Regimen Reference Order

LYMP – R-ICE (SUBCUTANEOUS Injection or RAPID IV riTUXimab)

ARIA: LYMP – [R-ICE (SUBCUT @ Cycle #1)]

Planned Course: Every 21 days up to 6 cycles
Indication for Use: Relapsed/Refractory Non-Hodgkin Lymphoma

CVAD: At Provider's Discretion

Proceed with treatment if:

ANC equal to or greater than 1 x 10^9/L AND Platelets equal to or greater than 75 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
Instruct patient to start vigorous oral pre-hydration (600-900 mL) the morning of ifosfamide treatment **(Self-administered at home)**		
allopurinol	300 mg	Orally once daily for 10 days to begin 3 days prior to Cycle **(Self-administered at home)** Only patients at risk of tumor lysis syndrome will be prescribed allopurinol Note: allopurinol should not be prescribed beyond 10 days unless under the direction of the hematologist. See *Additional Information*

Treatment Regimen
LYMP – R-ICE (SUBCUTANEOUS Injection or RAPID IV riTUXimab)

Establish primary solution 500 mL of: normal saline

Drug	Hours of Administration	Dose	CCMB Administration Guideline
Day 1 – riTUXimab SUBCUTANEOUS Injection			
cetirizine	Minus 1 hours and 50 minutes	10 mg	Orally 30 minutes prior to riTUXimab
acetaminophen	minus 1 hours and 50 minutes	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	minus 1 hour and 50 minutes	12 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medication(s) before starting riTUXimab			

Drug	Hours of Administration	Dose	CCMB Administration Guideline
riTUXimab (Subcutaneous)	minus 1 hour and 20 minutes	1400 mg (1400 mg = 11.7 mL)	**Subcutaneous:** Administer over 5 minutes into abdomen Syringe should be held in hand for 5 minutes to warm up and decrease viscosity Use 25G needle **Alert: rapid infusion and subcutaneous route not to be used for riTUXimab naïve patients* **Nursing Alert: Ensure subcutaneous riTUXimab formulation is used (riTUXimab-hyaluronidase, human)*
normal saline	minus 1 hour and 15 minutes	500 mL	IV over 1 hour (Pre hydration)
ondansetron	minus 30 minutes	16 mg	Orally 30 minutes pre-chemotherapy
mesna	minus 15 minutes	333 mg/m^2	IV in normal saline 50 mL over 15 minutes Immediately prior to ifosfamide
ifosfamide	Hour 0	1667 mg/m^2	IV in normal saline 250 mL over 1 hour
CARBOplatin	Hour 1	AUC 5 mg/mL.min; maximum dose 750 mg (see table below)	IV in D5W 250 mL over 30 minutes
etoposide	Hour 1 and 30 minutes	100 mg/m^2	IV in normal saline 500 mL over 1 hour *Use non-DEHP bags and non-DEHP administration sets*
normal saline	Hour 2 and 30 minutes	500 mL	IV over 90 minutes (Post hydration)
mesna	Hour 4	333 mg/m^2	IV in normal saline 50 mL over 15 minutes
mesna	Hour 6	666 mg/m^2	Orally with juice or soft drink **(Self-administered at home)** **Nursing Alert: Inform patient time to take dose*
OR			
Day 1 - riTUXimab Rapid INTRAVENOUS Infusion			
cetirizine	Minus 3 hours and 15 minutes	10 mg	Orally 30 minutes prior to riTUXimab
acetaminophen	minus 3 hours and 15 minutes	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	minus 3 hours and 15 minutes	12 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medication(s) before starting riTUXimab			

Drug	Hours of Administration	Dose	CCMB Administration Guideline
riTUXimab (IV brand name specific)	minus 2 hours and 45 minutes	375 mg/m^2	**Rapid infusion**: IV in normal saline over 90 minutes Infuse 50 mL of a 250 mL bag (100 mL of a 500 mL bag) of the dose over 30 minutes, then infuse the remaining 200 mL (or 400 mL of a 500 mL bag) over 60 minutes **Alert: Ensure brand name on prescription label (indicated in brackets on prescription label) matches prescribed order* **Alert: rapid infusion and subcutaneous route not to be used for riTUXimab naïve patients* **Alert: Pharmacy to ensure final volume on label*
normal saline	minus 1 hour and 15 minutes	500 mL	IV over 1 hour (Pre hydration)
ondansetron	minus 30 minutes	16 mg	Orally 30 minutes pre-chemotherapy
mesna	minus 15 minutes	333 mg/m^2	IV in normal saline 50 mL over 15 minutes Immediately prior to ifosfamide
ifosfamide	Hour 0	1667 mg/m^2	IV in normal saline 250 mL over 1 hour
CARBOplatin	Hour 1	AUC 5 mg/mL.min; maximum dose 750 mg (see table below)	IV in D5W 250 mL over 30 minutes
etoposide	Hour 1 and 30 minutes	100 mg/m^2	IV in normal saline 500 mL over 1 hour *Use non-DEHP bags and non-DEHP administration sets*
normal saline	Hour 2 and 30 minutes	500 mL	IV over 90 minutes (Post hydration)
mesna	Hour 4	333 mg/m^2	IV in normal saline 50 mL over 15 minutes
mesna	Hour 6	666 mg/m^2	Orally with juice or soft drink **(Self-administered at home)** **Nursing Alert: Inform patient time to take dose*
Days 2 and 3			
normal saline	minus 1 hour and 15 minutes	500 mL	IV over 1 hour (Pre hydration)
ondansetron	minus 30 minutes	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	minus 30 minutes	12 mg	Orally 30 minutes pre-chemotherapy
mesna	minus 15 minutes	333 mg/m^2	IV in normal saline 50 mL over 15 minutes Immediately prior to ifosfamide

ifosfamide	Hour 0	1667 mg/m^2	IV in normal saline 250 mL over 1 hour **Alert: start of ifosfamide infusion will be considered "Hour 0"*
etoposide	Hour 1	100 mg/m^2	IV in normal saline 500 mL over 1 hour *Use non-DEHP bags and non-DEHP administration sets*
normal saline	Hour 2	500 mL	IV over 2 hours (Post hydration)
mesna	Hour 4	333 mg/m^2	IV in normal saline 50 mL over 15 minutes
mesna	Hour 6	666 mg/m^2	Orally with juice or soft drink **(Self-administered at home)** **Nursing Alert: Inform patient time to take dose*
All doses will be automatically rounded that fall within CCMB Approved Dose Bands. See Dose Banding document for more information			

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)

All Cycles

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

INTRAVENOUS riTUXimab

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated
- No observation period is required. Patient can be discharged from treatment room if stable whether they had a reaction or not

SUBCUTANEOUS riTUXimab

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline, at discharge and as clinically indicated
- **15-minute observation period required after each dose**

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
pegfilgrastim (brand name specific)	6 mg	Subcutaneous once on Day 6 **Alert: pegfilgrastim to be given as a single dose once per chemotherapy cycle no sooner than 24 hours after chemotherapy*
dexamethasone	8 mg	Orally once daily on Days 4 and 5
metoclopramide	10 – 20 mg	Orally every 4 hours as needed for nausea and vomiting

DISCHARGE INSTRUCTIONS

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Ensure patient receives pegfilgrastim supply if patient is self-administering at home
- Instruct patient to:
    - Self-administer "Hour 6" of mesna by mixing the contents of the mesna syringe in juice (not grapefruit) or soft drink. If patient vomits within 2 hours of taking "Hour 6" mesna, they should be advised to contact their cancer team. Patient may require intravenous hydration
    - Avoid grapefruit and grapefruit juice, Seville oranges (i.e. orange marmalade) and starfruit
    - Continue taking anti-emetic(s) at home
    - Report changes in mental status; ifosfamide can cause encephalopathy (rare)
    - Maintain oral intake of 2000 mL (8 glasses) of fluid daily at home
    - Empty bladder every 2 hours while awake and at bedtime for 24 hours after each dose of ifosfamide
    - Obtain immediate assistance as per your clinic's contact instructions if:
        - Symptoms of hemorrhagic cystitis (e.g. dysuria, hematuria)
        - Unable to drink recommended amount of fluid
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

ADDITIONAL INFORMATION

- 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
- Unless patient was taking allopurinol for gout or other reasons unrelated to the patient's underlying lymphoma, allopurinol should not be prescribed with cycle 2 and onwards unless directed by hematologist
- Administering nurse must document any infusion-related reactions with any dose of riTUXimab
- Ensure there were **no Grade 3 or 4** infusion-related reactions with any previous dose prior to administering riTUXimab via subcutaneous injection or rapid infusion
- Intravenous riTUXimab formulation is available from more than one manufacturer and uses several different brand names. Brand name will be indicated in brackets after riTUXimab. **Ensure prescription label matches the brand name on prescribed order for intravenous riTUXimab**
- CARBOplatin dose considerations:
    - CCMB Lymphoproliferative DSG uses **actual body weight** to calculate GFR
    - CCMB Lymphoproliferative DSG uses a maximum CARBOplatin dose of 750 mg for this regimen
    - If calculated CARBOplatin dose differs **more than 10%** from prescribed CARBOplatin dose, contact the prescriber

CARBOplatin Dosing Calculations per CCMB Lymphoproliferative DSG

Calculation of CARBOplatin dose: (max.750 mg)

Dose (mg) = target AUC (GFR + 25)

$$\text{GFR} = \frac{\text{N} \times (140 - \text{age in years}) \times \text{Actual Body Weight (kg)}}{\text{serum creatinine in umol/L}} = \_\_\_ \text{ mL/min}$$

N = 1.23 in males
N = 1.04 in females

$$\frac{\text{AUC (mg/mL.min)}}{5} \times \frac{\text{GFR + 25 (mL/min)}}{\_\_\_\_ + 25} = \text{Total Dose (mg)}$$

AUC= Area Under Curve

The estimated creatinine clearance is based on limited evidence. Sound clinical judgment and interpretation of the estimation are required, because the equation above may not be appropriate for some patient populations (for example, acute renal failure).