Regimen Reference Order – LYMP – R-CODOX-M

ARIA: LYMP – [R-CODOX-M (age </= 65)]
LYMP – [R-CODOX-M (age > 65)]

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

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

CVAD: Preferred (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 Physician if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
allopurinol*	300 mg	Orally once daily for 10 days to begin 3 days prior to Cycle 1 (refer to inpatient orders for cycle 1) and at provider's discretion for subsequent cycles * Only patients at risk of tumor lysis syndrome will be prescribed allopurinol

Treatment Regimen – LYMP – R-CODOX-M (Outpatient)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Day 1		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	12 mg	IV in normal saline 50 mL over 15 minutes
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes
riTUXimab	1400 mg (1400 mg = 11.7 mL)	**Subcutaneous**: Administer over 5 minutes into abdomen Syringe should be held, in hand, at room temperature for 5 minutes to warm up and decrease viscosity Use 25G needle **Nursing Alert: Ensure subcutaneous riTUXimab formulation is used (riTUXimab-hyaluronidase, human)* **Alert: rapid infusion and subcutaneous route not to be used for riTUXimab naïve patients*
	OR	
	375 mg/m^2	**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 maximum of 400 mg/hr **Nursing Alert: IV tubing is primed with riTUXimab*

		OR **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 *Concentration dependent drug: Pharmacy will adjust diluent volume to ensure drug stability* **Alert: rapid infusion and subcutaneous route not to be used for riTUXimab naïve patients*
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
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
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)		

Flush after each medication:

- 50 mL over 6 minutes (500 mL/hr)

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

REQUIRED MONITORING (Outpatient)

All Cycles

- CBC, serum creatinine, urea, AST, ALT, total bilirubin, uric acid, sodium, potassium, calcium, albumin, magnesium, phosphate as per Physician Orders
- CBC prior to lumbar puncture

INTRAVENOUS riTUXimab

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

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
Grastofil® *(See Filgrastim Clinical Guide)*	5 mcg/kg (rounded to nearest 300 mcg or 480 mcg)	Subcutaneously once daily to start on Day 13 Discontinue when post-nadir ANC exceeds 1 x 10^9/L
ondansetron	8 mg	Orally once daily in the evening of days 1 to 5 then every 8 hours when needed for nausea and vomiting beginning day 6

DISCHARGE INSTRUCTIONS

- 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
  - 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
- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- 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 Low Risk Patients
- Refer to inpatient CODOX-M orders for supportive care medications and fluids given in hospital
- Refer to inpatient CODOX-M orders for required monitoring for methotrexate
- 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 the previous dose prior to administering riTUXimab via Rapid Infusion or Subcutaneous injection
- 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)
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 administered in LBMT Clinic
Day 3 (Cycles 2 and 3 only)		
cytarabine	70 mg	Intrathecal in 6 mL preservative free normal saline administered in LBMT Clinic
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
Day 10	
D5W with sodium bicarbonate	Sodium bicarbonate 100 mmol/L IV at 100 mL/m^2/hour on Day 10 and continue until methotrexate level is less than 0.1 micromole/L Do not adjust IV rate during methotrexate infusion
leucovorin	15 mg/m^2 IV every 3 hours starting 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 2400 hours 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
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

APPENDIX C

Inpatient – patients LESS THAN OR EQUAL to 65 years old

Drug	Dose
Day 10	
D5W with sodium bicarbonate	Sodium bicarbonate 100 mmol/L IV at 100 mL/m^2/hour on Day 10 and continue until methotrexate level is less than 0.1 micromole/L Do not adjust IV rate during methotrexate infusion
leucovorin	15 mg/m^2 IV every 3 hours starting 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 2400 hours 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
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