Regimen Reference Order – CLL – idelalisib + riTUXimab

ARIA: CLL – [idelalisib + riTUXimab]

Planned Course: **idelalisib until disease progression or unacceptable toxicity AND 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 and 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**

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
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 – 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 Swallow whole **(Self-administered at home)**
Day 1 ONLY		
cetirizine	10 mg	Orally 30 minutes prior to riTUXimab
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab

dexamethasone	40 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medications before starting riTUXimab		
riTUXimab (IV brand name specific)	375 mg/m^2	**<u>Slow infusion</u> (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 15 ONLY (SUBCUTANEOUS riTUXimab)		
cetirizine	10 mg	Orally 30 minutes prior to riTUXimab
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	Orally 30 minutes prior to riTUXimab
riTUXimab (Subcutaneous)	1600 mg (1600 mg = 13.4 mL)	**<u>Subcutaneous</u>:** 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)		
cetirizine	10 mg	Orally 30 minutes prior to riTUXimab
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes
riTUXimab (IV brand name specific)	500 mg/m^2	**<u>Rapid infusion</u>**: 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: 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*

Cycle 2 (SUBCUTANEOUS riTUXimab)		
Days 1 to 28		
idelalisib	150 mg	Orally twice daily with or without food Swallow whole **(Self-administered at home)**
Days 1 and 15 ONLY		
cetirizine	10 mg	Orally 30 minutes prior to riTUXimab
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	Orally 30 minutes prior to riTUXimab
riTUXimab (Subcutaneous)	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 to 28		
idelalisib	150 mg	Orally twice daily with or without food Swallow whole **(Self-administered at home)**
Days 1 and 15 ONLY		
cetirizine	10 mg	Orally 30 minutes prior to riTUXimab
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medications before starting riTUXimab		
riTUXimab (IV brand name specific)	500 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: 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*

Cycles 3 to 6 (SUBCUTANEOUS riTUXimab)		
Days 1 to 28		
idelalisib	150 mg	Orally twice daily with or without food Swallow whole **(Self-administered at home)**
Day 1 ONLY		
cetirizine	10 mg	Orally 30 minutes prior to riTUXimab
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	Orally 30 minutes prior to riTUXimab
riTUXimab (Subcutaneous)	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)		
Days 1 to 28		
idelalisib	150 mg	Orally twice daily with or without food Swallow whole **(Self-administered at home)**
Day 1 ONLY		
cetirizine	10 mg	Orally 30 minutes prior to riTUXimab
acetaminophen	650 mg	Orally 30 minutes prior to riTUXimab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes
Wait 30 minutes after completion of IV pre-medications before starting riTUXimab		
riTUXimab (IV brand name specific)	500 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: 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*
Cycle 7 and Onwards		
Days 1 to 28		
idelalisib	150 mg	Orally twice daily with or without food Swallow whole **(Self-administered at home)**
idelalisib (ZYDELIG®) available dosage strengths: 100 mg, 150 mg tablets **Classification: Non-Cytotoxic, Hazardous**		
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

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

Throughout treatment
- Hemoglobin A1C at baseline
- CMV via PCR at baseline and 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 and 2
Days 1 and 15
- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, glucose, uric acid and albumin as per Physician Orders

Cycle 3 and Onwards
Day 1
- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, glucose, uric acid and albumin as per Physician Orders

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 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
sulfamethoxazole-trimethoprim	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
- Instruct patient to report severe diarrhea, shortness of breath or rash to clinic
- idelalisib is a cancer therapy in this treatment regimen. 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 support medications at home

ADDITIONAL INFORMATION

- 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
- valACYclovir (shingles prophylaxis) and sulfamethoxazole-trimethoprim (*Pneumocystis jirovecii* pneumonia prophylaxis) 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 reactions with any previous dose prior to administering riTUXimab via subcutaneous injection or rapid infusion
- Note that this regimen has a higher riTUXimab dose Cycle 1 Day 15 onwards
- 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**
- idelalisib will be dispensed by CCMB Pharmacy