Regimen Reference Order – LEUK – azaCITIDine + venetoclax

ARIA: LEUK – [azaCITIDine + venetoclax]

Planned Course: **Every 28 days until disease progression or unacceptable toxicity**
Indication for Use: **Acute Myeloid Leukemia**

CVAD: At Provider's Discretion

Proceed with treatment if:

Cycle 1

- ***WBC less than or equal to 11 x 10^9/L***
- ***Creatinine clearance equal to or greater than 30 mL/minute***
- ***AST/ALT and total bilirubin less than 3 times upper limit of normal***
- ***Potassium less than 5 mmoL/L***
- ***Corrected calcium less than 2.6 mmol/L***
- ***Phosphate less than 1.5 mmol/L***

Cycle 2 and Onwards

- ***ANC equal to or greater than 0.5 x 10^9/L AND Platelets equal to or greater than 50 x 10^9/L***
- ***On Day 1, proceed with azaCITIDine only when venetoclax starts***
  - ❖ **Contact Leukemia DSG Physician if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Patient to drink 1.75 litres of water per day: • **Starting two days prior to starting venetoclax until end of Cycle 1, Day 4** **Alert: Contact physician if patient did not follow hydration as directed*		
allopurinol	300 mg	Orally once daily to begin 3 days prior to Cycle 1 and continue once daily until Cycle 1, Day 11 and at provider's discretion for subsequent cycles **(Self-administered at home)**

Treatment Regimen – LEUK – azaCITIDine + venetoclax

Drug	Dose	CCMB Administration Guideline
Cycle 1		
Day 1		
venetoclax*	100 mg	Orally once in the morning with food Swallow whole **Alert: venetoclax should be taken at 6:00 a.m.* **Alert: Post-dose biochemistry must be drawn 6 to 8 hours following venetoclax dose* *Do not proceed to next dose without confirmation and review of blood work* **(Self-administered at home)**
ondansetron	8 mg	Orally 30 minutes prior to azaCITIDine
azaCITIDine	75 mg/m^2	Subcutaneous into abdomen **Alert: Maximum volume at each injection site is 4 mL* **Nursing Alert: Air sandwich technique is recommended for administration*
Day 2		
venetoclax*	**If patient is on voriconazole or other azole:** 100 mg **If patient is not on voriconazole or other azole:** 200 mg	Orally once in the morning with food Swallow whole **Alert: venetoclax should be taken at 6:00 a.m.* **Alert: Post-dose biochemistry must be drawn 6 to 8 hours following venetoclax dose* *Do not proceed to next dose without confirmation and review of blood work* **(Self-administered at home)**
ondansetron	8 mg	Orally 30 minutes prior to azaCITIDine
azaCITIDine	75 mg/m^2	Subcutaneous into abdomen **Alert: Maximum volume at each injection site is 4 mL* **Nursing Alert: Air sandwich technique is recommended for administration*
Days 3 to 7		
venetoclax*	**If patient is on voriconazole or other azole:** 100 mg **If patient is not on voriconazole or other azole:** 400 mg	Orally once daily in the morning with food Swallow whole **Alert: On Days 3 and 4, venetoclax should be taken at 6:00 a.m.* **Alert: Post-dose biochemistry must be drawn 6 to 8 hours following Days 3 and 4 venetoclax dose only. Do not proceed to next dose without confirmation and review of blood work* **(Self-administered at home)**
ondansetron	8 mg	Orally 30 minutes prior to each dose of azaCITIDine

azaCITIDine	75 mg/m^2	Subcutaneous into abdomen **Alert: Maximum volume at each injection site is 4 mL* **Nursing Alert: Air sandwich technique is recommended for administration*
Days 8 to 28		
venetoclax*	**If patient is on voriconazole or other azole:** 100 mg	Orally once daily in the morning with food Swallow whole **(Self-administered at home)**
	If patient is not on voriconazole or other azole: 400 mg	
Cycle 2 and Onwards		
Days 1 to 7		
venetoclax*	**If patient is on voriconazole or other azole:** 100 mg	Orally once daily in the morning with food Swallow whole **(Self-administered at home)**
	If patient is not on voriconazole or other azole: 400 mg	
ondansetron	8 mg	Orally 30 minutes prior to each dose of azaCITIdine
azaCITIDine	75 mg/m^2	Subcutaneous into abdomen **Alert: Maximum volume at each injection site is 4 mL* **Nursing Alert: Air sandwich technique is recommended for administration*
Days 8 to 28		
venetoclax*	**If patient is on voriconazole or other azole:** 100 mg	Orally once daily in the morning with food Swallow whole **(Self-administered at home)**
	If patient is not on voriconazole or other azole: 400 mg	

**voriconazole increases the exposure of venetoclax. If voriconazole is discontinued, venetoclax dose should be increased only after a specified number of days at the discretion of the hematologist.*

venetoclax dose modifications will occur at the Leukemia DSG physician's discretion for cytopenias and drug-drug interactions.

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

venetoclax (VENCLEXTA®) available dosage strengths: 10 mg, 50 mg and 100 mg tablets
Classification: Cytotoxic, Hazardous

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

REQUIRED MONITORING

Baseline
- CBC, serum creatinine, urea, electrolytes, liver enzymes, LDH and albumin as per Physician Orders
- HIV and Hepatitis B and C serology
- EKG at physician's discretion

Cycle 1
Days 1, 2, 3, 4, 8, 15, 22
- CBC, serum creatinine, urea, electrolytes, liver enzymes, LDH and albumin as per Physician Orders

**Alert: Days 1 to 4: blood work must be done 6 to 8 hours post venetoclax*

Cycles 2 and 3
- CBC, serum creatinine, urea, electrolytes, liver enzymes, LDH and albumin as per Physician Orders

Cycle 4 and Onwards
- CBC, serum creatinine, urea, electrolytes, liver enzymes, LDH and albumin as per Physician Orders

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
levoFLOXacin	500 mg	Orally once daily
valACYclovir	500 mg	Orally twice daily
voriconazole	200 mg	Orally twice daily on an empty stomach Prescribed at physician's discretion for antifungal prophylaxis
sennosides-docusate sodium (8.6/50 mg) (Senokot-S®)	2 tablets	Orally at bedtime as needed for constipation
polyethylene glycol 3350 (RestoraLAX®)	17 g	Orally once daily as needed for constipation

DISCHARGE INSTRUCTIONS

- Instruct patient to drink 1.75 litres of water per day:
  - Two days prior to starting venetoclax
  - First four days of venetoclax
- venetoclax tablets should be swallowed whole. Do not spit, crush or chew
- Instruct patient to report to clinic if they are experiencing injection site reactions that are bothersome
- Remind patient to take supportive medications at home
- Patients should notify clinic prior to starting any new medication. venetoclax has potential for drug-drug interactions
- Avoid grapefruit and grapefruit juice, Seville oranges (i.e. orange marmalade) and starfruit
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

ADDITIONAL INFORMATION

- If patient is considered at moderate to high risk for tumor lysis at the physician's discretion, the following additions may be required:
  - rasburicase (7.5 mg dose) prior to starting venetoclax
  - IV hydration
- If rasburicase is required, follow rasburicase protocol (i.e. blood specimen must be put on ice). Refer to *Diagnostic Services of Manitoba Lab Information Manual* for further information
- Due to limited room temperature stability, azaCITIDine MUST be stored in the fridge until immediately prior to administration. DO NOT store at room temperature unless otherwise indicated by pharmacy
- venetoclax dosing in this regimen varies from the dosing in chronic lymphocytic leukemia protocols
- venetoclax may only be prescribed and dispensed by physicians and pharmacists who are registered with and adhere to the guidelines of the AbbVie distribution Program
- Administration site restrictions are in place for Cycle 1 of this regimen, as the patient must come for blood work monitoring at CCMB MacCharles site
- venetoclax will be dispensed by CCMB Pharmacy