

# 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
- pegaspargase is given independent of the above starting criteria as long as direct bilirubin is less than 50 micromol/L and fibrinogen is greater than or equal to 0.5 g/L
- ❖ Contact Leukemia/BMT (L/BMT) Physician if parameters not met

## 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 <sup>2</sup> /day (round to nearest 2 mg)	Orally divided twice a day with food on <b>Days 1 to 5</b> <b>(Self-administered at home)</b>
mercaptopurine	50 mg/m <sup>2</sup> (round to nearest 25 mg)	Orally once daily on an empty stomach <b>on Days 1 to 14</b> Do not take with milk or milk-based products <b>(Self-administered at home)</b>

**Day 1 ONLY**

ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
vinCRISStine	2 mg (standard dose)	IV in normal saline 25 mL over 2 to 3 minutes by gravity infusion
DOXOrubicin	30 mg/m <sup>2</sup>	IV push over 10 minutes
acetaminophen	650 mg	Orally <b>1 hour</b> prior to pegaspargase

hydrocortisone	100 mg	IV in normal saline 50 mL over 15 minutes <b>1 hour</b> prior to pegaspargase <i>*Nursing Alert: pegaspargase starts 1 hour after completion of hydrocortisone</i>
famotidine	20 mg	IV in normal saline 50 mL over 15 minutes
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes
<b>Wait 30 minutes after completion of IV pre-medication(s) before starting pegaspargase</b>		
pegaspargase	1000 units/m <sup>2</sup> ; 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 <sup>2</sup> (60 mg/m <sup>2</sup> during induction plus 30 mg/m <sup>2</sup> during CNS phase)		
Patients will receive Triple Intrathecal Therapy every 18 weeks while receiving intensification therapy <b>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</b> <b>See Appendix A – Intrathecal Therapy (IT)</b>		
mercaptopurine (PURINETHOL®) 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

### Baseline

- Hepatitis B serology

### 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 O<sub>2</sub> saturation) at baseline and as clinically indicated during pegaspargase administration
- Observe patient for 1 hour after administration of pegaspargase. 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

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## DISCHARGE INSTRUCTIONS

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- 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

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## ADDITIONAL INFORMATION

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- Physician or designate must be on site in case of reactions to pegaspargase
  - Do not administer on weekends or holidays
- pegaspargase can cause anaphylaxis. diphenhydrAMINE, hydrocortisone and EPINEPHrine must be available in case of reaction
- pegaspargase 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  $100 \times 10^9/L$
- pegaspargase dose reduction is recommended for patients with fatty liver or BMI over  $30 \text{ kg/m}^2$  (dose reduce to pegaspargase  $500 \text{ units/m}^2$ )
- 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 =  $90 \text{ mg/m}^2$  ( $60 \text{ mg/m}^2$  during induction plus  $30 \text{ mg/m}^2$  during CNS phase). Adjust the number of cycles at the beginning of this regimen to achieve a cumulative lifetime DOXOrubicin dose of  $300 \text{ mg/m}^2$  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)]	
Planned course: Every 18 weeks from the beginning of CNS Phase. Continue until the completion of AL4 (Continuation)	
<b><i>Proceed with treatment if:</i></b>	
<ul style="list-style-type: none"> <li>• <i>ANC equal to or greater than <math>0.5 \times 10^9/L</math> AND Platelets equal to or greater than <math>50 \times 10^9/L</math></i></li> <li>❖ <i>Contact L/BMT Physician if parameters not met</i></li> </ul>	
Drug and Dose	CCMB Administration Guideline
<b>Every 18 weeks (Starting with beginning of CNS phase)</b>	
<b><u>Triple Intrathecal:</u></b> methotrexate 12 mg cytarabine 40 mg hydrocortisone 50 mg	Intrathecal in 6 mL preservative free normal saline administered in L/BMT Clinic
IT is ordered as a separate cyclical Support regimen LEUK - [AL4 (IT)]	