Regimen Reference Order – CLL – idelalisib + riTUXimab

ARIA: CLL – [idelalisib + riTUXimab]

Planned Course: **idelalisib until disease progression or unacceptable toxicity; riTUXimab every 2 weeks for 5 doses, then every 4 weeks for 3 doses (1 cycle = 28 days)**

Indication for Use: **Chronic Lymphocytic Leukemia Relapsed/Refractory**

CVAD: At Provider's Discretion

Proceed with treatment if:

Cycle 1, Day 1 ONLY

- ***ANC equal to or greater than 0.9 x 10^9/L AND Platelets equal to or greater than 75 x 10^9/L***
- ***AST/ALT equal to or less than 5 times the upper limit of normal***

Cycle 1, Day 15 onwards

- ***ANC equal to or greater than 0.5 X 10^9/L AND Platelets equal to or greater than 75 x 10^9/L***
- ***AST/ALT equal to or less than 5 times the upper limit of normal***
  - **Contact Hematologist 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 – idelalisib + riTUXimab

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
Days 1 to 28		
idelalisib	150 mg	Orally twice daily with or without food on **Days 1 to 28**. Swallow tablets whole **(Self-administered at home)**
Day 1 ONLY		
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: (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 maximum of 400 mg/hr **Nursing Alert: IV tubing is primed with riTUXimab* **Slow infusion: (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 maximum of 400 mg/hr **Nursing Alert: IV tubing is primed with riTUXimab*
Day 15 ONLY (SUBCUTANEOUS riTUXimab)		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	Orally 30 minutes prior to riTUXimab
diphenhydrAMINE	50 mg	Orally 30 minutes prior to riTUXimab
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		
Day 15 ONLY (INTRAVENOUS riTUXimab)		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes
riTUXimab	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*

Cycle 2 (SUBCUTANEOUS riTUXimab)		
Days 1 to 28		
idelalisib	150 mg	Orally twice daily with or without food on **Days 1 to 28**. Swallow tablets whole **(Self-administered at home)**

Days 1 and 15 ONLY		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	Orally 30 minutes prior to riTUXimab
diphenhydrAMINE	50 mg	Orally 30 minutes prior to riTUXimab
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		
Cycle 2 (INTRAVENOUS riTUXimab)		
Days 1 and 15 ONLY		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes
riTUXimab	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*
Cycles 3 to 6 (SUBCUTANEOUS riTUXimab)		
Days 1 to 28		
idelalisib	150 mg	Orally twice daily with or without food on **Days 1 to 28**. Swallow tablets whole **(Self-administered at home)**
Day 1 ONLY		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	Orally 30 minutes prior to riTUXimab
diphenhydrAMINE	50 mg	Orally 30 minutes prior to riTUXimab
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)*

Cycles 3 to 6 (INTRAVENOUS riTUXimab)		
Day 1 ONLY		
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes
riTUXimab	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*
Cycle 7 onwards		
idelalisib	150 mg	Orally twice daily with or without food on **Days 1 to 28**. Swallow tablets whole **(Self-administered at home)**
idelalisib (Zydelig®) available dosage strengths: 100 mg, 150 mg tablets **Classification: Non-Hazardous**		
All doses will be automatically rounded that fall within the DSG Approved Dose Bands. 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

Throughout treatment

- Hepatitis B serology and Hemoglobin A1C at baseline
- CMV via PCR at baseline and to be performed once monthly while on idelalisib. If patient is experiencing symptoms of CMV viremia, then CMV via PCR should be monitored more frequently (i.e. once weekly)

Cycles 1 to 6

Each riTUXimab dose

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

Cycle 7 onwards (idelalisib only)

Each cycle

- CBC, serum creatinine, glucose, 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

DISCHARGE INSTRUCTIONS

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Remind patient to take idelalisib at home. idelalisib is continued daily throughout treatment until disease progression or unacceptable toxicity (continued after riTUXimab is complete)
- Remind patient to take valACYclovir (shingles prophylaxis) and sulfamethoxazole-trimethoprim (*Pneumocystis jirovecii* pneumonia prophylaxis) at home

ADDITIONAL INFORMATION

- Patient should report severe diarrhea, shortness of breath or rash to clinic
- valACYclovir and sulfamethoxazole-trimethoprim continue while on treatment and for 6 months after discontinuation of treatment
- 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 Rapid Infusion or Subcutaneous injection
- Note that this regimen has a higher riTUXimab dose 2 onwards
- idelalisib will be dispensed by CCMB Pharmacy