

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

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

Planned Course: 1 cycle = 21 days (usual 3 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

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – LEUK – AL4 (Intensification - methotrexate)*

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		
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		
vinCRIStine	2 mg (standard dose)	IV in normal saline 25 mL over 2 to 3 minutes by gravity infusion
calaspargase pegol	1000 units/m ² ; maximum dose 1875 units	IV in normal saline 100 mL over 1 hour
Days 2, 9 and 16		
methotrexate	60 mg/m ² (round to nearest 2.5 mg)	Orally on Days 2, 9 and 16 Take on an empty stomach in the evening (Self-administered at home)
<p>*This regimen is built as 3 cycles assuming 7 cycles of LEUK - [AL4 (Intens - DOXOrubicin)] have been administered. Target number of calaspargase pegol doses is 10 within the Intensification phase of AL4</p> <p>** If more than 3 cycles are needed, reduce dexamethasone dose to 6 mg/m²/day on Days 1 to 5 for additional cycles</p>		
<p>Patients will receive Triple Intrathecal Therapy every 18 weeks while receiving continuation 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)</p>		
<p>mercaptopurine available dosage strength: 50 mg tablets Classification: Cytotoxic, Hazardous</p> <p>methotrexate available dosage strength: 2.5 mg tablets Classification: Cytotoxic, Hazardous</p>		

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

REQUIRED MONITORING

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
- Instruct patient to hold sulfamethoxazole-trimethoprim on days when methotrexate is administered
- 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
- If nausea or mucositis develops, instruct patient to contact their L/BMT physician
- Reinforce safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

ADDITIONAL INFORMATION

- 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 methotrexate and 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)
- Treatment may be delayed if patient is experiencing moderate or severe mucositis
- If patient has recurrent mouth sores, they may be evaluated for HSV and considered for valACYclovir prophylaxis
- Goal of therapy is to administer ten 3-week cycles of vinCRISTine, dexamethasone, mercaptopurine, and DOXOrubicin/methotrexate. If additional cycles are needed to complete ten doses of calaspargase pegol, continue current regimen EXCEPT reduce dexamethasone to $6 \text{ mg/m}^2/\text{day}$ on Days 1 to 5
- Target number of calaspargase pegol doses is 10 within the Intensification phase of AL4. This regimen is built as 3 cycles assuming 7 cycles of LEUK - [AL4 (Intens - DOXOrubicin)] have been administered. Adjust number of cycles at the beginning of the regimen to ensure that 10 doses of calaspargase pegol are administered
- 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)

Proceed with treatment if:

ANC equal to or greater than $0.5 \times 10^9/L$ AND Platelets equal to or greater than $50 \times 10^9/L$

❖ **Contact L/BMT Physician if parameters not met**

Drug and Dose	CCMB Administration Guideline
Every 18 weeks (Starting with beginning of CNS phase)	
<u>Triple Intrathecal:</u> 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)]