

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
 - 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 - 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

vinCRISStine	2 mg (standard dose)	IV in normal saline 25 mL over 2 to 3 minutes by gravity infusion
acetaminophen	650 mg	Orally 1 hour prior to pegaspargase
hydrocortisone	100 mg	IV in normal saline 50 mL over 15 minutes 1 hour 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
Wait 30 minutes after completion of IV pre-medication(s) before starting pegaspargase		
pegaspargase	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 pegaspargase 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 (PURINETHOL®) available dosage strength: 50 mg tablets Classification: Cytotoxic, Hazardous 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 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

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 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 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 $100 \times 10^9/L$
- pegaspargase dose reduction is recommended for patients with fatty liver or BMI over 30 kg/m^2 (dose reduce to pegaspargase 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 pegaspargase, continue current regimen EXCEPT reduce dexamethasone to $6 \text{ mg/m}^2/\text{day}$ on Days 1 to 5
- Target number of pegaspargase 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 pegaspargase 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)]