Regimen Reference Order – CLL – oBINutuzumab + chlorambucil

ARIA: CLL – [oBINutuzumab + chlorambucil]

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

CVAD: At Provider's Discretion

Proceed with treatment if:

Day 1 of Cycle 1 ONLY

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

Day 1 and Day 15 of Each Cycle

- ***ANC equal to or greater than 1 x 10^9/L***
- ***Platelets decrease less than 50% from pre-treatment value (prior to Cycle 1, Day 1)***
  - ❖ **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 **(Self-administered at home)** *Only patients at risk of tumor lysis syndrome will be prescribed allopurinol

Treatment Regimen – CLL – oBINutuzumab + chlorambucil

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
Day 1		
cetirizine	10 mg	Orally 1 hour prior to oBINutuzumab
acetaminophen	650 mg	Orally 1 hour prior to oBINutuzumab
dexamethasone	40 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to oBINutuzumab **Nursing Alert: oBINutuzumab starts **1 hour after completion** of dexamethasone infusion*
Wait 1 hour after completion of IV pre-medication(s) before starting oBINutuzumab		
oBINutuzumab	100 mg	IV in normal saline 100 mL following administration rates below:

		• 0 to 60 minutes – 6 mL/hour • 60 to 120 minutes – 12 mL/hour • 120 minutes onwards – 24 mL/hour * *Alert: Pharmacy to ensure final volume in bag= 100 mL (1 mg/mL final concentration)* **Nursing Alert: IV tubing is primed with oBINutuzumab*
chlorambucil	0.25 mg/kg	Orally once on an empty stomach Swallow whole **(Self-administered at home)**
Day 2		
cetirizine	10 mg	Orally 1 hour prior to oBINutuzumab
acetaminophen	650 mg	Orally 1 hour prior to oBINutuzumab
dexamethasone	40 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to oBINutuzumab **Nursing Alert: oBINutuzumab starts **1 hour after completion** of dexamethasone infusion*
Wait 1 hour after completion of IV pre-medication(s) before starting oBINutuzumab		
oBINutuzumab	900 mg	IV in normal saline 250 mL following administration rates below: • 0 to 30 minutes – 14 mL/hour • 30 to 60 minutes – 28 mL/hour • 60 to 90 minutes – 42 mL/hour • 90 to 120 minutes – 56 mL/hour • 120 to 150 minutes – 69 mL/hour • 150 to 180 minutes – 83 mL/hour • 180 to 210 minutes – 97 mL/hour • 210 to 240 minutes – 111 mL/hour **Alert: Pharmacy to ensure final volume in bag = 250 mL (3.6 mg/mL final concentration)* **Nursing Alert: IV tubing is primed with oBINutuzumab*
Day 8		
cetirizine	10 mg	Orally 30 minutes prior to oBINutuzumab
acetaminophen	650 mg	Orally 30 minutes prior to oBINutuzumab
dexamethasone	20 mg	**ONLY** to be given if patient had a grade 3 or 4 infusion-related reaction with their previous oBINutuzumab infusion or if their lymphocyte count prior to Day 1 of current cycle was greater than 25 X 10^9/L. IV in normal saline 50 mL over 15 minutes **1 hour** prior to oBINutuzumab **Nursing Alert: oBINutuzumab starts **1 hour after completion** of dexamethasone infusion*
If applicable, wait 1 hour after completion of IV pre-medication(s) before starting oBINutuzumab		
oBINutuzumab	1000 mg	**Slow Infusion:** IV in normal saline 250 mL following

		administration rates below: • 0 to 30 minutes – 25 mL/hour • 30 to 60 minutes – 50 mL/hour • 60 to 90 minutes – 75 mL/hour • 90 minutes onwards – 100 mL/hour *Alert: Pharmacy to ensure final volume in bag = 250 mL (4 mg/mL final concentration)* *Nursing Alert: IV tubing is primed with oBINutuzumab*
Day 15		
cetirizine	10 mg	Orally 30 minutes prior to oBINutuzumab
acetaminophen	650 mg	Orally 30 minutes prior to oBINutuzumab
dexamethasone	20 mg	**ONLY** to be given if patient had a grade 3 or 4 infusion-related reaction with their previous oBINutuzumab infusion or if their lymphocyte count prior to Day 1 of current cycle was greater than 25 X 10^9/L. IV in normal saline 50 mL over 15 minutes **1 hour** prior to oBINutuzumab *Nursing Alert: oBINutuzumab starts **1 hour after completion** of dexamethasone infusion*
If applicable, wait 1 hour after completion of IV pre-medication(s) before starting oBINutuzumab		
oBINutuzumab	1000 mg	**Slow Infusion:** IV in normal saline 250 mL following administration rates below: • 0 to 30 minutes – 25 mL/hour • 30 to 60 minutes – 50 mL/hour • 60 to 90 minutes – 75 mL/hour • 90 minutes onwards – 100 mL/hour *Alert: Pharmacy to ensure final volume in bag= 250 mL (4 mg/mL final concentration)* *Nursing Alert: IV tubing is primed with oBINutuzumab*
chlorambucil	0.25 mg/kg	Orally once on an empty stomach Swallow whole **(Self-administered at home)**
Cycles 2 to 6		
Day 1		
cetirizine	10 mg	Orally 30 minutes prior to oBINutuzumab
acetaminophen	650 mg	Orally 30 minutes prior to oBINutuzumab
dexamethasone	20 mg	**ONLY** to be given if patient had a grade 3 or 4 infusion-related reaction with their previous oBINutuzumab infusion or if their lymphocyte count prior to Day 1 of current cycle was greater than 25 X 10^9/L. IV in normal saline 50 mL over 15 minutes **1 hour** prior to oBINutuzumab *Nursing Alert: oBINutuzumab starts **1 hour after completion** of dexamethasone infusion*

If applicable, wait 1 hour after completion of IV pre-medication(s) before starting oBINutuzumab		
oBINutuzumab	1000 mg	**Rapid Infusion:** IV in normal saline 250 mL following administration rates below: • 0 to 30 minutes – 25 mL/hour • 30 to 93 minutes – 225 mL/hour *Alert: Pharmacy to ensure final volume in bag = 250 mL (4 mg/mL final concentration)* *Nursing Alert: IV tubing is primed with oBINutuzumab*
		OR
		Slow Infusion: IV in normal saline 250 mL following administration rates below: • 0 to 30 minutes – 25 mL/hour • 30 to 60 minutes – 50 mL/hour • 60 to 90 minutes – 75 mL/hour • 90 minutes onwards – 100 mL/hour *Alert: Pharmacy to ensure final volume in bag = 250 mL (4 mg/mL final concentration)* *Nursing Alert: IV tubing is primed with oBINutuzumab*
chlorambucil	0.25 mg/kg to 0.5 mg/kg	Orally once on an empty stomach Swallow whole **(Self-administered at home)** Dose may be increased to 0.5 mg/kg **at Cycle 2 at physician's discretion**
Day 15		
chlorambucil	0.25 mg/kg to 0.5 mg/kg	Orally once on an empty stomach Swallow whole **(Self-administered at home)** Dose may be increased to 0.5 mg/kg **at Cycle 2 at physician's discretion**
chlorambucil (Leukeran®) available dosage strength: 2 mg tablets **Classification: Cytotoxic, Hazardous**		

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

REQUIRED MONITORING

Day 1

- CBC, serum creatinine, urea, electrolytes, liver enzymes, LDH, total bilirubin, uric acid and albumin as per Physician Orders

Day 15

- CBC as per Physician Orders

Cycle 1, Day 1 Only - oBINutuzumab

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated

- No observation period is required after oBINutuzumab administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
ondansetron	8 mg	Orally 30 minutes prior to chlorambucil on Days 1 and 15
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
- Instruct patient to continue taking anti-emetic(s) at home
- chlorambucil is a cancer therapy in this treatment regimen. Remind patient to take chlorambucil at home (Days 1 and 15)
- chlorambucil is stored in the refrigerator
- 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 oBINutuzumab
- Ensure there were **no Grade 3 or 4** infusion-related reactions with the three preceding infusions prior to administering oBINutuzumab via rapid infusion. Patients will be switched to rapid infusion at Cycle 2, Day 1 if lymphocyte count is less than 5 x 10^9/L
- **Note: For Cycles 2 to 6**, an entry called "***Physician Reminder – oBINutuzumab infusion time 1 Units Insert Miscellaneous once"*** will appear in the electronic drug order. No action is required. **This prompt is to remind the prescriber to confirm that patient is eligible for oBINutuzumab rapid infusion**
- For Cycle 1, Days 1 and 2, oBINutuzumab administration is 6 to 8 hours on average. Treatment should be booked for earliest morning appointment
- Administration site restrictions are in place for oBINutuzumab as per CCMB Drug Formulary. Cycle 1, Days 1 and 2 must be administered at CCMB MacCharles or Tache in Winnipeg