Regimen Reference Order – LYMP – R-ICE (Split Day SLOW IV riTUXimab)

ARIA: LYMP – [R-ICE (Split Day SLOW)]

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**

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 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 – R-ICE (Split Day SLOW IV riTUXimab)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Day 1		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
cetirizine	10 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	12 to 20 mg 20 mg for Cycle 1	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medication(s) before starting riTUXimab		
riTUXimab (IV brand name specific)	375 mg/m^2	**Slow infusion (if greater than 6 months since last riTUXimab dose or no previous riTUXimab):** IV made up to a final concentration of 1 mg/mL in normal saline. Start at 50 mg/hr for 60 minutes and escalate infusion rate in 50 mg/hr increments every 30 minutes to a maximum of 400 mg/hr **Nursing Alert: IV tubing is primed with riTUXimab* **Alert: Ensure brand name on prescription label (indicated in brackets on prescription label) matches prescribed order* **Alert: Pharmacy to ensure final volume on label*

		OR	
		<u>Slow infusion</u> (if equal to or less than 6 months since last riTUXimab dose): IV made up to a final concentration of 1 mg/mL in normal saline. Start at 100 mg/hr for 30 minutes and escalate infusion rate in 100 mg/hr increments every 30 minutes to a maximum of 400 mg/hr **Nursing Alert: IV tubing is primed with riTUXimab* **Alert: Ensure brand name on prescription label (indicated in brackets on prescription label) matches prescribed order* **Alert: Pharmacy to ensure final volume on label*	
Day 2			
Drug	**Hours of Administration**	**Dose**	**CCMB Administration Guideline**
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
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 3 and 4			
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
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

All Cycles

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

riTUXimab monitoring

- 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

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
pegfilgrastim (brand name specific) *(See Filgrastim Clinical Guide)*	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 5 and 6
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

- Administering nurse must document any infusion-related reactions with any dose of riTUXimab
- 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)***