Regimen Reference Order – LYMP – glofitamab

ARIA: LYMP - [glofitamab]

Planned Course: **Cycle 1: oBINutuzumab (Days 1 and 2) and glofitamab (Days 8 and 15)**
Cycle 2 and Onwards: glofitamab up to a maximum of 12 cycles
(1 cycle = 21 days)

Note: First dose of glofitamab is administered in hospital

Indication for Use: **Non-Hodgkin Lymphoma**

Drug Alert: T-Cell Engager

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***

Note: Hepatitis B serology results must be reviewed in accordance with CCMB Policy Hepatitis B Monitoring for Oncology and Hematology Patients

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Hydration for first three doses of glofitamab (Cycle 1, Day 8 (Step-up Dose 1), Cycle 1, Day 15 (Step-up Dose 2), and Cycle 2, Day 1 (first full dose)) *unless directed differently by clinic*): ○ **Day prior to glofitamab infusion**: ○ Ensure patient drinks 2 litres of fluids per day ○ **Day of glofitamab infusion**: ○ Ensure patient drinks 1.5 litres of fluids per day in addition to IV hydration given in treatment room ○ **Day after glofitamab infusion**: ○ 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 – glofitamab

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
Day 1		
cetirizine	20 mg	Orally **1 hour** prior to oBINutuzumab
acetaminophen	650 mg	Orally **1 hour** prior to oBINutuzumab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to oBINutuzumab **Nursing Alert: oBINutuzumab starts at least **1 hour after completion** of dexamethasone infusion*
Wait at least 1 hour after completion of IV pre-medication(s) before starting oBINutuzumab		
oBINutuzumab	100 mg	IV in normal saline 100 mL following administration rates below: • 0 to 60 minutes – 6 mL/hour • 60 to 120 minutes – 12 mL/hour • 120 minutes onwards – 24 mL/hour **Alert*: Pharmacy to ensure final volume in bag = 100 mL (1 mg/mL final concentration) **Nursing Alert*: IV tubing is primed with oBINutuzumab
Day 2		
cetirizine	20 mg	Orally **1 hour** prior to oBINutuzumab
acetaminophen	650 mg	Orally **1 hour** prior to oBINutuzumab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to oBINutuzumab **Nursing Alert: oBINutuzumab starts **1 hour after completion** of dexamethasone infusion*
Wait at least 1 hour after completion of IV pre-medication(s) before administering oBINutuzumab		
oBINutuzumab	900 mg	IV in normal saline following administration rates below: • 0 to 30 minutes – 14 mL/hour • 30 to 60 minutes – 28 mL/hour • 60 to 90 minutes – 42 mL/hour • 90 to 120 minutes – 56 mL/hour • 120 to 150 minutes – 69 mL/hour • 150 to 180 minutes – 83 mL/hour • 180 to 210 minutes – 97 mL/hour • 210 to 240 minutes – 111 mL/hour **Alert*: Pharmacy to ensure final volume in bag = 250 mL (3.6 mg/mL final concentration) **Nursing Alert*: IV tubing is primed with oBINutuzumab
Day 8 (glofitamab Step-up Dose 1)- Inpatient administration. Follow inpatient orders **Note**: Patients will be admitted to hospital for treatment with the first dose of glofitamab		
cetirizine	20 mg	Orally **1 hour** prior to glofitamab

acetaminophen	975 mg	Orally **1 hour** prior to glofitamab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to glofitamab **Nursing Alert: glofitamab starts at least **1 hour after completion** of dexamethasone infusion*
normal saline	500 mL	IV over 1 hour (Pre hydration)
glofitamab	2.5 mg	IV in normal saline over 4 hours **Alert: Pharmacy to ensure final volume in bag = 25 mL*
Day 9- Inpatient administration. Follow inpatient orders		
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 (glofitamab Step-up Dose 2)		
cetirizine	20 mg	Orally **1 hour** prior to glofitamab
acetaminophen	975 mg	Orally **1 hour** prior to glofitamab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to glofitamab **Nursing Alert: glofitamab starts at least **1 hour after completion** of dexamethasone infusion*
normal saline	500 mL	IV over 1 hour (Pre hydration)
glofitamab	10 mg	IV in normal saline 50 mL over 4 hours
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*
Cycle 2		
Day 1 (first full dose of glofitamab)		
cetirizine	20 mg	Orally **1 hour** prior to glofitamab
acetaminophen	975 mg	Orally **1 hour** prior to glofitamab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to glofitamab **Nursing Alert: glofitamab starts at least **1 hour after completion** of dexamethasone infusion*
normal saline	500 mL	IV over 1 hour (Pre hydration)
glofitamab	30 mg	IV in normal saline 50 mL over 4 hours
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*

Cycle 3		
Day 1		
cetirizine	20 mg	Orally **1 hour** prior to glofitamab
acetaminophen	975 mg	Orally **1 hour** prior to glofitamab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to glofitamab **Nursing Alert: glofitamab starts **1 hour after completion** of dexamethasone infusion*
normal saline	500 mL	IV over 1 hour (Pre hydration)
glofitamab	30 mg	IV in normal saline 50 mL over 2 hours
Cycles 4 to 12		
For **cycles 4 and onwards**, pre-medication with intravenous 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 glofitamab ARIA order for dexamethasone will be discontinued for patients who do not require premedication. Administer premedication if agents not discontinued by treating physician		
Day 1		
cetirizine	20 mg	Orally 30 minutes prior to glofitamab
acetaminophen	975 mg	Orally 30 minutes prior to glofitamab
dexamethasone	20 mg	dexamethasone only to be givenat **physician's discretion** IV in normal saline 50 mL over 15 minutes **1 hour** prior to glofitamab **Nursing Alert: glofitamab starts **1 hour after completion** of dexamethasone infusion*
glofitamab	30 mg	IV in normal saline 50 mL over 2 hours

*The dose of glofitmab 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 pre-treatment with oBINutuzumab, if glofitamab 2.5 mg dose is delayed by more than 1 week, then repeat pre-treatment with oBINutuzumab

Following glofitamab 2.5 mg or 10 mg dose, if there is a glofitamab treatment-free interval of 2 weeks to 6 weeks, then repeat the last tolerated glofitamab dose and resume the planned step-up dosing.

Following glofitamab 2.5 mg or 10 mg dose, if there is a glofitamab treatment-free interval of more than 6 weeks, then repeat pre-treatment with oBINutuzumab and glofitamab step-up dosing.

Following glofitamab 30 mg dose, if there is a glofitamab treatment-free interval of more than 6 weeks between cycles, then repeat pre-treatment with oBINutuzumab and glofitamab step-up dosing and then resume the planned treatment cycle (30 mg dose)

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

Hepatitis B serology

- Hepatitis B surface antigen and Hepatitis B core antibody (drawn within preceding 5 years)

Day of glofitamab and for two days after first three doses (Cycle 1, Days 8 to 10 and Cycle 2, Days 1 to 3)

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

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
Days 1, 8, 15

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin, glucose, LDH, uric acid, as per Physician Orders
- CRP and ferritin as per Physician Orders
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated
- Days 1 and 2: No observation period is required after oBINutuzumab administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

Cycle 2

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin, glucose, LDH and uric acid as per Physician Orders
- CRP and ferritin as per Physician Orders

Cycles 3 to 12

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

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
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)
- Patient needs to report any temperature over 38 degrees Celsius 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
- Remind patient to take recommended support medications at home
- valACYclovir and sulfamethoxazole-trimethoprim continue for 3 months after last dose of glofitamab is administered
- For cycles 1 and 2: Patient must remain located no greater than 1 hour from CancerCare Manitoba MacCharles site for 72 hours after glofitamab doses on cycle 1, Days 8 and 15 and cycle 2, Day 1

ADDITIONAL INFORMATION

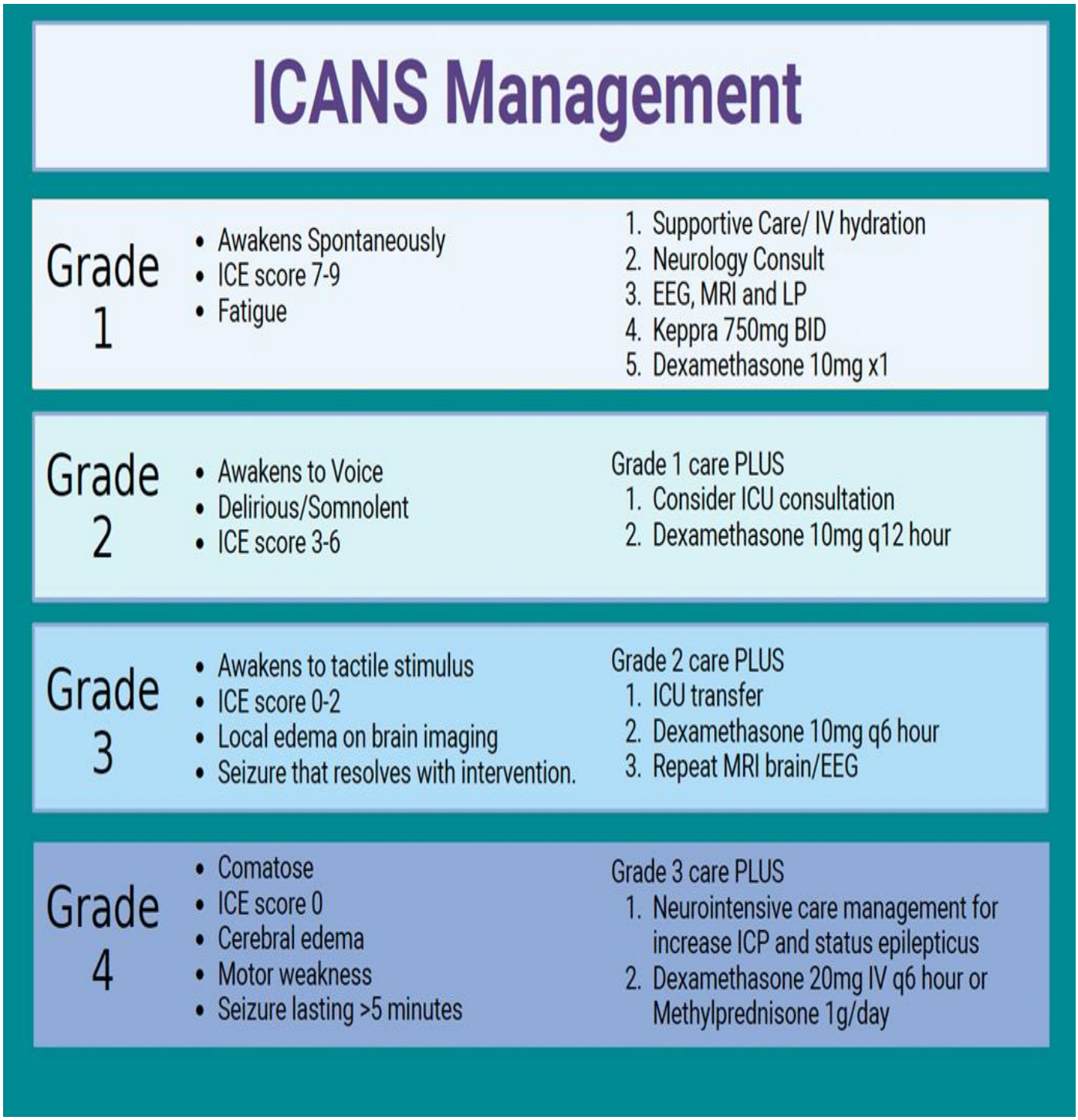
- glofitamab has been associated with Tumour Lysis Syndrome (TLS)
- glofitamab can cause tumor flare
- T-Cell Engagers can cause CRS and ICANS
- glofitamab treatment requires a dose of oBINutuzumab to be administered prior to the first glofitamab infusion as lymphodepletion to reduce risk of cytokine release syndrome (CRS)
- Due to the risk of reactivation of Hepatitis B virus (HBV) while on this treatment regimen, prescriber must adhere to CCMB Policy ***Hepatitis B Monitoring for Oncology and Hematology Patients*** for ordering and interpreting HBV serology and prescribing antiviral prophylaxis
- Administering nurse must document any infusion-related reactions with any dose of oBINutuzumab or glofitamab
- For cycle 1, Days 1 and 2, oBINutuzumab administration is 6 to 8 hours on average. Treatment should be booked for earliest morning appointment
- Administration site restrictions are in place for glofitamab. glofitamab must be administered at CCMB MacCharles or CCMB Tache in Winnipeg

Appendix "A" (adapted from 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