Regimen Reference Order – CLL – fludarabine + cyclophosphamide + riTUXimab

ARIA: CLL – [FCR]

Planned Course: Every 28 days for 6 cycles
Indication for Use: Chronic Lymphocytic Leukemia

CVAD: At Provider's Discretion

Proceed with treatment if:

Cycle 1

- ***Proceed regardless of blood counts***

Cycle 2 onwards

- ***ANC equal to or greater than 1 x 10^9/L AND Platelets equal to or greater than 50 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 and at provider's discretion for subsequent cycles * Only patients at risk of tumor lysis syndrome will be prescribed allopurinol

Treatment Regimen – CLL – fludarabine + cyclophosphamide + riTUXimab

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
Day 1		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	40 mg	IV in normal saline 50 mL over 15 minutes
diphenhydramine	50 mg	IV in normal saline 50 mL over 15 minutes
riTUXimab	375 mg/m^2	**Slow infusion:** 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 maximum of 400 mg/hr *Nursing Alert: IV tubing is primed with riTUXimab
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
fludarabine	25 mg/m^2	IV in normal saline 50 mL over 30 minutes
cyclophosphamide	250 mg/m^2	IV in normal saline 250 mL over 1 hour

Days 2 and 3		
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
fludarabine	25 mg/m^2	IV in normal saline 50 mL over 30 minutes
cyclophosphamide	250 mg/m^2	IV in normal saline 250 mL over 1 hour
Cycles 2 onwards		
Day 1		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	40 mg	IV in normal saline 50 mL over 15 minutes
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes
riTUXimab	1600 mg (1600 mg = 13.4 mL)	**Subcutaneous:** Administer **over 7 minutes** into abdomen Syringe should be held in hand for 5 minutes to warm up and decrease viscosity Use 25G needle **Nursing Alert: Ensure subcutaneous riTUXimab formulation is used (riTUXimab-hyaluronidase, human)*
	OR	
	500 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
fludarabine	25 mg/m^2	IV in normal saline 50 mL over 30 minutes
cyclophosphamide	250 mg/m^2	IV in normal saline 250 mL over 1 hour
Days 2 and 3		
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
fludarabine	25 mg/m^2	IV in normal saline 50 mL over 30 minutes
cyclophosphamide	250 mg/m^2	IV in normal saline 250 mL over 1 hour

All doses will be automatically rounded that fall within the DSG Approved Dose Bands or Agent Rounding. See LYMP DSG – Dose Banding document for more information

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

Day 1

- CBC, serum creatinine, BUN, AST, ALT, total bilirubin, uric acid, sodium, potassium, calcium, albumin, magnesium, phosphate as per Physician Orders

INTRAVENOUS riTUXimab

- Full vital signs (temperature, heart rate, blood pressure, respiration 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 had a reaction or not

SUBCUTANEOUS riTUXimab

- Full vital signs (temperature, heart rate, blood pressure, respiration 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
sulfamethoxazole-trimethoprim DS	800/160mg	Orally twice daily on Saturdays and Sundays only
valACYclovir	500 mg	Orally once daily
metoclopramide	10 – 20 mg	Orally every 4 – 6 hours as needed for nausea and vomiting

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
- Remind patient to take valACYclovir (shingles prophylaxis) and sulfamethoxazole-trimethoprim (*Pneumocystis jirovecii* pneumonia prophylaxis) at home
- 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

- Administering nurse must document any infusion-related reactions with any dose of riTUXimab
- Ensure there were **no Grade 3 or 4** infusion-related reaction with any previous dose prior to administering riTUXimab via Subcutaneous injection or Rapid Infusion
- Patients on fludarabine should receive irradiated blood products
- valACYclovir and sulfamethoxazole-trimethoprim DS continue during and for 12 months after completion of FCR due to risk of prolonged immunosuppression
- Note that this regimen has a higher riTUXimab dose Cycle 2 onwards