DukeMedicine
Division of Cellular Therapy

ADULT AND PEDIATRIC BLOOD AND MARROW TRANSPLANT PROGRAM

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Immune Effector Cell Administration and Patient Management

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APBMT-COMM-044
IMMUNE EFFECTOR CELL ADMINISTRATION AND PATIENT MANAGEMENT

1 PURPOSE

1.1 To outline the care and management of the adult and pediatric patients receiving immune effector cells (IECs), which includes post-infusion monitoring including but not limited to the recognition of cellular therapy complications and emergencies.

1.2 To describe the processes around IEC administration.

2 INTRODUCTION

2.1 Immune Effector Cells (IEC) are cells used to modulate an immune response for therapeutic intent, such as dendritic cells, natural killer cells, T cells, and B cells. This includes, but is not limited to, genetically engineered chimeric antigen receptor T cells (CAR-T cells) and therapeutic vaccines.

2.2 All staff involved in the prescribing, dispensing, or administration of IEC therapy are required to complete training modules, such as Risk Evaluation and Mitigation Strategy (REMS) specific to each individual product.

2.2.1 Components:

2.2.1.1 Training and assessment of knowledge include some or all of the following: prescribing information, medication guides, patient management, and adverse event management.

2.2.1.2 Training for all staff will include the detection of and management of immune effector cellular therapy complications. See related SOP APBMT-COMM-045 *Management of Immune Effector Cell Therapy Complications*.

2.2.2 Retraining:

2.2.2.1 As training is product specific, retraining for all applicable persons will occur if 12 months lapse without a product being utilized in the institution unless otherwise specified by institutional and/or product manufacturer policy.

2.2.3 Training Documentation and Storage:

2.2.3.1 Most retraining is completed and results stored via online modules through the product manufacturer training website. If such is not available, internal training (i.e. via Duke LMS training site) will occur in compliance with manufacturer recommendations.

2.2.3.2 Knowledge assessment are tracked, and when necessary will be kept on file locally, by staff in the Duke Center for Medication Policy.

2.2.3.3 Current Training Stats are available for review upon request from the Duke Center for Medication Policy.

3 SCOPE AND RESPONSIBILITES

3.1 Interdisciplinary

3.1.1 The physician, or physician designee, will screen the patient to determine eligibility and place an order for the IEC product and associated supportive care in the electronic medical record (EMR). The physician is ultimately responsible for the care of the patient pre, peri, and post IEC therapy.

3.1.2 The nurse will provide supportive care and administer any treatment ordered by physician.

3.1.3 The pharmacist will ensure immediate access to medications and targeted therapies adequate to manage and/or treat expected complications of IEC administration and in compliance with manufacturer's requirements, when applicable.

3.1.4 All staff involved in the care of the immune effector cell patient will be responsible for ongoing monitoring of the patient for complications associated with immune effector cell therapy.

3.1.5 In the event that the primary team deems an escalation of care is needed, patients will be promptly transferred to the care of the intensive care service and will include plans for patient monitoring before, during and after transfer and communication of the ongoing care plan.

4 DEFINITIONS/ACRONYMS

4.1	CAR	Chimeric Antigen Receptor
4.2	CRS	Cytokine Release Syndrome
4.3	EMR	Electronic Medical Record
4.4	IECs	Immune Effector Cells
4.5	IV	Intravenous
4.6	Licensed personnel	Physician, Advanced Practice Provider, Nurse
4.7	NS	Normal Saline
4.8	REMS	Risk Evaluation and Mitigation Strategy
4.9	SOP	Standard Operating Procedure
4.10	STCL	Stem Cell Transplant Laboratory

5 MATERIALS

5.1 NA

6 EQUIPMENT

6.1 NA

7 SAFETY

7.1 NA

8 PROCEDURE

8.1 **NOTE:** For all processes outlined below, first review the manufacturer-specific protocol for IEC therapy, as applicable for the product and patient. Examples include the Clinician Guides for:

- 8.1.1 Abecma (idecabtagene vicleucel)
- 8.1.2 Breyanzi (lisocabtagene maraleucel)
- 8.1.3 Carvykti (ciltacabtagene autoleucel)
- 8.1.4 Kymriah (tisagenlecleucel
- 8.1.5 Tecartus (brexucabtagene autoleucel)
- 8.1.6 Yecarta (axicabtagene ciloleucel)

8.2 After the patient is determined to be an IEC candidate and prior to therapy initiation, there shall be a consultation between the patient and a physician who is approved to prescribe IEC therapy, to review the goal and plan of treatment.

8.3 The patient will be screened by a financial care coordinator and social worker for appropriateness and to ensure adequate resources are in place for treatment.

8.4 The patient, parent and/or legally authorized representative, as applicable, will sign applicable consent(s) as per health system policy and product requirements.

8.5 A patient alert card will be provided to all IEC patients or their caregivers along with the following instructions:

- 8.5.1 The patient or caregiver will carry the patient alert card at all times.
- 8.5.2 The patient or caregiver will provide the patient alert card to any healthcare provider treating the patient.
- 8.5.3 The patient will be given instructions related to expectations on remaining within the proximity of the clinical program for follow-up care as medically indicated.
- 8.5.4 The patient will be reminded of the risks of cytokine release syndrome (CRS), neurologic toxicity, or other potential adverse effects and the need to monitor for these events and to seek immediate medical attention if they occur.
- 8.5.5 The patient will be instructed to refrain from driving and other hazardous activities following IEC administration when required per manufacturer's instructions.

8.6 The patient will receive IEC therapy either on the:

- 8.6.1 Adult Hematology Oncology inpatient unit

8.6.2 Pediatric Transplant and Cellular Therapy inpatient unit

8.6.3 Each program's corresponding outpatient clinic or infusion room

8.7 The pharmacist and physician will ensure timely availability of appropriate treatment for CRS prior to the initiation of the administration of the IEC product and during the recovery period.

8.8 The physician, advance practice provider (APP), or designee will ensure orders are available in the electronic medical record and include premedication and post intravenous (IV) hydration.

8.9 For first vendor product administration via infusion bag, the nurse manager or designee will request from the vendor, a sample bag for staff to view and practice administration set up, PRIOR to administering a new product. This will be housed in a dedicated location on each clinical service area.

8.10 IEC Administration

8.10.1 Patient will receive premedication 30-60 minutes before the start of the IEC infusion or as per physician orders.

8.10.2 IEC's will be delivered in a syringe or infusion bag. Tubing will be primed by nursing staff with normal saline (NS) and directly attached to the patient's central line.

8.10.3 PRIMING OF THE PRODUCT- ADULT PROGRAM

8.10.3.1 If the IEC product is prepared in a syringe, connect the syringe containing the product directly to port of the IV tubing that is closest to the patient (lowest port).

8.10.3.2 If the IEC product is prepared in an infusion bag, prime a secondary line with NS and attach to the first IV line at the proximal port to the patient. Next, remove NS bag used to prime secondary line from the tubing, ensuring to maintain sterility and attach the tubing to the infusion bag.

8.10.4 PRIMING OF THE PRODUCT- PEDIATRIC PROGRAM

8.10.4.1 If the IEC product is prepared in a syringe, it will be connected to a luer locking stopcock. The male end of the stopcock will be connected directly to the patient. The IEC product will then be administered via direct intravenous push with appropriate intravenous fluids provided at the bedside.

NOTE: Unless otherwise specified, as some products may require specific tubing requirements, do NOT use blood or filtered tubing; Do NOT Irradiate Product.

8.10.5 Carvykti (ciltacabtagene autoleucel) requires a non-leukocyte depleting filter commonly referred to as a blood filter. All blood and cell products must be administered through a filter in order to remove cell clots and thrombi. Must use a standard blood filter, with a pore size of 170 260 μm, to infuse product.

8.11 The product will be prepared in and released by the Stem Cell Transplant Laboratory (STCL) personnel and transported as outlined by product dispensing guidelines.

8.12 The product will be accepted from the courier by the clinical team and/or nurse. Two licensed personnel will verify the product to be infused by double-checking the paperwork to the product.

8.13 Two licensed personnel will verify the IEC product to the patient's armband at the bedside and confirm that the patient has received the prescribed pre-medications.

8.14 Vital signs will be monitored and documented at baseline, every 15 minutes until infusion is completed. Monitoring of VS should be completed 30 minutes after reinfusion is complete unless manufacture has specified specific post infusion monitoring time line.

8.15 If a complication occurs with the product administration, a time-out will occur immediately. The charge nurse and STCL personnel will be notified to determine next steps. As this will be a case by case basis.

8.15.1 Documentation will occur on the infusion flowsheet for any complication with administration. For a "line break" with possible administration volume loss, documentation should contain the comment "volume unknown" unless actual volume is determined by STCL personnel. Start and stop time will also be entered on infusion flowsheet.

8.15.2 In the nursing progress not, detailed documentation will occur on why the product was paused or not completely infused. If any additional steps were required with administration, these will be documented in the progress note.

8.15.3 RN will notify he primary physician of the event and resulting outcomes and provide documentation this communication occurred.

8.16 Begin IEC product infusion.

8.16.1 If the patient has a reaction, the physician will be notified, and appropriate medical intervention will be taken. This may include slowing or stopping the infusion.

8.16.2 Reactions may include the following:

- Chills and fever
- Decrease in blood pressure
- Dizziness or light-headedness
- Shortness of breath or difficulty breathing
- Fast heart rate
- Nausea and vomiting
- Muscle and joint aches
- Headache
- Symptoms of Cytokine Release Syndrome
- Symptoms of Macrophage Activation Syndrome
- Symptoms of Tumor Lysis Syndrome

8.16.3 If the patient stabilizes, the product may be resumed at a slower rate after consultation with physician or designee.

8.17 Materials used during the infusion will be discarded in accordance with hospital policy and in accordance with institutional and regulatory requirements. Contact leadership or the STCL manager for product-specific requirements.

8.18 The patient will be observed for a minimum of 1 hour following the infusion providing all vital signs are at baseline and patient is clinically stable. The patient will continue to be monitored for complications, including signs of cytokine release syndrome and neurologic dysfunction for a minimum of the next 2 to 3 weeks and in accordance with manufacturer's requirements.

8.18.1 In the event of suspected cytokine release syndrome or other complications, refer to APBMT-COMM-045 *Management of Immune Effector Cell Therapy Complications* for detailed management guidelines.

8.19 Should a deterioration in clinical status occur, there will be rapid escalation of care, increased intensity of monitoring, and relative workup to address complications and will include a written plan for communication of the transfer and ongoing management.

8.20 Communication to clinical staff, intensive care unit, emergency department, and pharmacy shall be comprehensive and timely, as applicable. (See Hospital Policies for Patient Transport).

8.21 Documentation:

8.21.1 Staff will document the infusion on the STCL-SOP-050 *Infusion Form* and in manufacturer specific databases, as required.

8.21.2 Staff will document the following into the electronic medical record:

8.21.2.1 Vital signs

8.21.2.2 Administration/Infusion times of all medications

8.21.2.3 Administration/Completion times of IEC infusion

8.21.3 Staff will document any adverse experiences on the STCL-GEN-050 *Infusion Form* and in accordance with regulatory and manufacturer's requirements, as applicable.

8.22 Once the patient meets criteria for discharge to home, discharge instructions will be reviewed in detail with the patient, caregiver and/or a legally authorized representative as applicable.

8.22.1 Discharge instructions will include any expectations for immediate follow-up care along with any restrictions, such as related to driving or other hazardous activity.

8.22.2 At this time, or during subsequent return visits, additional care plans incorporating additional follow-up requirements will be communicated.

8.23 Documents will be maintained per hospital document retention policies.

9 RELATED DOCUMENTS/FORMS

9.1 APBMT-COMM-045 Management of Immune Effector Cell Therapy Complications

9.2 STCL-SOP-050 Infusion Form

9.3 Product-specific Clinician Guides as provided by the manufacturer

10 REFFERENCES

10.1 NA

11 REVISION HISTORY

Revision No.	Author	Description of Change(s)
04	J. Frith	8.10.3.2 Updated If the IEC product is prepared in an infusion bag, prime a secondary line with NS and attach to the first IV line at the port proximal to the patient. Next, remove NS bag used to prime secondary line from the tubing, ensuring to maintain sterility and attach the tubing to the infusion bag. 8.14 Added Monitoring of VS should be completed for 30 minutes after reinfusion is complete unless specified differently from manufacture. 8.15 Added a time out procedure and how to document in flowsheet and notify provider.

Signature Manifest

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