Regimen Reference Order – LYMP – R-CODOX-M

ARIA: LYMP – [R-CODOX-M (age lt or equal to 65)]
LYMP – [R-CODOX-M (age greater than 65)]
LYMP – [R-CODOX-M (IT)]

Planned Course: **Every 21 days for 3 cycles (Note: Cycle 1 in hospital)**
AND
Intrathecal Therapy

Indication for Use: **Burkitt's Lymphoma (low risk)**

CVAD: At Provider's Discretion (VESICANT INVOLVED)

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 cyclophosphamide treatment **(Self-administered at home)**		
allopurinol	300 mg	Orally once daily for 10 days to begin 3 days prior to Cycle 1 **(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-CODOX-M (Outpatient)

Establish primary solution 500 mL of: normal saline

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

riTUXimab (Subcutaneous)	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)*
	OR	
riTUXimab (IV brand name specific)	375 mg/m^2	**Rapid infusion**: IV in normal saline over 90 minutes: Infuse 50 mL of a 250 mL bag (or 100 mL of a 500 mL bag) over 30 minutes, then infuse the remaining 200 mL (or 400 mL of a 500 mL bag) over 60 minutes **Alert: rapid infusion and subcutaneous route not to be used for riTUXimab naïve patients* **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
		Slow infusion: 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*
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
cyclophosphamide	800 mg/m^2	IV in normal saline 1000 mL over 2 hours
vinCRIStine	1.5 mg/m^2; maximum dose 2 mg	IV in normal saline 25 mL over 2 to 3 minutes by gravity infusion
DOXOrubicin	40 mg/m^2	IV Push over 10 to 15 minutes
Days 2 and 3		
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
cyclophosphamide	200 mg/m^2	IV in normal saline 1000 mL over 2 hours
Days 4 and 5		
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
cyclophosphamide	200 mg/m^2	IV in normal saline 1000 mL over 2 hours

Day 8		
vinCRIStine	1.5 mg/m^2; maximum dose 2 mg	IV in normal saline 25 mL over 2 to 3 minutes by gravity infusion
Day 10		
Patients will be admitted to hospital for high dose methotrexate (**See APPENDIX B** Inpatient – patients GREATER THAN 65 years old ***and*** **APPENDIX C** Inpatient – patients LESS THAN OR EQUAL to 65 years old)		

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

REQUIRED MONITORING (Outpatient)

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

Cardiac Monitoring
- Left Ventricular Ejection Fraction (LVEF) monitoring is recommended at baseline and as clinically indicated

All Cycles
- CBC, serum creatinine, urea, electrolytes, liver enzymes, LDH, total bilirubin, uric acid and albumin as per Physician Orders
- CBC prior to lumbar puncture

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

SUBCUTANEOUS riTUXimab
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) prior to each dose, 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 13 **Alert: pegfilgrastim to be given as a single dose once per chemotherapy cycle no sooner than 24 hours after chemotherapy*
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:
    - Continue taking anti-emetic(s) at home
    - 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 cyclophosphamide
    - 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

- Cycle 1 R-CODOX-M to be given in hospital
- Cycle 1 in ARIA refers to Cycle 1 of outpatient administration. Prescriber should order first cycle to be given as an outpatient as Cycle 1
- Patients will be admitted for the high dose methotrexate for all cycles (Day 10)
- Intrathecal therapy is part of regimen. See APPENDIX A Intrathecal Therapy (IT) Low Risk Patients
- Support protocol for intrathecal therapy is available under **R-CODOX-M (IT)** in the "Lymphoma" folder
- Refer to inpatient R-CODOX-M orders for supportive care medications and fluids given in hospital
- Refer to inpatient R-CODOX-M orders for required monitoring for methotrexate
- Cumulative DOXOrubicin dose should be calculated and should not exceed 450 mg/m^2
- 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**
- Administration site restrictions are in place for R-CODOX-M as per CCMB Drug Formulary. Administered only at CCMB MacCharles in Winnipeg

APPENDIX A

Intrathecal Therapy (IT) – LYMP – [R-CODOX-M (IT)]
Low Risk Patients

Proceed with treatment if:

Platelets equal to or greater than 50 x 10^9/L

- ❖ **Contact Physician if parameters not met**

Drug	Dose	CCMB Administration Guideline
Day 1 (Cycles 2 and 3 only)		
cytarabine	70 mg	Intrathecal in 6 mL preservative free normal saline
Day 3 (Cycles 2 and 3 only)		
cytarabine	70 mg	Intrathecal in 6 mL preservative free normal saline
Day 15 (Cycles 2 and 3 only)		
methotrexate	12 mg	Intrathecal in 6 mL preservative free normal saline

General Instructions:

- IT built as a separate cyclical support regimen with 2 cycles (21-day cycle)

APPENDIX B

Inpatient – patients GREATER THAN 65 years old

Drug	Dose
D5W with sodium bicarbonate	Sodium bicarbonate 100 mmol/L IV at 100 mL/m^2/hour starting at 1000 hours on Day 10 and continue until methotrexate level is less than 0.1 micromole/L Do not adjust IV rate during methotrexate infusion
methotrexate	100 mg/m^2 IV in D5W 250 mL over 1 hour starting at 1800 hours on Day 10 (total of 1 dose), followed immediately by the next methotrexate order Start and end infusion on time Start of methotrexate infusion = Hour 0
methotrexate	900 mg/m^2 IV in normal saline 1150 mL (final total volume) continuously over 23 hours starting immediately at 1900 hours immediately after methotrexate bolus infusion ends on Day 10 (total of 1 dose over 23 hours) Do not interrupt methotrexate infusion for other medications Adjust rate if necessary to ensure that infusion ends on time End of methotrexate infusion = Hour 24
leucovorin	15 mg/m^2 IV every 3 hours starting at 0600 hours on Day 12 (methotrexate hour 36) and continue until 1800 hours Day 12 (methotrexate hour 48) Doses must be given on time Total of 5 doses
leucovorin	15 mg/m^2 IV every 6 hours starting at 2400 hours on Day 12 (methotrexate hour 54) and continue until methotrexate level is less than or equal to 0.1 micromole/L Doses must be given on time

APPENDIX C

Inpatient – patients LESS THAN OR EQUAL to 65 years old

Drug	Dose
D5W with sodium bicarbonate	Sodium bicarbonate 100 mmol/L IV at 100 mL/m^2/hour starting at 1000 hours on Day 10 and continue until methotrexate level is less than 0.1 micromole/L Do not adjust IV rate during methotrexate infusion
methotrexate	300 mg/m^2 IV in D5W 250 mL over 1 hour starting at 1800 hours on Day 10 (total of 1 dose), followed immediately by the next methotrexate order Start and end infusion on time Start of methotrexate infusion = Hour 0
methotrexate	2700 mg/m^2 IV in normal saline 1150 mL (final total volume) continuously over 23 hours starting immediately at 1900 hours immediately after methotrexate bolus infusion ends on Day 10 (total of 1 dose over 23 hours) Do not interrupt methotrexate infusion for other medications Adjust rate if necessary to ensure that infusion ends on time End of methotrexate infusion = Hour 24
leucovorin	15 mg/m^2 IV every 3 hours starting at 0600 hours on Day 12 (methotrexate hour 36) and continue until 1800 hours Day 12 (methotrexate hour 48) Doses must be given on time Total of 5 doses
leucovorin	15 mg/m^2 IV every 6 hours starting at 2400 hours on Day 12 (methotrexate hour 54) and continue until methotrexate level is less than or equal to 0.1 micromole/L Doses must be given on time