Regimen Reference Order – LYMP – epcoritamab

ARIA: LYMP - [epcoritamab]

Planned Course: **Until disease progression or unacceptable toxicity (1 cycle = 28 days)**
Indication for Use: **Non-Hodgkin Lymphoma**

CVAD: At Provider's Discretion

Proceed with treatment if:
ANC equal to or greater than 0.5 x 10^9/L AND Platelets equal to or greater than 50 x 10^9/L
- ***Contact Hematologist if parameters not met***

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Hydration for Cycle 1 (unless directed differently by clinic): • **Day prior to epcoritamab**: o please ensure patient drinks 2 litres of fluids per day • **Day of epcoritamab**: o please ensure patient drinks 1.5 litres of fluids per day in addition to IV hydration given in treatment room (or directed by clinic) • **Day after epcoritamab**: o ensure patient is booked for 1 L IV hydration in treatment room and ensure patient drinks an additional 1 litre of fluids per day		
allopurinol	300 mg	Orally once daily for **30 days** to begin 3 days prior to Cycle 1 and at provider's discretion for subsequent cycles **(Self-administered at home)** Only patients at risk of tumor lysis syndrome will be prescribed allopurinol

Treatment Regimen – LYMP – epcoritamab

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
predniSONE	100 mg	**Cycle 1 ONLY:** Orally once daily on **Days 2 to 4**, **9 to 11, 16 to 18 and 23 to 25** **(Self-administered at home)**
Day 1 – "Priming dose"		
cetirizine	20 mg	Orally **1 hour** prior to epcoritamab
acetaminophen	975 mg	Orally **1 hour** prior to epcoritamab

dexamethasone	16 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to epcoritamab **Nursing Alert: epcoritamab starts at least **1 hour after completion** of dexamethasone infusion*
Wait at least 1 hour after completion of IV pre-medication(s) before administering epcoritamab		
normal saline	500 mL	IV over 1 hour (Pre hydration)
epcoritamab	0.16 mg	**Subcutaneous**: Administer into abdomen or thigh Use 25G needle **Pharmacy Alert: Use the 5 mg/mL concentration of epcoritamab for "Priming dose". Two dilutions are required*
Day 2		
normal saline	1000 mL	IV over 2 hours **Nursing Alert: Vital signs and immune effector encephalopathy (ICE) score needs to be done prior to hydration. Prescriber must be contacted with vital sign values and ICE score*
Day 8 – "Intermediate dose"		
cetirizine	20 mg	Orally **1 hour** prior to epcoritamab
acetaminophen	975 mg	Orally **1 hour** prior to epcoritamab
dexamethasone	16 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to epcoritamab **Nursing Alert: epcoritamab starts at least **1 hour after completion** of dexamethasone infusion*
Wait at least 1 hour after completion of IV pre-medication(s) before administering epcoritamab		
normal saline	500 mL	IV over 1 hour (Pre hydration)
epcoritamab*	0.8 mg	**Subcutaneous:** Administer into abdomen or thigh Use 25G needle **Pharmacy Alert: Use the 5 mg/mL concentration of epcoritamab for "Intermediate dose". One dilution is required*
Day 9		
normal saline	1000 mL	IV over 2 hours **Nursing Alert: Vital signs and immune effector encephalopathy (ICE) score needs to be done prior to hydration. Prescriber must be contacted with vital sign values and ICE score*
Day 15 – First "Full dose" **Patient may be admitted to hospital for Cycle 1, Day 15**		
cetirizine	20 mg	Orally **1 hour** prior to epcoritamab
acetaminophen	975 mg	Orally **1 hour** prior to epcoritamab
dexamethasone	16 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to epcoritamab **Nursing Alert: epcoritamab starts at least **1 hour after completion** of dexamethasone infusion*
Wait at least 1 hour after completion of IV pre-medication(s) before administering epcoritamab		
normal saline	500 mL	IV over 1 hour (Pre hydration)

epcoritamab*	48 mg	**Subcutaneous:** Administer into abdomen or thigh Use 25G needle **Pharmacy Alert: Use the 60 mg/mL concentration of epcoritamab for "Full dose". No dilution is required*
Day 16		
normal saline	1000 mL	IV over 2 hours **Nursing Alert: vital signs and immune effector encephalopathy (ICE) score needs to be done prior to hydration. Prescriber must be contacted with vital sign values and ICE score*
Day 22 – "Full dose"		
cetirizine	20 mg	Orally **1 hour** prior to epcoritamab
acetaminophen	975 mg	Orally **1 hour** prior to epcoritamab
dexamethasone	16 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to epcoritamab **Nursing Alert: epcoritamab starts at least **1 hour after completion** of dexamethasone infusion*
Wait at least 1 hour after completion of IV pre-medication(s) before administering epcoritamab		
normal saline	500 mL	IV over 1 hour (Pre hydration)
epcoritamab*	48 mg	**Subcutaneous:** Administer into abdomen or thigh Use 25G needle **Pharmacy Alert: Use the 60 mg/mL concentration of epcoritamab for "Full dose". No dilution is required*
Day 23		
normal saline	1000 mL	IV over 2 hours **Nursing Alert: vital signs and immune effector encephalopathy (ICE) score needs to be done prior to hydration. Prescriber must be contacted with vital sign values and ICE score*
Cycles 2 and 3		
For **cycles 2 and onwards**, pre-medication with cetirizine, acetaminophen and dexamethasone is required for patients who: • Repeat doses within the step-up dosing schedule following a dose delay AND/OR • Experience CRS following the prior dose of epcoritamab ARIA orders for cetirizine, acetaminophen and dexamethasone will be discontinued for patients who do not require premedication. Administer premedication if agents not discontinued by treating physician		
cetirizine	20 mg	cetirizine only to be given ***at physician's discretion*** Orally **1 hour** prior to epcoritamab
acetaminophen	975 mg	acetaminophen only to be given ***at physician's discretion*** Orally **1 hour** prior to epcoritamab
dexamethasone	16 mg	dexamethasone only to be given ***at physician's discretion*** Orally **1 hour** prior to epcoritamab

epcoritamab*	48 mg	**Subcutaneous:** Administer into abdomen or thigh on **Days 1, 8, 15 and 22** Use 25G needle **Pharmacy Alert: Use the 60 mg/mL concentration of epcoritamab for "Full dose". No dilution is required*
Cycles 4 to 9		
cetirizine	20 mg	cetirizine only to be given ***at physician's discretion*** Orally **1 hour** prior to epcoritamab
acetaminophen	975 mg	acetaminophen only to be given ***at physician's discretion*** Orally **1 hour** prior to epcoritamab
dexamethasone	16 mg	dexamethasone only to be given ***at physician's discretion*** Orally **1 hour** prior to epcoritamab
epcoritamab*	48 mg	**Subcutaneous:** Administer into abdomen or thigh on **Days 1 and 15** Use 25G needle **Pharmacy Alert: Use the 60 mg/mL concentration of epcoritamab for "Full dose". No dilution is required*
Cycle 10 and Onwards		
cetirizine	20 mg	cetirizine only to be given ***at physician's discretion*** Orally **1 hour** prior to epcoritamab
acetaminophen	975 mg	acetaminophen only to be given ***at physician's discretion*** Orally **1 hour** prior to epcoritamab
dexamethasone	16 mg	dexamethasone only to be given ***at physician's discretion*** Orally **1 hour** prior to epcoritamab
epcoritamab*	48 mg	**Subcutaneous:** Administer into abdomen or thigh on **Day 1** Use 25G needle **Pharmacy Alert: Use the 60 mg/mL concentration of epcoritamab for "Full dose". No dilution is required*

*The dose of epcoritamab may be delayed *as per the Lymphoma DSG or Leukemia/BMT (L/BMT)* Physician's discretion (*usual c*riteria for dose delay: ANC less than 0.5 x 10^9/L; platelets less than 50 x 10^9/L or if patient is bleeding, signs or symptoms of infection, signs or symptoms of cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity (ICANS) or other adverse reactions that are Grade 3 or higher).

Following a dose delay, epcoritamab dose schedule may require modification. If dosing of epcoritamab is interrupted for more than 8 days after the "Priming dose" of Cycle 1 Day 1, more than 14 days after the "Intermediate dose" on Cycle 1 Day 8 or more than 6 weeks after any "Full dose" on Cycle 1 Day 15 and Onwards, dose re-escalation may be required. Refer to Health Canada Product Monograph for recommendations after a dose delay.

Any non-hematologic toxicity other than CRS or ICAN must resolve to equal to or less than grade 1 or baseline with no evidence of active bacterial, viral, or fungal infection before proceeding to the next dose. CRS and ICANS must fully resolve before proceeding to the next dose.

(**See APPENDIX A – Cytokine Release Syndrome (CRS) and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) monitoring and management**)

In the event of an infusion-related hypersensitivity reaction, refer to the **'Hypersensitivity Reaction Standing Order'**

REQUIRED MONITORING

Baseline

- Hepatitis B serology

Throughout therapy

- Monitor for signs and symptoms of cytokine release syndrome (CRS). Serious adverse events that may be associated with CRS include: pyrexia, headache, nausea, asthenia, hypotension, and elevations in serum aminotransferases and bilirubin
- Monitor for signs and symptoms of neurotoxicity. Symptoms may include: trembling, disturbance or loss of movement of parts of the body, speech or coordination disorders, apraxia, dizziness, confusion, disorientation, reversible seizures, encephalopathy, somnolence and agitation

Cycle 1 ONLY

Days 1 to 4, 8 to 11, 15 to 18 and 22 to 25 (day of epcoritamab and for three days after each dose)

- Patient to self-monitor body temperature with thermometer, three times a day

Cycles 1

Days 1, 8, 15 and 22

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders

Cycles 2 and 3

Day 1

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders

Day 15

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders

Cycle 4 and Onwards

Day 1

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
prednisone	100 mg	Orally once daily on Days 2, 3, 4, 9, 10, 11, 16, 17, 18 and 23, 24 and 25 of **Cycle 1 only**
valACYclovir	500 mg	Orally once daily
sulfamethoxazole-trimethoprim	800/160 mg	Orally once daily on Mondays, Wednesdays and Fridays

DISCHARGE INSTRUCTIONS

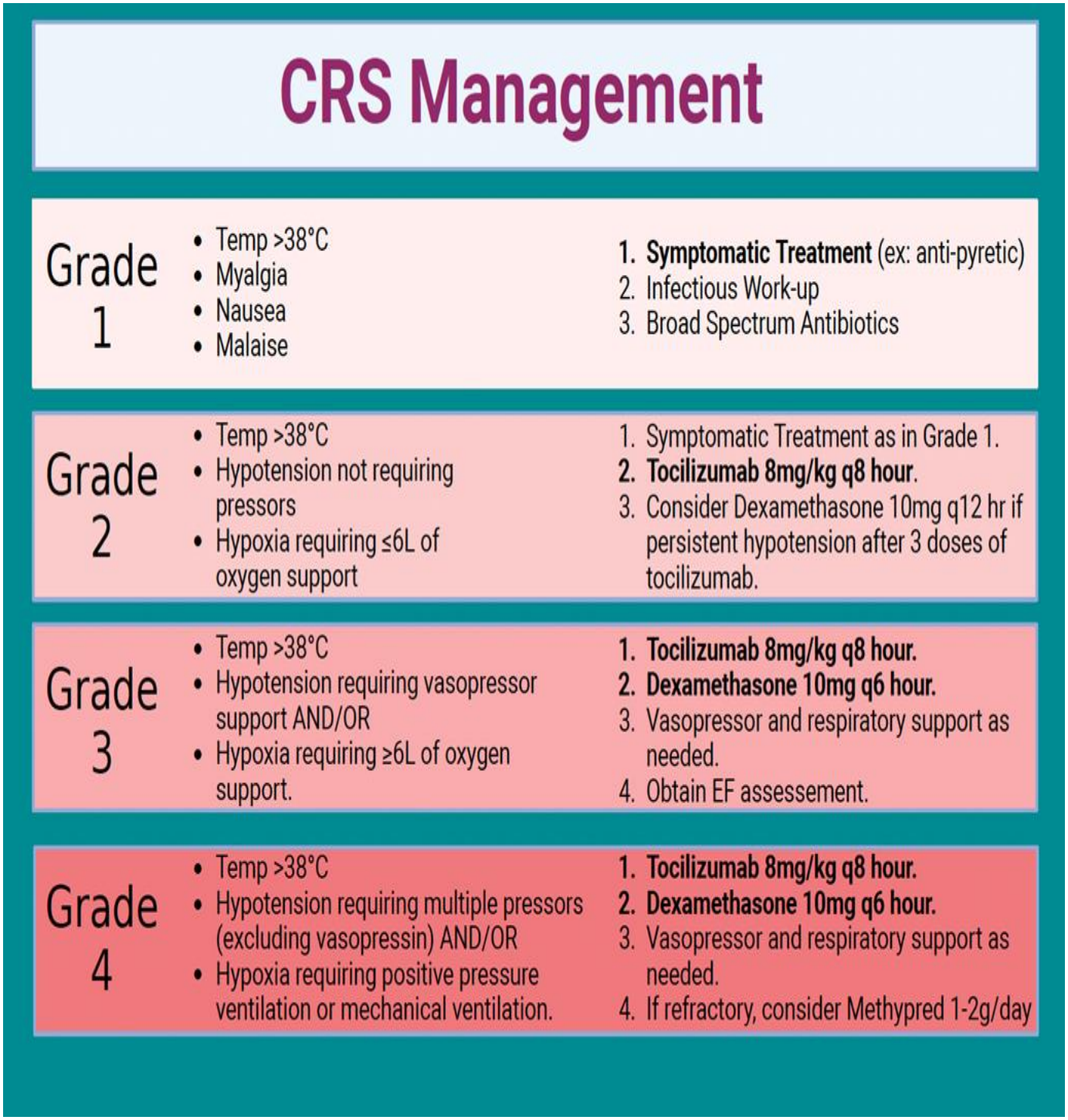
- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Advise patient to immediately report any symptoms of cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity (ICANS)
- For cycle 1 only: patient is to self-monitor body temperature 3 times daily, beginning on the day of each epcoritamab injection and continuing for 3 days after each injection
- Patient needs to report any temperature over 38 degrees Celsius or other potential symptoms of cytokine release syndrome to clinic team (adult hematology consult service for HSC or St. Boniface on call for evenings, weekends and holidays)
- Patient should be instructed to notify about any signs or symptoms of infection or unusual bruising or bleeding
- predniSONE is being prescribed for the prevention of CRS in this treatment regimen. Remind patient to take predniSONE at home on Cycle 1 and support medications at home
- For cycle 1 only: Patient must remain located no greater than 1 hour from CancerCare Manitoba MacCharles site

ADDITIONAL INFORMATION

- epcoritamab has been associated with tumor lysis syndrome
- Administration site restrictions are in place for epcoritamab

APPENDIX A (adapted from MBMT SOP CLI030):

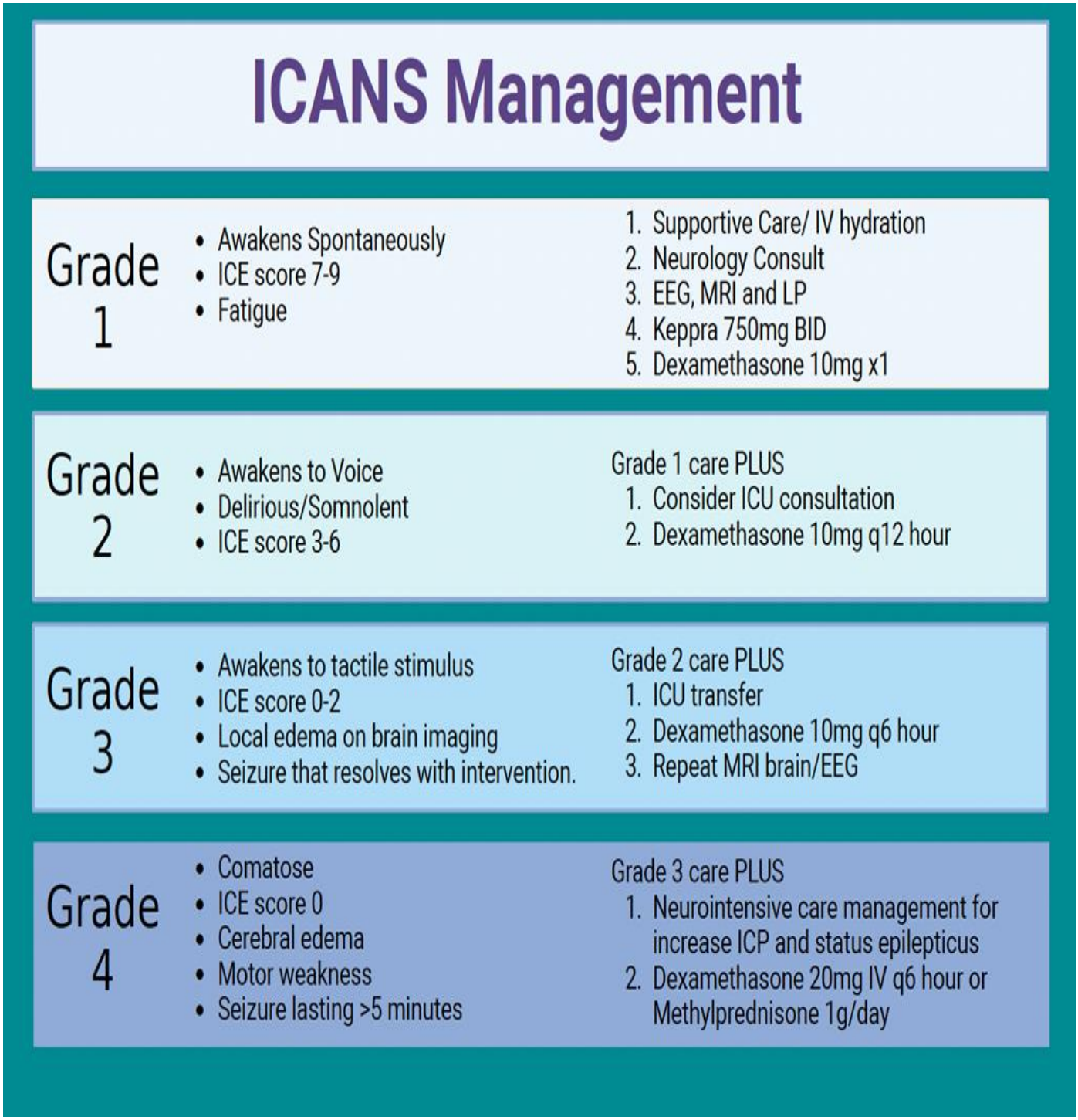
Cytokine Release Syndrome (CRS) and Immune effector cell-associated neurotoxicity syndrome (ICANS) monitoring and management



ICANS Monitoring

Immune Effector Cell Encephalopathy (ICE) Scoring
(Routinely performed twice daily)

- ***Orientation:*** Orientation to year, month, city, hospital: 4 points
- ***Naming:*** Ability to name 3 objects (e.g., point to clock, pen, button): 3 points
- ***Following commands:*** Ability to follow simple commands (e.g., "show me 2 fingers"): 1 point
- ***Writing:*** Ability to write a standard sentence (e.g., "The sky is blue"): 1 point
- ***Attention:*** Ability to count backwards from 100 by 10: 1 point


ICANS Management
Grade 1
• Awakens Spontaneously
• ICE score 7-9
• Fatigue
1. Supportive Care/ IV hydration
2. Neurology Consult
3. EEG, MRI and LP
4. Keppra 750mg BID
5. Dexamethasone 10mg x1
Grade 2
• Awakens to Voice
• Delirious/Somnolent
• ICE score 3-6
Grade 1 care PLUS
1. Consider ICU consultation
2. Dexamethasone 10mg q12 hour
Grade 3
• Awakens to tactile stimulus
• ICE score 0-2
• Local edema on brain imaging
• Seizure that resolves with intervention.
Grade 2 care PLUS
1. ICU transfer
2. Dexamethasone 10mg q6 hour
3. Repeat MRI brain/EEG
Grade 4
• Comatose
• ICE score 0
• Cerebral edema
• Motor weakness
• Seizure lasting >5 minutes
Grade 3 care PLUS
1. Neurointensive care management for increase ICP and status epilepticus
2. Dexamethasone 20mg IV q6 hour or Methylprednisone 1g/day