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Navigating Bispecifics Outpatient step-up dosing: A Roadmap To Help improve SafeTy and Access in the Real-world (NORTHSTAR)

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Key Takeaway

This expert consensus-driven mDelphi study informs practical recommendations to support safe outpatient step-up dosing of teclistamab or talquetamab.

Conclusions

Experts support the safe and feasible implementation of outpatient step-up dosing for teclistamab or talquetamab for appropriately selected patients with RRMM.

The resulting consensus-based implementation guide will provide practical guidance on patient selection, AE monitoring and management, education and care coordination to support implementation of outpatient step-up dosing across diverse clinical settings.

Accordingly, the implementation guide is expected to improve the ability of US healthcare providers to operationalize outpatient step-up dosing, optimize healthcare resource utilization, and expand patient access to teclistamab or talquetamab.

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Introduction

- Teclistamab and talquetamab are standard-of-care bispecific antibody (BsAb) T-cell engagers that demonstrate deep and durable responses in clinical trials as monotherapy and in combination therapy for patients with relapsed/refractory multiple myeloma (RRMM).[1-3]
- To mitigate the risk of class-wide adverse events (AEs) associated with BsAbs, particularly cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), treatment is initiated using a step-up dosing (SUD) schedule that has traditionally been administered in the inpatient (IP) setting.[4,5]
- In 2026, the Food and Drug Administration removed the recommendation for hospitalization after the first treatment dose of teclistamab, providing flexibility for administration in outpatient (OP) settings.[4]
- Growing evidence supports that OP SUD can be administered safely and is an effective approach that may reduce healthcare resource utilization and improve patient access, particularly in community practices which may have limited resources for IP SUD.[6]
- However, the absence of standardized guidance remains a barrier to broader implementation of OP SUD.

Aim

- To establish expert consensus supporting the safe administration of OP SUD for teclistamab or talquetamab and translate these recommendations into a practical, provider-facing implementation guide.

Results

- Fifteen US providers (7 hematologist-oncologists; 8 pharmacists) leading their respective BsAbs programs in academic (n=3) and community (n=12) settings comprised the panel.
  - 9 panelists had prior teclistamab or talquetamab OP SUD experience
  - 6 panelists provided insights on perceived barriers to operationalizing OP SUD
- Patient eligibility criteria, AE monitoring and management workflows, and patient and caregiver education are presented in **Figures 2-6**.

Figure 2: Patient eligibility decision tree for OP SUD

Start: Patient Being Evaluated for OP SUD

1 Does the patient have any of these?
- ❑Grade ≥3 infection or untreated active infection
- ❑ECOG performance status ≥3
- ❑Moderate to severe neurologic/cognitive impairment limiting symptom reporting or ICANS assessment
- ❑Actively symptomatic congestive heart failure
- ❑AE risk not controllable with prophylaxis (e.g., tocilizumab, steroids), per clinician judgment
- ❑No eligible caregiver available during OP SUD period (see Figure 5)

Yes → **IP SUD preferred, or wait until symptom resolution**: Use when immediate clinical risk makes OP SUD unsuitable.

No ↓

2 Are any of these additional risk factors present?

Unstable or uncontrolled comorbidities:
- ❑Cardiovascular, pulmonary, or autoimmune disease
- ❑Renal impairment
- ❑Bone marrow dysfunction or neutropenia
- ❑Concomitant malignancy

Factors indicating severe disease:
- ❑High tumor burden
- ❑Extramedullary disease
- ❑History of Grade ≥3 CRS or ICANS with prior CAR-T therapy

Other risk factors:
- ❑Oxygen dependence
- ❑Mild or severe frailty
- ❑Recent stabilized fracture
- ❑Age ≥80

Yes → Provider determines whether these factors exclude the patient from OP SUD.

No → **OP SUD appropriate**: Proceed when eligibility and OP monitoring requirements are met.

Figure 3: Access to care decision tree for OP SUD

Assess Access-to-care Requirements
Confirm proximity, transportation, and monitoring capability before OP SUD

1. Resides ≤60 minutes of administering site? — Yes → step 2; No → Temporary lodging ≤60 minutes of administering site? — Yes → step 2; No → Can the practice support lodging*?
2. Resides ≤60 minutes of designated ER**? — Yes → step 3; No → Temporary lodging ≤60 minutes of designated ER**? — Yes → step 3; No → Can the practice support lodging*? (Yes → step 3; No → IP SUD preferred)
3. Reliable transportation to/from administering site/designated ER**? — Yes → step 4; No → Can the practice support transportation*? — Yes → step 4; No → IP SUD preferred
4. Access to at-home thermometer, BP cuff, pulse oximeter? — Yes → OP SUD may proceed; No → Can practice provide monitoring equipment*? — Yes → OP SUD may proceed; No → IP SUD preferred

***Lodging, transportation, and equipment support could be coordinated through social workers and may include:**
- Ride-share services
- Non-profit support programs
- Grant funding
- Pharmaceutical industry support programs

****Recommendations for designated ER**
- Availability of tocilizumab for timely management of CRS
- Located within ≤60 minutes of the patient's residence (or temporary lodging)
- Should be informed that they may receive patients undergoing BsAb therapy
- Educated on recognition and management of CRS and ICANS symptoms

Methods

Study design and study population

- A three-round modified Delphi (mDelphi) study (**Figure 1**) was initiated in January 2026 with a panel of hematologist-oncologists and/or pharmacists leading BsAbs programs and caring for patients with RRMM in the United States (US) who:
  - Had ≥6 months of experience managing multiple myeloma (MM).
  - Had treated or managed ≥5 adult patients with RRMM requiring teclistamab or talquetamab SUD within the prior year.

Analysis

- Panelists' level of agreement with the consensus statements was rated on a 5-point Likert scale from 1 (strongly disagree) to 5 (strongly agree).
- Consensus was defined as ≥80% concordance in responses, achieved when ≥80% of panelists selected either 4 (agree) or 5 (strongly agree), or when ≥80% selected 1 (strongly disagree) or 2 (disagree).
- Consensus statements presented here reflect findings of Rounds 1 and 2 of the mDelphi panel. The third round of mDelphi panel is ongoing.
- To facilitate the adoption of OP SUD in real-world clinical practice, consensus statements will be synthesized into a healthcare provider-facing implementation guide that will be supplemented with existing literature, expert opinion and external treatment protocols, where appropriate.

Figure 1: mDelphi study design

1 Expert interviews
- 90-minute semi-structured interviews with the expert panel
- Responses coded and synthesized into draft consensus statements
- 156 preliminary consensus statements

2 Rating survey
- Online survey rating 156 statements
- 66 achieved consensus
- 90 items consolidated for re-rating
- 69* statements with no consensus

3 Revised re-rating
- Online survey rating the 69 revised statements
- Final consensus set to be confirmed
- Analysis ongoing

*Some statements were combined or removed.

Figure 4a: Roles and responsibilities for SUD administration and AE monitoring

At-a-glance Care Team Workflow:
Eligibility → Authorization → Treatment Day Dosing → AE Monitoring

Core workflow
1. **Hematologist-oncologist**: Determine OP SUD eligibility →
2. **Designated staff member**: Manage treatment authorizations →
3. **Healthcare provider/APP**: Administer SUD on treatment days

Flexible treatment day support
1. **Hematologist-oncologist**: Administer or oversee SUD administration →
2. **Healthcare provider/APP**: Administer step-up doses →
3. **On-site pharmacist**: Develop and adjust the treatment plan, provide education, and review medications with patient →
4. **Social worker or financial coordinator**: Assist with psychological support, lodging, transportation, and financial assistance

AE monitoring during clinic hours
- ✓ Healthcare provider/APP

Responsibilities
- ❑Educate patients on AE monitoring (may be done by pharmacist or nurse navigator)
- ❑Provide pre-medications
- ❑Administer prophylaxis
- ❑Escalate to physician or IP admission

AE monitoring during non-clinic hours
- ✓ On-call physician
- ✓ On-call healthcare provider/APP

Responsibilities
- ❑24/7 phone support
- ❑Escalate to physician or IP admission

Figure 4b: AE monitoring and risk mitigation

1 Educate patients on AE monitoring

Manual symptom monitoring
- ❑CRS: assess for fever, low BP, low oxygen with **home monitoring kit†**
- ❑ICANS: assess neurologic symptoms (e.g., confusion/disorientation, shaky handwriting, difficulty waking the patient)
- ❑Assess for infection, and oral toxicity symptoms
- ❑Caregiver-led vital sign checks every 4–8 hours

†CRS home monitoring kit
- ❑Thermometer
- ❑BP cuff
- ❑Pulse oximeter

Optional — keep a vitals log: record readings to review with the provider

Remote symptom monitoring
Educate patients on the use of each wearable device per its device-specific instructions
- ❑**Wearable device** to record temperature, heart rate, and oxygen saturation; BP (manually obtained)
- ❑**Practice-level electronic remote patient monitoring platform** to receive physiologic data
- ❑**Automatic notification/alert to on-call physician** for abnormal vital signs or reported symptoms

2 Provide pre-medications*

*1–3 hours before each SUD
- ❑Dexamethasone (16 mg PO/IV or per institutional guidelines)
- ❑Diphenhydramine (50 mg PO/IV or per institutional guidelines)
- ❑Acetaminophen (650 mg–1,000 mg PO/IV)

3 Administer prophylaxis**

**Administration and dosing per institutional guidelines and patient attributes
- ❑Tocilizumab (8 mg/kg IV, max. 800 mg)
- ❑Acyclovir (400–800 mg PO BID) or valacyclovir (500 mg PO BID), with sulfamethoxazole/trimethoprim (1 DS tab PO three times weekly)
- ❑Levofloxacin (500 mg PO daily) or oral cephalosporin (e.g., cefpodoxime 200 mg PO BID) and fluconazole (200–400 mg PO daily)
- ❑Immunoglobulin replacement (~0.4–0.5 g/kg IV every 4 weeks; maintain IgG ≥400 mg/dL)

4 Recommended infrastructure
- ❑Phone, in-person, or remote monitoring capabilities
- ❑EMR alerts and pre-built order sets for CRS and ICANS monitoring
- ❑Patient's EMR profile could contain educational materials or emergency guidance to facilitate easier access during OP SUD monitoring, management and emergency care

Figure 4c: AE management pathway and escalation to IP admission

CRS Management

	Grade 1: Fever	Grade 2: Fever + Low BP/ Low oxygen	Grade ≥3: Fever + Low BP needing support medication, or high-flow oxygen
Patient action	❑Call provider ❑Take dexamethasone + acetaminophen	❑Call provider ❑Go to clinic or designated ER	❑Go directly to designated ER
Provider action	❑Check-in again	❑Tocilizumab (8 mg/kg IV, max. 800 mg) ❑Supportive care per provider discretion (e.g., transfusions, supplemental oxygen, IV fluids)	❑Tocilizumab (8 mg/kg IV, max. 800 mg) ❑Supportive care per provider discretion (e.g., transfusions, supplemental oxygen, IV fluids)
Symptoms resolved: Yes	❑OP SUD may continue	❑OP SUD may continue after symptom resolution	❑Remain IP for remainder of SUD
Symptoms resolved: No	❑Call provider ❑May need in-person visit	❑Escalate to IP admission	❑Hold SUD until resolution ❑Discontinue if not manageable, recurrent, or lasts ≥48 hours

ICANS Management

	Grade 1: ICE score 7-9	Grade 2: ICE score 3-6	Grade ≥3: ICE score 0-2
Patient action	❑Call provider	❑Go directly to designated ER	❑Go directly to designated ER
Provider action	❑Check-in again	❑Levetiracetam 500 mg PO/IV BID ❑Supportive care per provider discretion (e.g., transfusions, supplemental oxygen, IV fluids)	❑Levetiracetam 500 mg PO/IV BID ❑Supportive care per provider discretion (e.g., transfusions, supplemental oxygen, IV fluids)
Symptoms resolved: Yes	❑OP SUD may continue with dose monitoring if resolved	❑Remain IP for remainder of SUD	❑Remain IP for remainder of SUD
Symptoms resolved: No	❑Escalate to IP admission	❑Hold SUD until resolution ❑Discontinue if recurrent Grade ≥3 ICANS or not manageable	❑Hold SUD until resolution ❑Discontinue if recurrent Grade ≥3 ICANS or not manageable

Other triggers for IP admission
- Major social destabilization (e.g., housing loss, death of a caregiver)
- **Grade ≥3 infection (or infection requiring IV antibiotics)**

Figure 5: Caregiver eligibility for OP SUD

Caregiver Eligibility Screening
Caregiver eligibility requires reliable support, communication, continuous presence, symptom monitoring, and appointment participation throughout OP SUD

1 Responsibilities and availability
- ❑Be physically present with the patient for the entire SUD period
- ❑Monitor with thermometer, BP cuff, pulse oximeter
- ❑Assess and report CRS and ICANS symptoms every 4–8 hours
- ❑Attend all patient SUD appointments and communicate concerns to providers

2 Capability
- ❑No cognitive impairment impacting patient support abilities
- ❑No physical limitations impairing emergency response or patient transport
- ❑Ability to reliably communicate with the patient and providers

Figure 6: Patient and caregiver education for OP SUD

Education Package Prior to OP SUD Monitoring

Post-treatment medications
- ❑Dexamethasone and acetaminophen
- ❑Instruct patient to take these medications for Grade 1 CRS (see Figure 4c)

Whom and when to call
- ❑Who: administering site contact information during and after hours
- ❑When: any grade CRS or ICANS (see Figure 4c)

ER guidance
- ❑Which ER: designated CRS/ICANS-capable site where possible (see Figure 3)
- ❑When to go: see Figure 4c
- ❑What to bring: wallet care card or patient bracelet
- ❑What to inform ER providers: on bispecific therapy and last dose date; at risk for CRS/ICANS; ask ER staff to contact the administering site

Wallet care card or patient bracelet
- ❑Current therapy and dosing
- ❑AEs to monitor: CRS, ICANS, infection
- ❑Providers: administering site 24/7 contact number and on-call provider 24/7 contact number

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Abbreviations

AE: adverse event; APP: advanced practice provider; BID: twice per day; BP: blood pressure; BsAb: bispecific antibody; CAR-T: chimeric antigen receptor T-cell; CRS: cytokine release syndrome; DS: double strength; ECOG: Eastern Cooperative Oncology Group; EMR: electronic medical record; ER: emergency room; ICANS: immune effector cell-associated neurotoxicity syndrome; ICE: immune effector cell-associated encephalopathy; IgG: immunoglobulin G; IP: inpatient; IV: intravenous; MM: multiple myeloma; OP: outpatient; PO: taken orally; RRMM: relapsed/refractory multiple myeloma; SUD: step-up dosing.

Multiple Myeloma

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