari et al., 2024; Inoue et al., 2004). Although the cause of dysgeusia is unclear and characteristics of taste disturbances vary among patients, dysgeusia has now been established as an AE associated with GPRC5D-targeting therapies. Other oral side effects include dysphagia and xerostomia (Chari et al., 2024).

TALQUETAMAB SAFETY PROFILE

The detailed safety profile and clinical management of talquetamab from MonumenTAL-1 have been previously published (Chari et al., 2024; Chari et al., 2022). A total of 339 patients were evaluated in one of three cohorts: SC talquetamab at 0.4 mg/kg QW (n = 143), SC talquetamab at 0.8 mg/kg Q2W (n = 145), or SC talquetamab at QW or Q2W in patients who had received prior T-cell redirection therapies (n = 51; Chari et al., 2024; Schinke et al., 2023).

Talquetamab monotherapy had a clinically manageable safety profile in patients with RRMM (Chari et al., 2024; Chari et al., 2022). Adverse events in MonumenTAL-1 were consistent with other bispecific agents and GPRC5D-targeting therapies (Chari et al., 2024). GPRC5D-related AEs were predominantly grades 1 to 2 (per Common Terminology Criteria for Adverse Events classification; Chari et al., 2024). The incidence of infection (including grade 3/4 infection) was lower than with B-cell maturation antigen (BCMA)-directed bispecific antibody therapies (Lesokhin et al., 2023; Moreau et al., 2022; Schinke et al., 2023; Usmani et al., 2021). Treatment delays or discontinuations were infrequent at both doses, and AEs were manageable.

PREVENTION AND MANAGEMENT STRATEGIES FOR AES ASSOCIATED WITH TALQUETAMAB

Incidence, Severity, and Treatment Options for AEs

Various supportive measures and treatment options for common AEs reported after treatment with talquetamab are provided in Table 1; however, efficacy data for certain interventions are pending for oral, skin, and nail toxicities. In the following sections, the incidence and severity of AEs from the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts of MonumenTAL-1 are summarized (Chari et al., 2024), followed by perspectives and prevention strategies based on pharmacist experience.

Pretreatment Medication

For both dose cohorts, all patients received a glucocorticoid, antihistamine, and antipyretic as protocol-required pretreatments before step-up dosing and first treatment dose. Per study protocol, for patients who experienced grade ≥ 2 cytokine release syndrome (CRS), glucocorticoid pretreatment was administered before the next two subsequent doses of talquetamab. Other classes of pretreatment medications administered to ≥ 20% of patients included histamine-2 receptor antagonists (e.g., famotidine) and serotonin receptor antagonists (e.g., ondansetron). Additionally, prophylactic antivirals (e.g., acyclovir, valacyclovir) were prescribed for most patients.

Cytokine Release Syndrome

Results from MonumenTAL-1 indicated that CRS occurred in 79% and 75% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively. No grade 4 or 5 CRS was reported; one patient discontinued treatment due to CRS. Patients with CRS grade 1, 2, or 3 in the 0.4 mg/kg QW cohort were 62.2%, 14.7%, and 2.1%, respectively, and 57.2%, 16.6%, and 0.7% in the 0.8 mg/kg Q2W cohort, respectively. Median time to CRS onset was 25.9 and 28.0 hours and median duration was 14.5 and 18.0 hours in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively. The talquetamab treatment schedule included step-up doses given 2 to 4 days apart at 0.01 mg/kg and 0.06 mg/kg for the 0.4 mg/kg QW cohort, as well as an additional step-up dose of 0.3 mg/kg (which was changed to 0.4 mg/kg in the FDA/European Medicines Agency labels to ensure that the first three doses were the same for both dosing schedules) for the 0.8 mg/kg Q2W cohort before the first full dose (Figure 1). Inpatient admissions were required during initial step-up dosing but not required for repeat step-up doses later in treatment when scheduled dosing was interrupted. To minimize the incidence and severity of CRS, pretreatment was administered as mentioned previously. The management of CRS included supportive measures, interleukin-6 receptor antagonist tocilizumab, corticosteroids, and acetaminophen. For CRS not responding to initial therapies, other immunosuppressants were considered. For severe CRS (grade 3/4), vasopressors and/or high-flow oxygen were also utilized (Table 1).

Per study protocol, talquetamab rechallenge was permitted for the first occurrence of grade 3 CRS. However, pretreatment medications including dexamethasone were required for the next two infusions. Talquetamab was permanently discontinued with a second occurrence of grade 3 or any occurrence of grade 4 CRS. This aligns closely with guidance in the prescribing information and summary of product characteristics (European Medicines Agency, 2024; Janssen Biotech Inc., 2023a).

There is a growing body of evidence that suggests prophylactic tocilizumab may reduce the risk of drug-induced CRS (Rodriguez-Otero et al., 2024). Data from a trial of cevostamab, a bispecific antibody targeting Fc receptor-homolog 5 and CD3, showed that prophylactic tocilizumab

Table 1. Incidence, Severity, and Timing of AEs Associated With Talquetamab in MonumenTAL-1 and Pharmacist-Suggested Interventions

AE type	Symptoms	Timing and duration of onset	Severity/grade	Interventions[a] (including prophylactic treatment)
Oral	Dysgeusia (altered sense of taste)	0.4 mg/kg group: Median time to onset was 20.0 days and median duration was 95.0 days 0.8 mg/kg group: Median time to onset was 15.0 days and median duration was 102.0 days	0.4 mg/kg group: Grade 1 (42.7%) Grade 2 (29.4%) 0.8 mg/kg group: Grade 1 (41.4%) Grade 2 (29.7%)	• Dose skipping • Dose delay • Dose reduction • Oral hydration • Oral salivary stimulants • Dexamethasone mouth wash with nystatin suspension (alcohol-free swish and spit)
	Dysphagia (trouble swallowing)	0.4 mg/kg group: Median time to onset was 20.5 days and median duration was 109.0 days 0.8 mg/kg group: Median time to onset was 28.5 days and median duration was 73.0 days	0.4 mg/kg group: Any grade (23.8%) 0.8 mg/kg group: Any grade (24.8%)	• Dose skipping • Dose delay • Dose reduction
	Xerostomia (dry mouth)	0.4 mg/kg group: Median time to onset was 26.0 days and median duration was 57.0 days 0.8 mg/kg group: Median time to onset was 22.0 and median duration was 89.0 days	0.4 mg/kg group: Grade 1 (15.4%) Grade 2 (11.2%) 0.8 mg/kg group: Grade 1 (26.9%) Grade 2 (13.1%)	• Xylitol • Sorbitol • Glycerol • Artificial saliva • Lysozyme • Lactoferrin • Pilocarpine
Skin	Rash-related (maculopapular rash, erythematous rash, erythema) Non-rash-related (skin exfoliation, dry skin, pruritus, palmar-plantar erythrodysesthesia)	Rash-related: 0.4 mg/kg group: Median time to onset was 20.0 days and median duration was 28.0 days 0.8 mg/kg group: Median time to onset was 22.0 days and median duration was 26.0 days Non-rash-related: 0.4 mg/kg group: Median time to onset was 29.5 days and median duration was 36.0 days 0.8 mg/kg group: Median time to onset was 27.0 days and median duration was 39.0 days	Rash-related: 0.4 mg/kg group: Grade 1 (19.6%) Grade 2 (18.9%) Grade 3 (1.4%) 0.8 mg/kg group: Grade 1 (16.6%) Grade 2 (7.6%) Grade 3 (5.5%) Non-rash-related: 0.4 mg/kg group: Grade 1 (30.1%) Grade 2 (25.9%) 0.8 mg/kg group: Grade 1 (44.8%) Grade 2 (27.6%)	• Oral hydration Rash • Topical » Hydrocortisone (injection site rash) » Corticosteroids » Triamcinolone • Oral » Corticosteroids (e.g., prednisone) » Dexamethasone » Methylprednisolone dose pack » Antihistamines (e.g., loratadine, diphenhydramine, or hydroxyzine) Non-rash • Topical » Emollients (e.g., heavy moisturizers) » Ammonium lactate » Triamcinolone » Betamethasone • Oral » Cetirizine

Note. AE = adverse event; COVID-19 = coronavirus disease 2019; CRS = cytokine release syndrome; EMA = European Medicines Agency; HSV = herpes simplex virus; ICANS = immune effector cell–associated neurotoxicity syndrome; IL = interleukin; IVIG = intravenous immunoglobulin; PJP = pneumocystis pneumonia; VZV = vesicular stomatitis virus. Information from Chari et al. (2024).
[a]Efficacy data for certain interventions are pending for skin, nail, and oral side effects.
[b]EMA-approved package insert includes CRS and ICANS management.

Table 1. Incidence, Severity, and Timing of AEs Associated With Talquetamab in MonumenTAL-1 and Pharmacist-Suggested Interventions (cont.)

AE type	Symptoms	Timing and duration of onset	Severity/grade	Interventions[a] (including prophylactic treatment)
Nail	• Discoloration • Disorder • Onycholysis (separation of nail from nail bed) • Onychomadesis (detachment of nail from nail bed) • Onychoclasis (nail breakage) • Nail dystrophy • Nail ridging	0.4 mg/kg group: Median time to onset was 68.5 days and median duration was 88.5 days 0.8 mg/kg group: Median time to onset was 67.5 days and median duration was 74.0 days	0.4 mg/kg group: Grade 1 (37.1%) Grade 2 (17.5%) 0.8 mg/kg group: Grade 1 (46.9%) Grade 2 (6.9%)	• Dose skipping • Dose delay • Dose reduction • Oral hydration • Emollients • Vitamin E oil • Biotin (vitamin B7) • Triamcinolone 0.025% ointment • Protective nail coverings (socks and gloves) • Routine nail care (keep well-trimmed) • Avoid nail soaks due to risk of fungal infections
CRS[b]	• Fever/pyrexia • Hypoxia • Hypotension • Headache • Confused state	0.4 mg/kg group: Median time to onset was 25.9 hours and median duration was 14.5 hours 0.8 mg/kg group: Median time to onset was 28.0 hours and median duration was 18.0 hours	0.4 mg/kg group: Any grade (79%) Grade 3–4 (2.1%) 0.8 mg/kg group: Any grade (74.5%) Grade 3–4 (0.7%)	• Corticosteroids • Antipyretics • Tocilizumab (or another anti–IL-6 alternative) • Oxygen • Vasopressor Pretreatment with • Corticosteroids • Antihistamine • Antipyretic
ICANS[b]	• Confusion • Lethargy • Somnolence • Bradyphrenia	0.4 mg/kg group: Median time to onset was 23.6 hours and median duration was 15.5 hours 0.8 mg/kg group: Median time to onset was 31.9 hours and median duration was 7.8 hours	Only reported in phase II: 0.4 mg/kg group: Any grade (10.7%) Serious ICANS (4.1%) 0.8 mg/kg group: Any grade (11.0%) Serious ICANS (3.7%) ICANS concurrent with CRS: 0.4 mg/kg group (66.7%) 0.8 mg/kg group (66.7%)	• Corticosteroids • Tocilizumab (if concurrent with CRS) • Anakinra (for refractory CRS and steroid refractory ICANS) Prophylactic medication • Levetiracetam at onset of grade 1 ICANS
Infections	Fever (overlaps with CRS; thus, need to rule out CRS) Symptoms related to: • Upper respiratory tract infection • COVID-19 • Urinary tract infection • Pneumonia • Bronchitis • Nasopharyngitis • Sepsis	0.4 mg/kg group: Median time to onset was 148.0 days and median duration was 11.5 days 0.8 mg/kg group: Median time to onset was 108.0 days and median duration was 12.0 days	0.4 mg/kg group: Any grade (58.7%) Grade 3–4 (19.6%) 0.8 mg/kg group: Any grade (66.2%) Grade 3–4 (14.5%)	• Antibiotics • Antifungals Prophylactic medication • HSV/VZV: acyclovir or valacyclovir • Consider PJP (follow institutional guidelines): sulfamethoxazole-trimethoprim, pentamidine, dapsone, or atovaquone • IVIG (for hypogammaglobulinemia) • Hepatitis B screening

Note. AE = adverse event; COVID-19 = coronavirus disease 2019; CRS = cytokine release syndrome; EMA = European Medicines Agency; HSV = herpes simplex virus; ICANS = immune effector cell–associated neurotoxicity syndrome; IL = interleukin; IVIG = intravenous immunoglobulin; PJP = pneumocystis pneumonia; VZV = vesicular stomatitis virus. Information from Chari et al. (2024).
[a]Efficacy data for certain interventions are pending for skin, nail, and oral side effects.
[b]EMA-approved package insert includes CRS and ICANS management.

Table 1. Incidence, Severity, and Timing of AEs Associated With Talquetamab in MonumenTAL-1 and Pharmacist-Suggested Interventions (cont.)

AE type	Symptoms	Timing and duration of onset	Severity/grade	Interventions[a] (including prophylactic treatment)
Rare AEs	Tumor lysis syndrome		1 patient, grade 3/4	• Hydration • Allopurinol or febuxostat (prophylaxis) • Rasburicase (hyperuricemia treatment)
	Tumor flare and pseudoprogression (mild to severe site-specific pain, such as bone pain)			• Analgesic (opioids) • Corticosteroids

Note. AE = adverse event; COVID-19 = coronavirus disease 2019; CRS = cytokine release syndrome; EMA = European Medicines Agency; HSV = herpes simplex virus; ICANS = immune effector cell–associated neurotoxicity syndrome; IL = interleukin; IVIG = intravenous immunoglobulin; PJP = pneumocystis pneumonia; VZV = vesicular stomatitis virus. Information from Chari et al. (2024).
[a]Efficacy data for certain interventions are pending for skin, nail, and oral side effects.
[b]EMA-approved package insert includes CRS and ICANS management.

significantly reduced the risk of patients with RRMM developing cevostamab-induced CRS, without impacting antimyeloma activity (Trudel et al., 2022). A single dose of prophylactic tocilizumab in patients treated with teclistamab appeared to reduce the incidence of CRS relative to the overall study population (Martin et al., 2023; van de Donk et al., 2023). Finally, a single dose of tocilizumab before talquetamab and increased dexamethasone use post dose reduced the incidence and severity of CRS compared with the overall MonumenTAL-1 population (Schinke et al., 2023). However, per International Myeloma Working Group (IMWG) guidelines, prophylactic tocilizumab is currently considered investigational and not recommended outside of a clinical trial (Rodriguez-Otero et al., 2024). Therefore, further work is required to assess potential prophylactic strategies with tocilizumab in patients treated with talquetamab.

Pharmacist Experience and Perspective on CRS

In MonumenTAL-1, inpatient admissions were required during initial step-up dosing and patient vitals were checked routinely (every 4 hours) to monitor for onset of CRS: fever, chills, hypotension, headache, elevated liver function tests, hypoxia, and/or signs of neurotoxicity. Treatments for CRS included acetaminophen, tocilizumab, siltuximab, anakinra, and dexamethasone. Of the

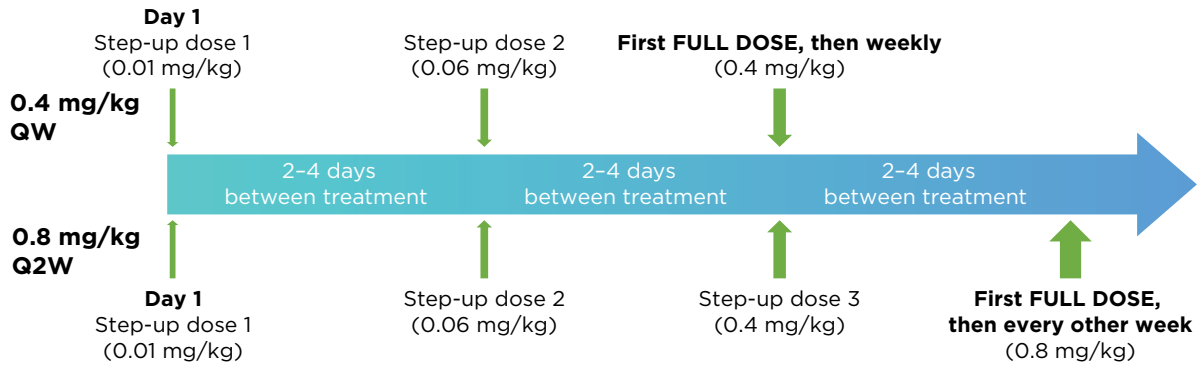

Figure 1. Diagram of step-up dosing schedules.

available immunosuppressive biologics, tocilizumab was used most, whereas anakinra and siltuximab were rarely used for CRS with bispecific antibody treatments. Certain institutions opted for starting tocilizumab treatment with grade 1 CRS to prevent symptoms from worsening

Select institutions have initiated administering talquetamab step-up dosing in an outpatient setting. In general, several factors should be considered for suitability of outpatient administration of bispecific antibodies such as talquetamab, including comorbidities and frailty of the patient, availability of a 24-hour caregiver, proximity to a treatment center, and vital sign monitoring systems (CancerNetwork, 2024). In a patient deemed eligible for outpatient treatment, the role of pharmacists is to review drugs that may mask or exacerbate symptoms during a pretreatment education visit and discuss any drugs, such as antipyretics or sedative medications, which should be held or adjusted during the step-up dosing phase. The patient is provided with a remote monitoring kit to capture any abnormal signs and is instructed to report CRS symptoms to the care team. Advanced practice providers use American Society for Transplantation and Cellular Therapy grading for CRS (Chari et al., 2024; Lee et al., 2019), and document grade and treatment in the patient's charts. Pharmacists are then notified of events by provider or routine chart reviews.

Special considerations for talquetamab outpatient administration are generally given to patients who are older in age and/or have lower body weight; while overall response rates with talquetamab are consistent across patient subgroups regardless of age (< 65, 65–< 75, and ≥ 75 years) and body weight (≤ or ≥ median; Ma et al., 2023), older and/or frailer patients may be more susceptible to comorbidities and may be less likely to recover from adverse events, including infections (Willan et al., 2016). If there is concern that a patient is more likely to decompensate in the event of CRS or if they do not have a caregiver available, step-up dosing and monitoring are completed in the inpatient setting. Overall, pharmacists play a critical role in premedication management for patients.

Neurological AEs

Immune effector cell–associated neurotoxicity syndrome (ICANS) was reported in 11% of patients in all cohorts, and 4% of all patients had serious ICANS. The median time to onset was 24 hours after administration of talquetamab for the 0.4 mg/kg QW cohort and 32 hours for the 0.8 mg/kg Q2W cohort; 67% of cases of ICANS were concurrent with CRS in both cohorts. Supportive measures included corticosteroids (7% and 3%) and tocilizumab (3% and 5%) in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively. ICANS resolved in 86% and 80% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively; 2% of patients had dose modifications for ICANS in both cohorts during the trial.

Pharmacist Experience and Perspective on Neurological AEs

Neurological AEs during the trial were described via immune effector cell–associated encephalopathy scores and most were successfully managed by dexamethasone. Tocilizumab was only used if ICANS was concurrent with CRS, because tocilizumab does not cross the blood-brain barrier. In rare instances, anakinra, methylprednisolone, or levetiracetam were prescribed.

Oral Side Effects

Oral side effects in MonumenTAL-1 consisted of dysgeusia (includes dysgeusia, ageusia, hypogeusia, and general taste disorders), dysphagia, xerostomia, and stomatitis.

Dysgeusia was the most commonly reported oral side effect in ~70% of patients in both cohorts, with median time to onset of 20 and 15 days in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively; it resolved in 46% and 31% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts of patients, with median duration of 95 and 102 days, respectively. Various supportive measures were implemented in patients with dysgeusia, including dose modification (reduction and/or skipping), salivary stimulants, oral hydration, and/or dexamethasone mouthwash.

Dysphagia occurred in ~24% of patients and appeared to be secondary to dry mouth in MonumenTAL-1; median duration was 73–103 days in the two cohorts. Xerostomia was reported in 27% and 40% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, with median duration of 57 and 89 days, respectively. Supportive measures

included dose modification, xylitol, lysozyme, pilocarpine, and/or artificial saliva. Stomatitis incidence was 13% and 6% in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively. Management of dysphagia and dry mouth included instructing patients to increase fluid and food intake. Weight loss (≥ 10% from baseline) was observed in 32–37% of patients in both cohorts. More detailed treatment approaches are listed in Table 1.

Pharmacist Experience and Perspective on Oral Side Effects

Currently in clinical practice, depending on the institution, patient education is detailed on what to potentially expect. Pharmacists are notified by nursing or provider teams after patients report symptoms (e.g., taste changes, dry mouth, dysphagia, glossitis, thrush) or via routine chart review of patients receiving talquetamab in the clinic; pharmacists and other health-care personnel would then assist with management strategies. More significant oral-related changes are expected to occur during outpatient follow-up after start of full doses.

As there are currently no proven effective treatments for such taste changes, efforts are made primarily to alleviate symptoms. Patients are instructed to maintain good oral hydration throughout therapy, use artificial saliva sprays and lozenges if needed, and to report any worsening symptoms to the care team. Supportive care options for oral side effects include saliva stimulants, pilocarpine tablets, sodium chloride rinses, dexamethasone/nystatin swish and spit, and/or dexamethasone mouthwash, depending on severity. Eating or drinking should be avoided immediately after use of rinses and patients with dry mouth should avoid hot beverages. Sour citrus fruits or candies can be taken before a meal to potentially stimulate the taste buds.

Dysphagia can potentially be managed by adjusting eating habits, such as taking small bites, eating upright, taking sips of liquids with food, and avoiding dry foods (e.g., meats). Glossitis and thrush management should be started as soon as possible with initiation of nystatin or clotrimazole. Since dry mouth can lead to dental issues, patients should receive routine dental care and cleanings, and education on maintaining good oral hygiene. Toothpastes with sodium lauryl sulfate and mouthwashes containing alcohol should be avoided. An icing neck wrap can also help to alleviate symptoms.

Oral side effects and taste changes can often result in weight loss and anorexia. Patients may need a nutrition consult for dietary modifications or start an appetite stimulant if indicated (e.g., dronabinol, mirtazapine). Baseline weight is documented before start of therapy and measured at each clinic visit to track changes that may affect dosing. In general, most recent weight will be used for patients who receive dose reductions or repriming. Specific verbiage can be included in the treatment plan for nurses to alert providers if there is ≥ 10% weight loss (grade ≥ 2) from baseline and discuss with providers to consider holding therapy for ≥ 20% weight loss (grade ≥ 3).

Nail Toxicity

Nail toxicities (e.g., onycholysis, onychomadesis, onychoclasis, nail disorder, nail discoloration, nail dystrophy, nail ridging) were reported in 54% of patients, with median time to onset of 68 days from initial dose. Patients experienced nail-related AEs for median duration of 89 and 74 days for the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively. Dose modification occurred in one patient between the two cohorts, and other potential treatments (e.g., vitamin E oil, nail coverings) are detailed in Table 1.

Pharmacist Experience and Perspective on Nail Toxicity

Nail toxicities were not observed during step-up dosing during the trial; however, in real-world practice, symptoms have appeared within the first 1 to 2 months of starting therapy. Pharmacists are notified by nursing or provider teams when patients report symptoms. Patients complain and present with thin, peeling nails that are lifting off the nail bed (Narayan et al., 2023). Current treatments for nail toxicity are primarily symptomatic and of unclear efficacy. Patients are instructed to keep nails trimmed short to avoid breaking/tearing and are recommended to use an over-the-counter nail hardener or topical triamcinolone 0.025% to 0.5% ointment if nails are inflamed. Topical vitamin E oil may be used to moisturize cuticles and nail soaks should be avoided due to risk of fungal infection.

Skin Toxicity

Rash and non-rash toxicities (e.g., skin exfoliation, dry skin, pruritus, erythrodysesthesia syndrome) were reported in 40% and 56% of patients in the 0.4 mg/kg QW cohort and 30% and 73% in the 0.8 mg/kg Q2W cohort, respectively. Most skin AEs were grade 1 or 2 in both cohorts, with grade 3 rash in 1% and 6% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively.

For skin rashes, topical medications such as corticosteroids and petroleum jelly (white soft paraffin) were used in 22% and 16% of patients, and oral medications such as cetirizine and corticosteroids were used in 15% and 12% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively. For rash-related skin toxicities, dose modifications occurred in 6% and 4% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively.

For non-rash skin AEs, topical and oral medications were used in 26% and 16% of patients in the 0.4 mg/kg QW cohort, and in 32% and 7% in the 0.8 mg/kg Q2W cohort, respectively. For non-rash skin toxicities, dose modifications occurred in 8% and 1% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively.

Pharmacist Experience and Perspective on Skin Toxicity

During step-up dosing of talquetamab, injection site reaction such as a mild rash can occur but does not always need intervention; if a patient experiences pain, a topical steroid can be used. Treatment-related rashes usually appear in the first cycle and spread throughout the torso; more significant skin toxicities are expected to occur during outpatient follow-up after initiation of full doses. Depending on rash severity, this could lead to treatment holds and/or dose reductions, and early management of the rash is important to mitigate dose modifications. Rashes are treated with a topical or oral steroid depending on the percentage of body surface area covered.

Ammonium lactate lotion is provided to patients to use on hands and feet twice daily at the start of talquetamab therapy, and patients are advised to continue using lotion throughout treatment. Hydration and unscented moisturizers are used for dry skin, and hydroxyzine or other antihistamines can be used if itching is significant. Patients are counseled to avoid extremes of temperature and soaking hands/feet in hot tubs or a sink with dishwater. Patients are counseled to apply emollients or moisturizer after showering and throughout the day.

Infection

In MonumenTAL-1, 59% and 66% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts experienced at least one incidence of infection, including 20% and 15% of patients with grade 3/4 infections, respectively. Opportunistic infection occurred in five patients (4%) in the 0.4 mg/kg QW cohort (esophageal candidiasis: n = 2; adenovirus infection, fungal sepsis, viral retinitis: n = 1 each) and eight patients (6%) in the 0.8 mg/kg Q2W cohort (esophageal candidiasis: n = 3; adenovirus infection, herpes ophthalmic, cytomegalovirus infection, cytomegalovirus viremia, human herpes virus 6 infection: n = 1 each). There were no cases of pneumocystis pneumonia (PJP).

Patients with RRMM are at risk for hypogammaglobulinemia, as the overproduction of malignant plasma cells causes elimination of normal plasma cells and decreased levels of functional immunoglobulin G (IgG), leading to increased risk of infections (Saltarella et al., 2024). While teclistamab may increase the risk of hypogammaglobulinemia due to its BCMA-directed mechanism of action and its on-target, off-tumor elimination of normal (non-MM) BCMA-expressing plasma cells, talquetamab (GPRC5D-directed) does not deplete plasma cells (Nooka et al., 2024; Rodríguez-Otero et al., 2023). As GPRC5D is highly expressed on MM cells, with limited expression on normal hematopoietic cells, including B cells, talquetamab allows the maintenance of key elements of humoral immunity (Kodama et al., 2019; Rodríguez-Otero et al., 2023; Verkleij et al., 2021). Following talquetamab treatment, CD19+ B-cell levels showed no reduction over time; however, a transient decrease in both neutrophil counts and IgG levels were observed in cycle 1 of treatment before each recovered during cycle 2 (Rodríguez-Otero et al., 2023). While no definitive conclusion exists at present, this transient neutropenia may be an underlying cause of the infections observed in MonumenTAL-1.

In MonumenTAL-1, IgG levels were monitored for hypogammaglobulinemia (i.e., functional IgG < 400 mg/dL) on a monthly basis, and the administration of replacement intravenous immunoglobulin (IVIG) was protocol-recommended for the prevention of infections and was consistent with current treatment guidelines (Lancman et al., 2023; Ludwig & Kumar, 2023). Intravenous immunoglobulin was used in 15% and 13% of patients in the 0.4 mg/kg QW and 0.8 mg/kg Q2W cohorts, respectively. When monitoring IgG levels, IgG concentration could be higher than the cutoff of 400 mg/dL due to the long half-life of the immunoglobulin as well as a high prevalence of IgG-type myeloma; therefore, it is important to subtract the clonal (myeloma) IgG from the overall serum IgG to obtain an accurate estimate of functional IgG levels. IMWG guidelines recommend an early start of IVIG replacement regardless of a particular cutoff, considering that first infections typically occur early after the start of bispecific antibody therapy (Rodriguez-Otero et al., 2024).

The most common reason for prophylaxis was prevention of herpes infection. Acyclovir and valacyclovir were the two most common prophylactic medications, used in 52% and 37% of patients in the 0.4 mg/kg QW cohort and 72% and 11% in the 0.8 mg/kg Q2W cohort, respectively.

Pharmacist Experience and Perspective on Infections

Infections were usually observed in outpatient follow-up visits. Degree of pharmacist intervention may differ depending on the institution. In certain institutions, IVIG is prescribed if hypogammaglobulinemia occurs and the patient has recent history of more than one infection; in other institutions, IVIG is given for hypogammaglobulinemia regardless of whether the patient has a history of infection or recurrent infections. Some sites routinely prescribe prophylactic anti-infective drugs for patients with hypogammaglobulinemia due to potential issues in insurance coverage or financial toxicity to patients. Antiviral (e.g., acyclovir, valacyclovir) and anti-PJP (e.g., sulfamethoxazole-trimethoprim, atovaquone) prophylaxes are strongly recommended, whereas antibacterial (e.g., levofloxacin) and antifungal (e.g., fluconazole) drugs are only recommended during periods of neutropenia. Prophylactic medications should be given following institutional guidelines.

Rare AEs

Tumor lysis syndrome (TLS) was reported in one patient in the 0.8 mg/kg Q2W group (grade 3/4) whose bone marrow plasma cell percentage was 90% via biopsy and 60% via aspirate. Hydration and prophylaxis with a xanthine oxidase inhibitor (e.g., allopurinol, febuxostat) should be used for patients at higher risk for TLS.

Tumor flare was also observed as pain in specific sites (e.g., bone pain), which may appear like early disease progression. Pain was managed using analgesics and inflammation was controlled with corticosteroids.

Pharmacist Experience and Perspective on Rare AEs

Regarding TLS, patients should have recent glucose-6-phosphate dehydrogenase activity documented in the chart in case there is a need for rasburicase. Pain flares at tumor sites were observed during step-up dosing during the trial. Patients were treated with non-acetaminophen analgesics (e.g., opioids) to avoid masking fevers. If initial analgesic treatment was ineffective, individualized dosing of dexamethasone (instead of a standing regimen) was utilized.

ADDITIONAL CONSIDERATIONS FOR PHARMACISTS AND HEALTH-CARE TEAMS

Key considerations for pharmacists and healthcare personnel involved in talquetamab selection and use are detailed in Figure 2 and Table 2. Clinical pharmacists play a significant role in ensuring transparent communication between inpatient and outpatient teams regarding the patient's treatment schedule and whether premedication, dose adjustments, repriming, and/or schedule adjustments are being implemented. This communication mitigates medication errors/delays and ensures proper drug inventory is kept on hand. During onboarding of new bispecific treatments, clinical pharmacists provide education to pharmacy, provider, and nursing teams regarding operational considerations, anticipated AEs, and

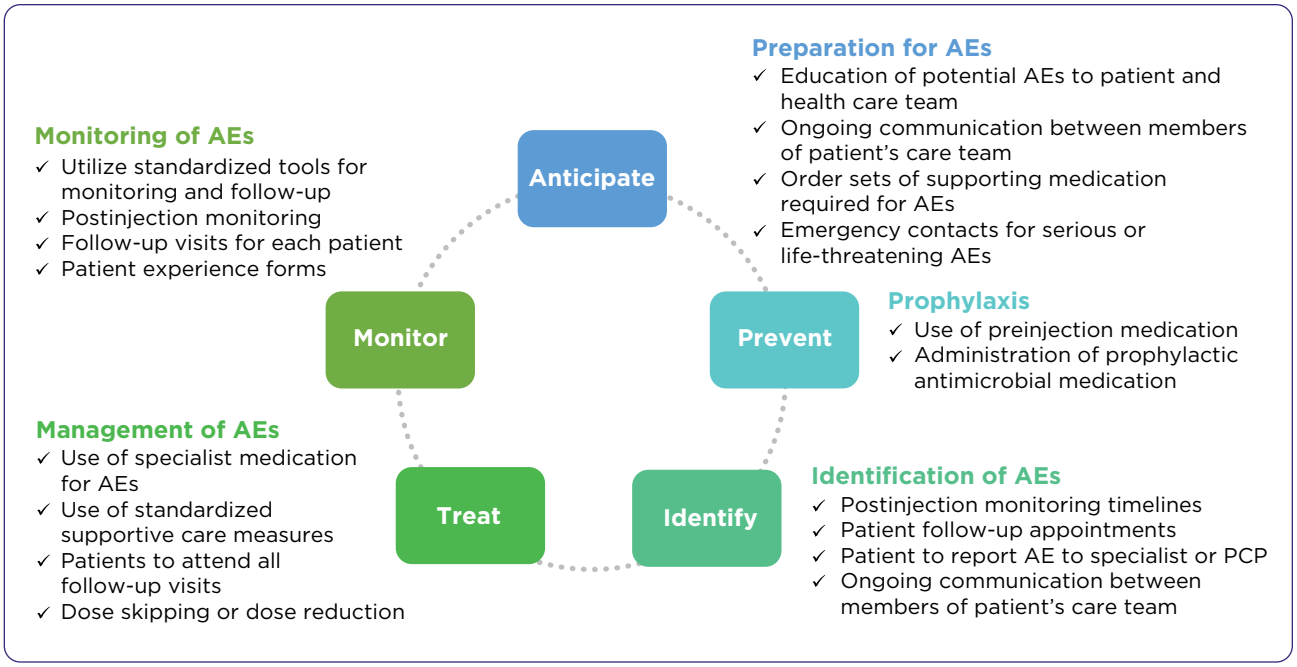

Figure 2. Flow chart summarizing considerations for pharmacy teams. AEs = adverse events; PCP = primary care provider.

supportive care recommendations to ensure consistency in practice.

A patient's primary oncologist should always be available to provide direction and supportive care in the event of any AEs or serious AEs. Sufficient resources (e.g., wallet card, off-hour contact information) should also be available for appropriate symptom awareness and management of any AEs. Subsequent overlaps in care (e.g., inclusion of dermatologists and nutritionists for AE management) and varying management considerations among different health-care team members, including nurses and advanced practice providers, must also be considered. Additional consulting teams included otolaryngologists or nutritionists (oral AEs) and dermatologists (skin and nail AEs). Social workers are often consulted at the start of therapy for coping and consultations.

ROLE OF THE PHARMACIST IN TALQUETAMAB ADMINISTRATION

A multidisciplinary team, including pharmacists, provides care and education of patients who receive talquetamab. Figure 3 summarizes roles of pharmacists at different sites of talquetamab administration and follow-up. This provides an overview of how and when pharmacists can assist with mitigating and managing talquetamab-associated AEs. Key roles for pharmacists are discussed below.

Patient Education

Pharmacists can provide education to patients on (1) mechanism of action for talquetamab and an overview of dosing/administration; (2) anticipated toxicities and how to proactively minimize them; (3) new supportive care medication(s) (e.g., prophylaxis, antiemetics, skin care); and (4) options for management at home. Pharmacists can discuss with patients on how to monitor and report side effects to the care team, to aid with AE management before symptoms worsen.

Step-up Dosing

Step-up dosing is a critical component of talquetamab administration and should be carefully monitored by providers and pharmacists. Pharmacists' roles include vigilant monitoring of patient vital signs alongside all health-care team members. Pharmacists ensure that step-up dosing dates are accurate and interventions for CRS and/or ICANS are administered correctly. If a delay in treatment due to AEs occurred and re–step-up is required, pharmacists ensure that proper doses are ordered.

Table 2. Considerations for Pharmacists and Multidisciplinary Teams

Area	Consideration
Prescribing and management	• Patient eligibility and consent (including intent of therapy) • Details of drug information • Management of AEs (order sets of supportive medication for potential AEs), e.g., CRS/ICANS order sets to allow for quick ordering of tocilizumab and steroids • Medication use review/care plan and patient medical history collection before talquetamab administration • Documentation of care plan and strong transitions of care between teams involved in step-up dosing and treatment dosing phase • Using collaborative practice agreements, pharmacists may independently see certain patients during step-up dosing and maintenance therapy, freeing the APP and physicians to treat more complex patients
Monitoring and follow-up	• Post-infusion monitoring (e.g., vital signs, electrolytes) and potential dose reductions. Ongoing monitoring should occur at each clinical encounter • Collaborative agreements, including lab monitoring, should exist in all clinical settings where clinical oncology HCPs are part of the multidisciplinary team • Ongoing communication with the oncology team and the patient's PCP and local hematologist
Education	HCP education • Education surrounding dosing, administration, efficacy, AE management, REMS requirements (Janssen Biotech Inc., 2023), operational logistics, workflows, and patient support tools • Standardized education materials (e.g., pamphlets, information booklets, guidelines) should be consistent across all care sectors, including outpatient clinics, inpatient care areas, emergency department providers, and critical care teams involved in the care of patients receiving talquetamab • Site-specific workflow education, including who in the multidisciplinary team is responsible for each step (e.g., provider identifies patients, contacts nursing and pharmacy to coordinate care, patient goes to one unit for step-up dosing then onto outpatient infusion center for subsequent doses) • Shared-care agreement (including concordance between patient and relevant HCP) • Specialist care contact details, including after-hours contacts Patient education • Dosing schedule and how administered • Education should include how to recognize AEs, any self-care recommendations, and when to contact care team for assistance • Specific monitoring parameters and education on how to use any technology provided (e.g., remote monitoring kits or devices) • Education on supportive care medications, including antimicrobials, antiemetics, and skin protection • Nutrition recommendations • Provider contact information for each stage of treatment, including after-hours contacts • Caregiver attendance strongly encouraged at education sessions
Properties/dispensing/distribution	• Concentration of talquetamab: 3 mg/1.5 mL (2 mg/mL) or 40 mg/mL vial • Does not require dilution • Potential areas of error when dispensing talquetamab (e.g., talquetamab vs. teclistamab) and any supportive medications required • Order sets/EMR • Near-miss errors and error reporting procedures
Extra resources	• Any extra resources for HCPs on standardized care for patients • Emergency contacts (for any serious or life-threatening AEs) • Pre-and post-financial assessments, clinical quality measures including patient experience forms and assessments for continuous clinical quality improvements

Note. Modified from Mackler et al. (2019) for talquetamab. AE = adverse event; APP = advanced practice provider; EMR = electronic medical record; HCP = health care professional; PCP = primary care physician; REMS = Risk Evaluation and Mitigation Strategy; TEAE = treatment-emergent adverse event.

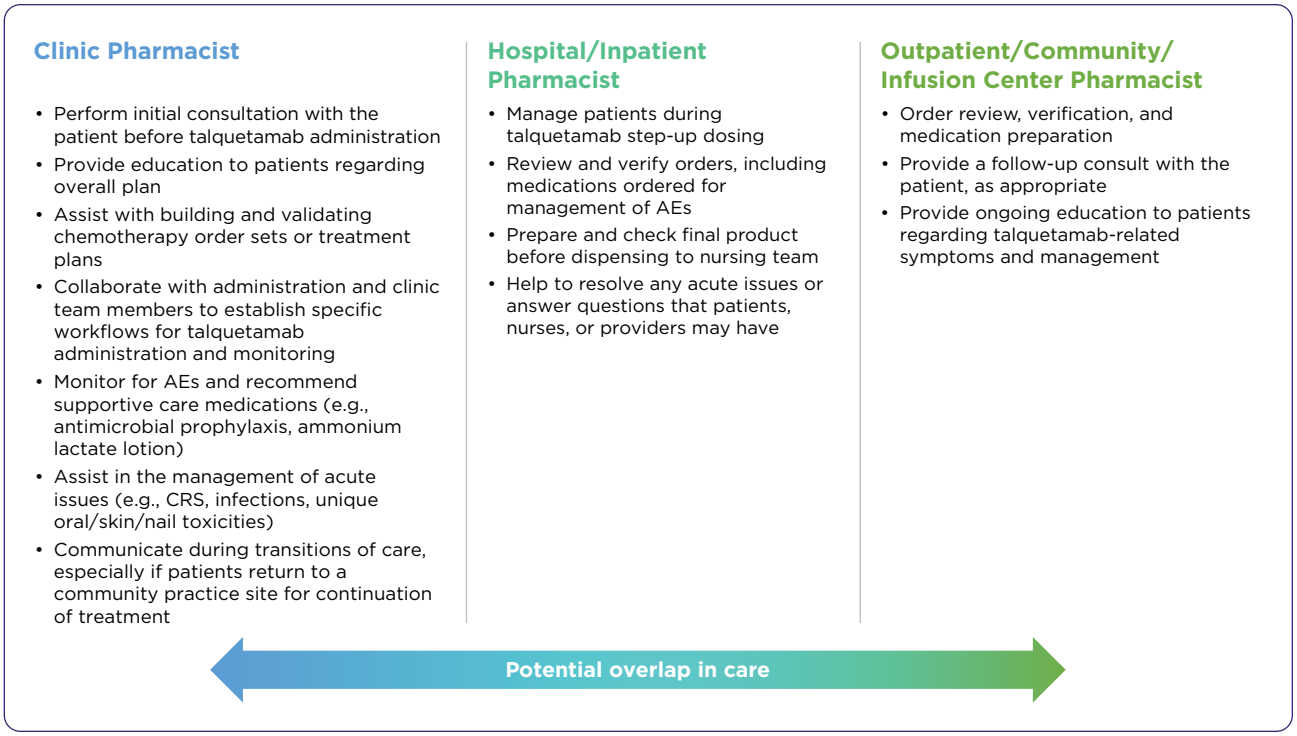

Figure 3. Chart summarizing roles of pharmacists. AEs = adverse events; CRS = cytokine release syndrome.

Pharmacists should also be aware of any drugs that can potentially confound/interfere with CRS or ICANS interpretation. For example, analgesics with antipyretic activity (e.g., acetaminophen) can be held during step-up dosing to avoid missing any new fevers; alternate analgesics (e.g., low-dose oxycodone, tramadol) can be utilized as appropriate. Antihypertensives (e.g., carvedilol, nifedipine) or diuretics (e.g., furosemide) can have specific holding parameters to mitigate profound hypotension. Drugs with neurologic or sedation AEs (e.g., opioids, gabapentin) can also have specific holding parameters to mitigate oversedation.

The pharmacy team can also lead the charge in talquetamab implementation within the institution to ensure the hospitalization plan minimizes inpatient stay while facilitating transition to outpatient care. Furthermore, the team can also optimize drug utilization among inpatient and outpatient settings.

Other Considerations

Pharmacies and clinics must be Risk Evaluation and Mitigation Strategy (REMS) enrolled and certified for talquetamab use. A REMS dispense authorization code must be generated before dispensing of each talquetamab dose.

There exists a potential for mix-up with talquetamab and teclistamab. The names and vials can look similar (although the vials have different cap colors), but pharmacies should ensure drugs that look-alike and sound-alike are stored separately to avoid confusion. The strategy of tall man lettering can be considered (e.g., talQUEtamab, TECListamab) and drug targets (e.g., GPRC5DxCD3, BCMAxCD3) be added to the medication order to further differentiate drugs with similar names (Institute for Safe Medication Practices, 2023).

When dispensing a dose with volume > 2 mL, volume of talquetamab should be split as evenly as possible into multiple syringes to maintain a maximum injection volume of 2 mL, and the medication order should contain this information. The talquetamab package insert contains more detailed injection volume information based on body weight (Janssen Biotech Inc., 2023a).

Allergic reactions to common talquetamab-related AE mitigation medications have been observed in the clinic and alternatives should remain available. For example, if the patient is allergic to

tocilizumab, alternative options for CRS management can be siltuximab (Patel et al., 2022) and/or corticosteroid (e.g., dexamethasone).

OVERALL PHARMACIST PERSPECTIVE AND FUTURE DIRECTION

Pharmacists are pivotal in the administration and management of talquetamab and ensure adherence to the REMS program (Janssen Biotech Inc., 2023b). If there are dose delays or holds, pharmacists help with checking if orders are entered appropriately, especially given the different parameters and concentrations that are available. Pharmacists provide recommendations on premedications (e.g., reinitiation, taper/discontinuation, and/or additions). Dose modifications should be considered on an individual basis. For active infections, talquetamab therapy would be placed on hold; for CRS/ICANS, the subsequent dose would be held until symptoms have fully resolved. The package insert has more detailed recommendations about treatment delays and doses.

In the future, to overcome barriers of travel and housing for patients who live far from a large academic center, talquetamab may be administered in an outpatient setting for both step-up and treatment dosing. Adverse events may be managed by other members of the health care team in smaller clinics that do not have a pharmacist on staff or pharmacists may provide consultations through telehealth processes to help with AE management. Patients' health records from an outpatient clinic to the primary care site will need to be reconciled (whether scheduled or out of necessity, e.g., urgent care or emergency department visits), facilitated by electronic medical record interoperability between sites and patient/family communications to the primary care site. Using collaborative practice agreements, pharmacists may independently see patients during step-up dosing, freeing advanced practice practitioners and physicians to treat more complex patients. Pharmacists will continue to have key roles in clear and transparent communication among patients, caregivers, care providers, and different care institutions.

CONCLUSIONS

Wider multidisciplinary teams, including pharmacists and other advanced practitioners, have vital roles in supportive care of patients who experience AEs associated with talquetamab treatment. Talquetamab is a novel therapy showing promising safety and efficacy results in patients with triple-class–exposed RRMM (Chari et al., 2024). Prophylaxis, education, support, and effective medication to treat common AEs associated with talquetamab treatment all help to improve patient experience and adherence. ●

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