[Clinic or Hospital Logo]

SOP #	[Number]
Effective	[Date]
Approved	[Date]
Next Review	[Date]
Owner	[Name]
Department	[Name]
Tags	[Tags]
Applicability	[Name of sites]

Bispecific T-Cell Engager Ordering and REMS Compliance

Where Did This Resource Come From?	
Clinic/Hospital Type	Mid-sized, community-based clinic with satellite clinics
What's Unique?	• Coordinated multidisciplinary roles ensure REMS enrollment, training, and mandatory reporting are met. • Designated a pharmacist manager as an Authorized Representative to oversee implementation and compliance with REMS requirements. • Integrated safety and documentation adhere to regulations.

1. Purpose

The purpose of this SOP is to establish a standardized process for ordering and ensuring Risk Evaluation and Mitigation Strategy (REMS) compliance for bispecific therapies within the oncology clinic. This procedure supports patient safety, regulatory compliance, and operational efficiency in drug procurement and administration.

2. Scope

This SOP applies to all clinical and pharmacy staff involved in the ordering, procurement, administration, and monitoring of BTCEs. It includes pharmacists, pharmacy technicians, oncology nurses, ordering physicians, and administrative personnel responsible for compliance and documentation.

3. Definitions

- **Bispecific T-Cell Engager (BTCE)**: Synthetic proteins that bind two distinct antigens: one targets the CD3 protein on T cells, and the other targets a specific cancer antigen, redirecting T cells to activate an antitumor immune response.

- **REMS (Risk Evaluation and Mitigation Strategy):** A safety program required by the United States Food and Drug Administration (FDA) to ensure that the benefits of certain medications outweigh their risks.
- **GPO (Group Purchasing Organization):** An entity that helps healthcare providers procure medications at negotiated rates.
- **CIN (Clinically Integrated Network):** A group of healthcare providers collaborating to improve quality and cost-effectiveness of care.
- **Cytokine Release Syndrome (CRS):** A potentially severe inflammatory response that occurs when immune effector cell therapy leads to the release of cytokines into the bloodstream. This syndrome causes symptoms such as fever, hypotension, hypoxia, chills, tachycardia, dyspnea, nausea, rash, headache, and myalgia.
- **Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS):** A neurological complication caused by inflammation in the central nervous system following immune effector cell therapy. Symptoms can range from mild, such as headache and confusion, to severe, including seizures and coma, which may be life-threatening.

4. Responsibilities

- **Oncology Pharmacists:** Responsible for reviewing bispecific therapy requests, ensuring formulary adherence, obtaining necessary approvals, and verifying REMS compliance.
- **Pharmacy Technicians:** Assist with ordering, inventory management, and ensuring availability of required pre-medications.
- **Ordering Physicians/Advanced Practice Providers (APPs):** Submit medication requests and oversee clinical appropriateness.
- **Nurses:** Maintain up-to-date certifications on training required for dispensing/administering REMS medications, ensure patients complete required consent forms, verify that required laboratory tests or monitoring are completed prior to dispensing REMS medications, and submit required REMS reports.
- **Administrative Compliance Team:** Ensures adherence to REMS requirements and documentation of patient and provider enrollment.

5. Procedure

Drug Procurement and Ordering

- **Step 1:** Coordinate with the designated specialty distributor or GPO for product availability.
- **Step 2:** Ensure pricing considerations, including rebates and discounts from CIN or provider networks, are factored into purchasing decisions.
- **Step 3:** Educate purchasing staff on proper ordering procedures.
- **Step 4:** Order the product from specialty distributor.
- **Step 5:** Arrange for the ordering of pre-medications and supportive therapies as needed.

- **Step 6**: Maintain a small stock of critical supportive medications such as tocilizumab if required.

REMS Compliance and Registration

- **Step 1:** Verify if the prescribed therapy requires REMS enrollment through REMS@FDA.
- **Step 2**: Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with REMS requirements.
    - Authorized Representatives are typically pharmacist or nurse managers.
- **Step 3:** The Authorized Representative must enroll the pharmacy or setting in the REMS program by completing and submitting the Pharmacy and Healthcare Setting Enrollment Form to the REMS. Work with manufacturers to ensure the clinic and prescribers are registered as required.
    - Individual pharmacists may be required to complete training, verify safe use conditions (e.g., verifying required laboratory monitoring or that a patient or prescriber is enrolled in the REMS), counsel patients, and/or provide the patient with educational materials or a medication guide.
- **Step 4:** Train all relevant staff involved in dispensing BTCEs with REMS requirements, with retraining occurring for new staff and when needing to address updates.
- **Step 5:** Document REMS registration and compliance on each order in the Electronic Health Record (EHR).

6. Safety and Compliance Considerations

- Follow all federal and institutional regulations regarding bispecific therapy ordering and administration.
- Ensure REMS compliance, including provider and patient education requirements. Nurse Educator provides training on the REMS program and side effect management to newly hired nurses and as needed in response to clinical updates.
- Providers must complete a REMS certification test to prescribe REMS-required BTCEs.
- Providers and nurses must educate patients on REMS-required BTCEs and provide a medication guide and wallet card, if available.
- Verify pre-medication availability and ensure emergency preparedness for potential adverse reactions.
- Report any serious adverse events suggestive of cytokine release syndrome (CRS) and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), to the REMS.

7. Records and Documentation

- Maintain records of all drug orders electronically, including approvals, procurement, and dispensing details. Records may be requested by REMS and/or wholesale distributors.
- Ensure an up-to-date inventory by routinely monitoring stock levels, removing expired medications, and upholding proper storage conditions.
- Maintain records of personnel training and schedule retraining per institutional protocols.
- Document REMS enrollment and verification in the electronic health record (EHR) with every dispense
- Track medication usage and compliance audits.

8. REMS Resources

- BTCE Requiring REMS:
    - Elranatamab-bcmm (ELREXFIO™)
    - Talquetamab-tgvs (TALVEY®) & Teclistamab-cqyv (TECVAYLI®)
        - Note: Both of these BTCEs are on the same REMS.
- Access the Currently Approved REMS Drugs for resources on specific REMS program requirements.
- Roles of Different Participants in REMS

9. References

1. FDA. Approved Risk Evaluation and Mitigation Strategies (REMS). https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm. Accessed February 2025.
2. FDA. REMS Compliance Program. https://www.fda.gov/drugs/risk-evaluation-and-mitigation-strategies-rems/rems-compliance-program. Accessed February 2025.
3. ACCP. Oncology Practice Management. https://www.accp.com/docs/meetings/ONC15/handouts/OPC15_Oncology_Practice_Management.pdf. Updated 2015. Accessed February 2025.

10. Revision History

Version #	Date	Description of Changes	Reviewed / Approved By