Updating Your Therapeutic Armamentarium: Operating Procedures and Personnel

Brooke Peters, PharmD, BCOP

Brooke.Peters@aoncology.com

AON American Oncology Network | Pharmacy Services

Outline

- Review updates to Cellular Therapy Initiation SOP
  - New table for display of hospitalization recommendations
- Discuss updates to Cellular Therapy Toxicity Prevention and Management SOP
  - Refined recommendations for infection prevention
- Introduce new nurse protocols for CRS/ICANS monitoring
- Review updated data for formulary review

Cellular Therapy Initiation SOP Review

- Purpose
  - To establish guidance for providers and clinic staff seeking to initiate cellular therapies (**bispecific T-cell-engaging therapies**).
- Outline roles/responsibilities
- Introduce cellular therapy requirements
  - Drug preparation/administration instructions
  - REMS instructions
  - Tocilizumab considerations
  - **New table for display of hospitalization recommendations**

AON American Oncology Network | Pharmacy Services

Cellular Therapy Initiation SOP UPDATE

- Hospital requirements

5.6.4 Hospital recommendations per drug (per package insert, schedules can vary)

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Tecvayli																						
Lunsumio																						
Epkinly																						
Columvi								*														
Talvey QW																						
Talvey Q2W																						
Elrexfio																						

Key
Blue – hospital for observation +/- drug administration (24 hours per block) *PI recommends hospitalization for dose administration, not just after dose
Green – outpatient administration

Toxicity Prevention and Management SOP Review

- CRS Management
- ICANS Management
- Infection Prevention
  - **Refined recommendations for infection prevention** 

AON American Oncology Network | Pharmacy Services

Toxicity Prevention and Management SOP: Infection UPDATE

AON American Oncology Network Pharmacy Services

Pathogen	Intervention	All patients	High risk patients
Bacterial	Levofloxacin 500 mg PO daily (alternatives cefdinir 300 mg PO BID or Augmentin 875 mg PO BID)	Consider during the first month of therapy	Strongly consider for ANC <500 occurring after the first month and continue until neutrophil recovery. Consider ongoing prophylaxis for high risk patients[2]
	IVIG 400 mg/kg once every 4 weeks	Consider starting month two and continuing until therapy complete or IgG >400 (whichever is longer)	Strongly consider for IgG < 500
	Growth factor	N/A	Consider for ANC <500 and continue until neutrophil recovery
Pneumococcus	Pneumococcus conjugated vaccine	Update vaccination status prior to starting therapy	N/A
HSV/VZV	Acyclovir 400–800 mg PO twice a day or valacyclovir 500 mg PO once or twice a day	Strongly consider for all patients during therapy	N/A
Influenza	Immunization	Strongly consider seasonally	N/A
HBV	Entecavir 0.5 mg PO daily	N/A	Strongly consider for HBs Ag-positive or HBs Ag-negative, HBc Ab- IgG positive
Fungal	Fluconazole 400 mg PO daily	N/A	Strongly consider for ANC <500 and continue until neutrophil recovery. Consider ongoing prophylaxis for high risk patients[2]
PCP	Trimethoprim 80 mg/sulfamethoxazole 400 mg daily or 160/800 mg 3 times a week[3]	Strongly consider starting with therapy and continue for its duration or until CD4 ≥ 200/µL (whichever is longer)	N/A

1. Mohan M, Chakraborty R, Bal S, et al. Recommendations on prevention of infections during chimeric antigen receptor T-cell and bispecific antibody therapy in multiple myeloma. Br J Haematol. 2023;203(5):736-746.
2. History of prolonged steroid use or active high-dose corticosteroid use or are undergoing high-dose lymphodepletion or anticytokine therapy
3. Alternatives: Dapsone 100 mg PO daily, atovaquone suspension 750 mg/5 mL—1500 mg = 10 mL PO daily, pentamidine inhalation or IV every 4 weeks

Mohan M, Chakraborty R, Bal S, et al. Recommendations on prevention of infections during chimeric antigen receptor T-cell and bispecific antibody therapy in multiple myeloma. Br J Haematol. 2023;203(5):736-746.

New nurse protocols for CRS/ICANS monitoring

This document serves two primary purposes:

1. Provide instructions for triage nurses to make regularly scheduled calls on the outpatient days which a patient is at highest risk for CRS/ICANS and is not seeing a provider. This nurse triage activity will be built into flowsheets on additional days where a phone call may not be needed, simply as a reminder that this document is available should a patient call with signs/symptoms of CRS/ICANS
2. Provide instructions for the triage of patients experiencing signs/symptoms of CRS/ICANS.

New nurse protocols for CRS/ICANS monitoring

	JBI ATTACHMENT		RN
AON AMERICAN ONCOLOGY NETWORK, LLC	**Bispecific T-Cell Engager Triage Instructions**	Document Number	RN-JBI-041-ATT2
		Revision Number	1
		Effective Date	1/31/2024

This patient is receiving a bispecific T-cell engager, which has a risk of CRS/ICANS. Complete information about the identification and management of CRS/ICANS can be found in RN-JBI-041-ATT Cellular Therapy Toxicity Prevention and Management (please review this document for education on CRS/ICANS if you are not familiar with these toxicities).

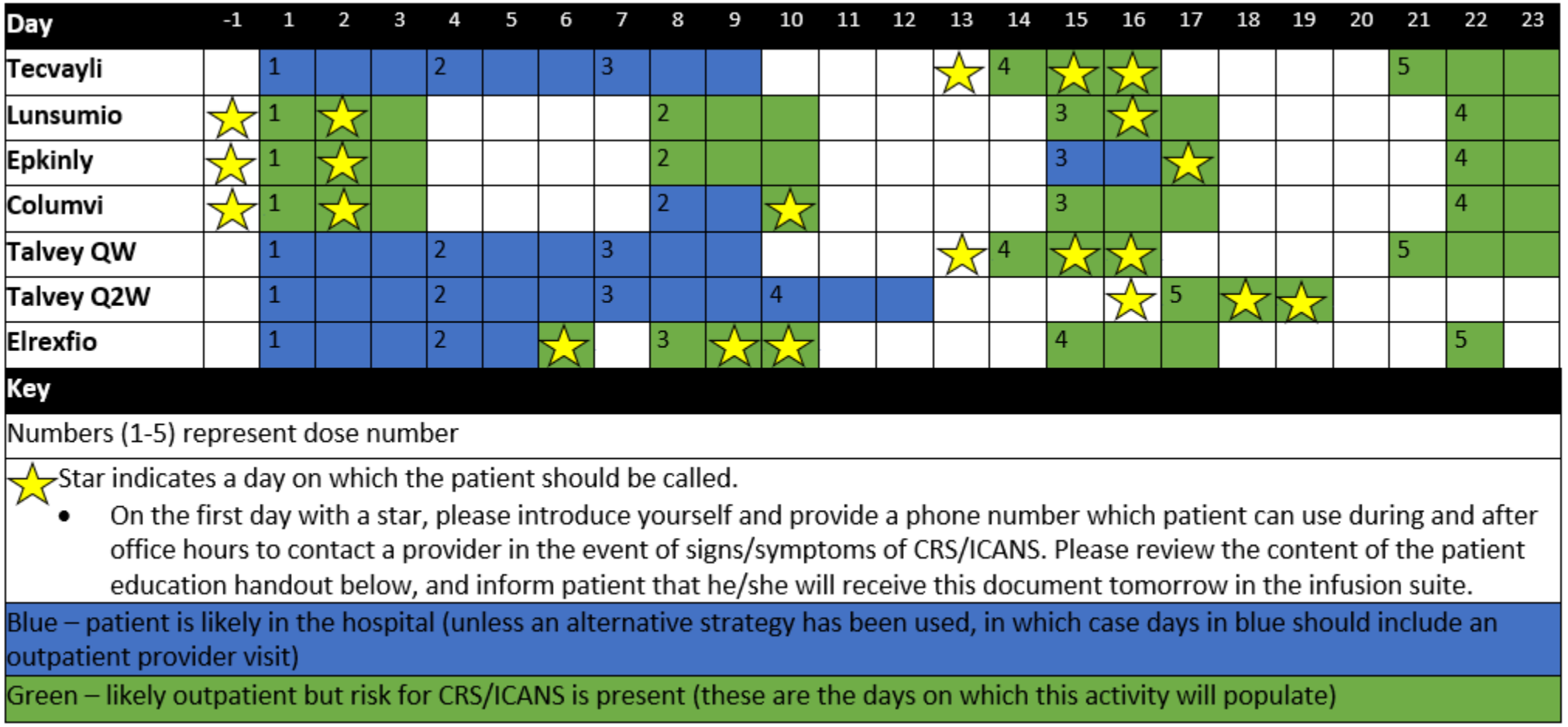
This document serves two primary purposes:

1. Provide instructions for triage nurses to make regularly scheduled calls on the outpatient days which a patient is at highest risk for CRS/ICANS and is not seeing a provider. This nurse triage activity will be built into flowsheets on additional days where a phone call may not be needed, simply as a reminder that this document is available should a patient call with signs/symptoms of CRS/ICANS
2. Provide instructions for triage of patients experiencing signs/symptoms of CRS/ICANS.

If this patient or caregiver calls to report side effects at any time, please consider CRS/ICANS. Side effects of CRS/ICANS may include:

· Difficulty breathing	· Dizziness/lightheadedness
· Fever (100.4°F/38°C or higher)	· Headache
· Chills/shaking chills	· Seizures
· Severe nausea, vomiting, diarrhea	· Confusion
· Severe muscle or joint pain or weakness	· Aphasia
· Hypotension (generally defined as an SBP < 90 mm Hg or <75% of patient baseline)	· Tremors

New nurse protocols for CRS/ICANS monitoring



Day	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Tecvayli		1			2			3						★	4	★	★					5		
Lunsumio	★	1	★						2							3	★						4	
Epkinly	★	1	★						2							3		★					4	
Columvi	★	1	★						2		★					3							4	
Talvey QW		1			2			3						★	4	★	★					5		
Talvey Q2W		1			2			3			4						★	5	★	★				
Elrexfio		1			2		★		3	★	★					4							5	

Key

Numbers (1-5) represent dose number

★ Star indicates a day on which the patient should be called.

- On the first day with a star, please introduce yourself and provide a phone number which patient can use during and after office hours to contact a provider in the event of signs/symptoms of CRS/ICANS. Please review the content of the patient education handout below, and inform patient that he/she will receive this document tomorrow in the infusion suite.

Blue – patient is likely in the hospital (unless an alternative strategy has been used, in which case days in blue should include an outpatient provider visit)

Green – likely outpatient but risk for CRS/ICANS is present (these are the days on which this activity will populate)

New nurse protocols for CRS/ICANS monitoring

Please reach out to the patient regarding these side effects on each of the three days indicated with a star in the table below (if he/she is not currently in the hospital or being seen by a provider on this day)

- The treatment schedule may vary.
- This activity serves as a reminder that the patient may call with signs/symptoms of CRS/ICANS on this day (days highlighted in blue and green)
- Days on which the patient should be **proactively called** for education or a review of signs/symptoms of CRS/ICANS are marked with a **star** below
    - On the day of the first call, please review the patient education pearls for CRS/ICANS at the end of this document and provide patient with a phone number to get in touch with a nurse and/or provider during and after business hours.
    - On subsequent days, please inquire about any sings/symptoms of CRS/ICANS and triage per instructions included in this document.
- Days highlighted in blue represent days that the patient is likely in the hospital for observation, and days highlighted in green reflect days that the patient is likely outpatient/home, unless they have experienced significant CRS/ICANs with a previous dose. **If days highlighted in blue are actually planned for outpatient administration**, dose please contact the patient to review instructions prior to the first outpatient treatment day.

New nurse protocols for CRS/ICANS monitoring

AON American Oncology Network Pharmacy Services

What to do if patient reports any side effects of CRS/ICANS:

Send the patient to the ER (or direct admit if able) for the following side effects:

- Difficulty breathing
- Confusion, aphasia, tremors
- Severe nausea, vomiting, diarrhea
- Severe muscle or joint pain or weakness
- Symptomatic hypotension (SBP < 90 mm Hg or <75% of patient baseline with other symptoms)
- Severe Dizziness/lightheadedness

Bring to the clinic for evaluation for the following side effects. If this is not an option, send patient to the ER (or direct admit if able):

- Fever (100.4°F/38°C or higher) ***see fever management below***
- Mild chills/shaking chills
- Mild muscle or joint pain or weakness
- Asymptomatic hypotension (SBP < 90 mm Hg or <75% of patient baseline without other symptoms)
- Headache

New nurse protocols for CRS/ICANS monitoring

Fever management

Fever (100.4°F/38°C or higher) with no other symptoms AND no suspected neutropenia (ANC >3000 1-2 days prior to fever documented)

- Instructions for patient:
  - Drink plenty of fluids and take acetaminophen 625-1000 mg PO Q6H for 24 hours
  - If two hours after acetaminophen your fever has not resolved to less than 100.4, take PO dexamethasone 10-12 mg once if your provider has prescribed this for you
  - If your fever has not resolved after 12 hours despite supportive care, OR if you develop any other symptoms, please contact your provider and/or report to the ER. Please review the symptoms above with patient.
  - If you have a blood pressure monitor at home, check your blood pressure regularly and please contact your provider and/or report to the ER for any confirmed (repeat) reading with SBP <90.
- Instructions for RN:
  - Notify provider
    - If during clinic hours, provider may prefer to instruct patient to take acetaminophen 625-1000 mg PO once and then come into clinic for IV hydration +/- dexamethasone. Consult with provider about this option if able.
  - Please contact patient before the end of the business day and 24 hours after initial call (or at the start and end of the next business day if call is made after-hours) to check-in.

New nurse protocols for CRS/ICANS monitoring

AON American Oncology Network Pharmacy Services

Fever (100.4°F/38°C or higher) with no other symptoms AND possible neutropenia (ANC >3000 1-2 days prior to fever NOT documented)

- Instructions for patient:
  - During clinic hours: Take acetaminophen 625-1000 mg PO once and then come into clinic for labs and possible IV hydration.
  - After clinic hours: Report to ER
- Instructions for RN:
  - Notify provider
    - Provider may prefer to send patient to ER rather than brining into clinic for further workup. Consult with provider about this option if able.
  - Coordinate for patient to come in for the following
    - Labs (febrile neutropenia workup): CBC with differential, blood cultures x2, others per provider discretion
    - 1L NS or other hydration fluid +/- dexamethasone 10 mg at provider discretion (dexamethasone should be reserved for patients without neutropenia, for the treatment of CRS)
    - Provider visit if able
  - See RN-JBI-041-ATT Cellular Therapy Toxicity Prevention and Management for further CRS/ICANS treatment guidelines

New nurse protocols for CRS/ICANS monitoring

AON American Oncology Network Pharmacy Services

Patient education pearls for CRS/ICANS (Appendix 1 (last page) of RN-JBI-041-ATT Cellular Therapy Toxicity Prevention and Management)

Cytokine Release Syndrome and Related Side Effects

- Cytokine release syndrome, or CRS, is a systemic inflammatory response that occurs when the immune system is over-activated.
- CRS may occur in response to infection or receipt of certain medications, such as chimeric antigen receptor (CAR) T-cell therapy or bispecific T-cell engaging antibodies.
- Symptoms of CRS may include flu-like symptoms (fever, chills, body aches), low blood pressure, or difficulty breathing.
- Immune effector cell-associated neurotoxicity syndrome, or ICANS, is a neurological condition that may occur with or without CRS. Symptoms of ICANS include confusion, dizziness, headaches, or hallucinations.

- You will be closely monitored for these symptoms after receiving therapy with a risk for CRS or ICANS.
- Occasionally, these symptoms can become severe enough to require inpatient admission for management.
- Early recognition of these symptoms may result in less severe complications.

Contact your health care provider immediately if you experience any of these symptoms or note any changes in behavior:

Chills	Dizziness
Fever	Hallucinations
Low blood pressure	Seizures
Difficulty breathing	Anxiety
Confusion	Headaches

Formulary Considerations: Updated Data

AON American Oncology Network | Pharmacy Services

Formulary Considerations: Updated Data

	Tecvayli (teclistamab) *formulary status*	Lunsumio (mosunetuzumab) *formulary status*	Epkinly (epcoritamab) *formulary status*	Columvi (glofitamab) *formulary status*	Talvey (talquetamab) *formulary status*	Elrexfio (elranatamab) *formulary status*
Manufacturer	Janssen	Genentech	Genmab	Genentech	Janssen	Pfizer
FDA Approval	10/25/22	12/22/22	5/19/23	6/15/23	8/9/23	8/14/23
Targets	BCMA/CD3	CD20/CD3	CD20/CD3	CD20/CD3	GPRC5D/CD3	BCMA/CD3
Indication	Myeloma	FL	DLBCL	DLBCL	Myeloma	Myeloma
REMs	Yes	No	No	No	Yes	Yes
Hospital Recommended	Yes	No	Yes	Yes	Yes	Yes
Perma JCode	J9380	J9350	J9321	J9286	Pending	J1323 Effective 4/1/24
Contract	*contract and availability information*	*contract and availability information*	*contract and availability information*	*contract and availability information*	*contract and availability information*	*contract and availability information*
#active pt/ # planned	#/#	#/#	#/#	#/#	#/#	#/#

Updating Your Therapeutic Armamentarium: Operating Procedures and Personnel

Brooke Peters, PharmD, BCOP

Brooke.Peters@aoncology.com

AON American Oncology Network | Pharmacy Services