

Regimen Reference Order – LEUK – AL4 (Intensification - DOXOrubicin)

ARIA: LEUK - [AL4 (Intens - DOXOrubicin)]

Planned Course: 1 cycle = 21 days (maximum of 7 cycles*)

Indication for Use: Acute Lymphoblastic Leukemia

CVAD: Preferred (VESICANT INVOLVED)

Proceed with treatment if:

Cycle 1 Day 1

- ANC equal to or greater than $1 \times 10^9/L$ AND Platelets equal to or greater than $100 \times 10^9/L$
- AST less than 8 times the upper limit of normal
- Direct bilirubin less than 25 micromol/L
- calaspargase pegol is given independent of the above starting criteria as long as direct bilirubin is less than 50 micromol/L and fibrinogen is less than 0.5 g/L
 - ❖ Contact Leukemia/BMT (L/BMT) Physician 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
Not Applicable		

Treatment Regimen – LEUK – AL4 (Intensification - DOXOrubicin)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
dexamethasone	18 mg/m ² /day (round to nearest 2 mg)	Orally divided twice a day with food on Days 1 to 5 (Self-administered at home)
mercaptopurine	50 mg/m ² (round to nearest 25 mg)	Orally once daily on an empty stomach on Days 1 to 14 Do not take with milk or milk-based products (Self-administered at home)

Day 1 ONLY

ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
vinCRISine	2 mg (standard dose)	IV in normal saline 25 mL over 2 to 3 minutes by gravity infusion
DOXOrubicin	30 mg/m ²	IV push over 10 minutes

famotidine	40 mg	Orally 1 hour prior to calaspargase pegol
cetirizine	20 mg	Orally 1 hour prior to calaspargase pegol
acetaminophen	650 mg	Orally 1 hour prior to calaspargase pegol
hydrocortisone	100 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to calaspargase pegol <i>*Nursing Alert: calaspargase pegol starts 1 hour after completion of hydrocortisone</i>
Wait 1 hour after completion of IV pre-medication(s) before starting calaspargase pegol		
calaspargase pegol	1000 units/m ² ; maximum dose 1875 units	IV in normal saline 100 mL over 1 hour
* LEUK - [AL4 (Intens - DOXOrubicin)] is built as 7 cycles assuming an initial cumulative DOXOrubicin = 90 mg/m ² (60 mg/m ² during induction plus 30 mg/m ² during CNS phase)		
Patients will receive Triple Intrathecal Therapy every 18 weeks while receiving intensification therapy Patient is placed on support regimen – LEUK - [AL4 (IT)] beginning with CNS phase which occurs every 126 days = 18 weeks). Intrathecal is given at the start of treatment cycles where possible See Appendix A – Intrathecal Therapy (IT)		
mercaptopurine available dosage strength: 50 mg tablets Classification: Cytotoxic, Hazardous		

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)

Cardiac monitoring

- Left Ventricular Ejection Fraction (LVEF) monitoring is recommended at baseline and as clinically indicated

All Cycles

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin and glucose as per Physician Orders
- Glucose and lipase as per Physician Orders
- Fibrinogen as per Physician Orders
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O₂ saturation) at baseline and as clinically indicated during calaspargase pegol administration
- Observe patient for 1 hour after administration of calaspargase pegol. Full vital signs prior to discharge

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
sulfamethoxazole-trimethoprim	800/160mg	Orally twice daily on Saturdays and Sundays only

DISCHARGE INSTRUCTIONS

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Remind patient to take sulfamethoxazole-trimethoprim (*Pneumocystis jirovecii* pneumonia prophylaxis) at home
- mercaptopurine should not be taken at the same time as milk or milk-based products. Cow's milk in particular, contains high concentrations of xanthine oxidase which inactivates mercaptopurine
- Reinforce safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

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
- If HBV serology results are positive, patient is prescribed antiviral prophylaxis (usually tenofovir 300 mg orally once daily) during treatment and continued until 6 to 12 months after last dose of treatment
- Physician or designate must be on site in case of reactions to calaspargase pegol
 - Do not administer on weekends or holidays
- calaspargase pegol can cause anaphylaxis. cetirizine, hydrocortisone and EPINEPHrine must be available in case of reaction
- calaspargase pegol can cause serious side effects such as hemorrhage, pancreatitis and thrombotic events
- Dose adjustments are made to mercaptopurine to achieve a desired nadir ANC of $0.5 \times 10^9/L$ to $0.75 \times 10^9/L$ and platelets of $75 \times 10^9/L$ to $100 \times 10^9/L$
- calaspargase pegol dose reduction is recommended for patients with fatty liver or BMI over 30 kg/m^2 (dose reduce to calaspargase pegol 500 units/m^2)
- If patient has recurrent mouth sores, they may be evaluated for HSV and considered for valACYclovir prophylaxis
- LEUK - [AL4 (Intens - DOXOrubicin)] is built as 7 cycles assuming an initial cumulative DOXOrubicin = 90 mg/m^2 (60 mg/m^2 during induction plus 30 mg/m^2 during CNS phase). Adjust the number of cycles at the beginning of this regimen to achieve a cumulative lifetime DOXOrubicin dose of 300 mg/m^2 or until 9 months post complete remission date
- Intrathecal therapy is part of this regimen and is given every 18 weeks. See *Appendix A*

APPENDIX A

Intrathecal Therapy (IT) – LEUK - [AL4 (IT)]	
<p>Planned course: Every 18 weeks from the beginning of CNS Phase. Continue until the completion of AL4 (Continuation)</p>	
<p><i>Proceed with treatment if:</i> <i>ANC equal to or greater than $0.5 \times 10^9/L$ AND Platelets equal to or greater than $50 \times 10^9/L$</i> ❖ Contact L/BMT Physician if parameters not met</p>	
Drug and Dose	CCMB Administration Guideline
Every 18 weeks (Starting with beginning of CNS phase)	
<p><u>Triple Intrathecal:</u> methotrexate 12 mg cytarabine 40 mg hydrocortisone 50 mg</p>	<p>Intrathecal in 6 mL preservative free normal saline administered in L/BMT Clinic</p>
<p>IT is ordered as a separate cyclical Support regimen LEUK - [AL4 (IT)]</p>	