

Regimen Reference Order

LEUK – CALGB 10403 (Remission Consolidation)

ARIA: LEUK - [CALGB 10403 (Rem Cons)]

ARIA Support: LEUK - [CALGB 10403(Cons) IT]

Planned Course: Single cycle (1 Cycle = 56 days)

Indication for Use: Newly Diagnosed Precursor B-Cell Acute Lymphoblastic Leukemia

CVAD: Preferred (VESICANT INVOLVED)

Proceed with treatment if:

Days 1 and 29

ANC equal to or greater than $0.75 \times 10^9/L$ AND Platelets equal to or greater than $75 \times 10^9/L$

❖ Contact Leukemia/BMT (L/BMT) Physician if parameters not met

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Instruct patient to start vigorous oral pre-hydration (600-900 mL) the morning of cyclophosphamide treatment (Self-administered at home)		

Treatment Regimen – LEUK – CALGB 10403 (Remission Consolidation)

Establish primary solution 500 mL of: normal saline		
Drug	Dose	CCMB Administration Guideline
Day 1		
normal saline	1000 mL	IV over 1 hour (Pre hydration)
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
cyclophosphamide	1000 mg/m^2	IV in normal saline 250 mL over 1 hour
cytarabine	75 mg/m^2	IV push over 2 to 5 minutes
mercaptopurine	60 mg/m^2 (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once on an empty stomach Do not crush or chew (Self-administered at home)
Days 2 to 4		
cytarabine	75 mg/m^2	IV push over 2 to 5 minutes
mercaptopurine	60 mg/m^2 (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once daily on an empty stomach Do not crush or chew (Self-administered at home)

Days 5 to 7		
mercaptopurine	60 mg/m ² (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once daily on an empty stomach Do not crush or chew (Self-administered at home)
Days 8 to 11		
cytarabine	75 mg/m ²	IV push over 2 to 5 minutes
mercaptopurine	60 mg/m ² (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once daily on an empty stomach Do not crush or chew (Self-administered at home)
Days 12 to 14		
mercaptopurine	60 mg/m ² (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once daily on an empty stomach Do not crush or chew (Self-administered at home)
Day 15		
vinCRIS ^t ine	1.5 mg/m ² ; maximum dose 2 mg	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
Day 22		
vinCRIS ^t ine	1.5 mg/m ² ; maximum dose 2 mg	IV in normal saline 25 mL over 2 to 3 minutes by gravity infusion
Day 29		
normal saline	1000 mL	IV over 1 hour (Pre hydration)
aprepitant	125 mg	Orally 1 hour pre-chemotherapy
ondansetron	16 mg	Orally 30 minutes pre-chemotherapy
dexamethasone	12 mg	Orally 30 minutes pre-chemotherapy
cyclophosphamide	1000 mg/m ²	IV in normal saline 250 mL over 1 hour
cytarabine	75 mg/m ²	IV push over 2 to 5 minutes
mercaptopurine	60 mg/m ² (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once on an empty stomach Do not crush or chew (Self-administered at home)

Days 30 to 32		
cytarabine	75 mg/m ²	IV push over 2 to 5 minutes
mercaptopurine	60 mg/m ² (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once daily on an empty stomach Do not crush or chew (Self-administered at home)
Days 33 to 35		
mercaptopurine	60 mg/m ² (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once daily on an empty stomach Do not crush or chew (Self-administered at home)
Days 36 to 39		
cytarabine	75 mg/m ²	IV push over 2 to 5 minutes
mercaptopurine	60 mg/m ² (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once daily on an empty stomach Do not crush or chew (Self-administered at home)
Days 40 to 42		
mercaptopurine	60 mg/m ² (see <i>Appendix A</i> mercaptopurine Dosing Instructions)	Orally once daily on an empty stomach Do not crush or chew (Self-administered at home)
Day 43		
vinCRISStine	1.5 mg/m ² ; maximum dose 2 mg	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
Day 50		
vinCRISStine	1.5 mg/m ² ; maximum dose 2 mg	IV in normal saline 25 mL over 2 to 3 minutes by gravity infusion
Patients will receive methotrexate Intrathecal Therapy with this regimen (See Appendix B – Intrathecal Therapy (IT))		
mercaptopurine (PURINETHOL®) available dosage strength: 50 mg tablet Classification: Cytotoxic, Hazardous		

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

REQUIRED MONITORING

Days 1 and 29

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin and glucose as per Physician Orders

Days 8, 22, 36 and 50

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin and glucose as per Physician Orders
- Lipase as per Physician Orders

Days 15 and 43

- CBC, fibrinogen, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin and glucose as per Physician Orders
- Lipase 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 vitals prior to discharge

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
valACYclovir	500 mg	Orally twice daily
sulfamethoxazole-trimethoprim	800/160 mg	Orally once daily on Mondays, Wednesdays and Fridays
aprepitant	80 mg	Orally once daily on Days 2 and 3 and on Days 30 and 31
metoclopramide	10 – 20 mg	Orally every 4 hours as needed for nausea and vomiting

DISCHARGE INSTRUCTIONS

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Instruct patient to:
 - Continue taking anti-emetic(s) at home
 - Maintain oral intake of 2000 mL (8 glasses) of fluid daily at home
 - Empty bladder every 2 hours while awake and at bedtime for 24 hours after cyclophosphamide treatment
 - Obtain immediate assistance as per your clinic’s contact instructions if:
 - Symptoms of hemorrhagic cystitis (e.g. dysuria, hematuria)
 - Unable to drink recommended amount of fluid
- mercaptopurine is a cancer therapy in this treatment regimen. Remind patient to take mercaptopurine at home
- mercaptopurine should not be taken with milk or citrus based products. Cow’s milk in particular, contains high concentrations of xanthine oxidase which inactivates mercaptopurine
- Remind patient to take valACYclovir (shingles prophylaxis) and sulfamethoxazole-trimethoprim (*Pneumocystis jirovecii* pneumonia prophylaxis) at home
- Instruct patient to hold sulfamethoxazole-trimethoprim on days when IT methotrexate is administered
- 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
- sulfamethoxazole-trimethoprim should not be administered on days when intrathecal methotrexate is administered due to potential drug interaction
- pegaspargase dose reduction is recommended for patients with fatty liver or BMI over 30 kg/m² (dose reduce to pegaspargase 500 units/m²)
- mercaptopurine is dosed with a weekly target dose of 420 mg/m² (Days 1 to 14 and 29 to 42). Doses are given at least one hour after the evening meal. Different daily doses rounded to the nearest 25 mg are to be given on alternating days when required to attain the weekly target dose. See *Appendix A* for administration instructions for mercaptopurine prescriptions
- mercaptopurine may be eligible for Home Cancer Drug Program coverage
- Intrathecal therapy is part of this regimen to start on Day 1 of CALGB 10403 (Remission Consolidation). See *Appendix B* regarding dosing for the support regimen LEUK - [CALGB 10403(Cons) IT]. Support protocol is available under **CALGB (Cons IT)** in the “Leukemia” folder

Appendix A

mercaptopurine Dosing – LEUK – CALGB 10403 (Remission Consolidation)

mercaptopurine dose is calculated by the Leukemia/BMT clinic

In the LEUK – CALGB 10403 (Remission Consolidation) regimen, mercaptopurine should be dosed at 60 mg/m²/day on Days 1 to 14 and Days 29 to 42 of the 56-day cycle (Weekly dose of 420 mg/m²). Because mercaptopurine is only available as a 50 mg tablet, there is limited flexibility in delivering the appropriate daily dose. As such, the dosing schedule may require different daily doses to ensure an appropriate dose over the course of the cycle.

While the Medical Oncology Manager (ARIA®) application is used for order entry and a specific regimen for the LEUK – CALGB 10403 (Remission Consolidation) regimen is available, the dosing instructions for this regimen are too complex to build into the ARIA-based regimen. Manual calculation and manual entry of the dosing instructions (e.g. number of tablets per dose) is required. The table below outlines required tablets per dose according to dose intensity and patient body surface area.

Administration Instructions on Day 1:

Take dose orally once daily for 14 days starting Day 1
Take on an empty stomach at least one hour after the evening meal
Avoid milk and citrus based products at the same time as the dose

Target dose = 60 mg/m² PO on Days 1 to 14 (Weekly dose 420 mg/m²/week)

Medication may be eligible for Home Cancer Drug Program coverage

Administration Instructions on Day 29:

Take dose orally once daily for 14 days starting Day 29
Take on an empty stomach at least one hour after the evening meal
Avoid milk and citrus based products at the same time as the dose

Target dose = 60 mg/m² PO on Days 29 to 42 (Weekly dose 420 mg/m²/week)

Medication may be eligible for Home Cancer Drug Program coverage

mercaptopurine Dosing Instructions

mercaptopurine dosing for daily doses of 60 mg/m² (Target weekly dose of 420 mg/m²) administered on Days 1 to 14 and Days 29 to 42

BSA (m ²)	7-day daily dose* 1 tab = 50 mg	Dosing Instructions for Days 1 to 14 and Days 29 to 42**
1.26 – 1.3	2 tablets/day x 1; 1½ tablets/day x 6 (550 mg/week)	Take 100 mg (2 tablets) once daily on Thursdays and 75 mg (1 & 1/2 tablets) once daily on Mondays, Tuesdays, Wednesdays, Fridays, Saturdays, and Sundays Qty: 22 x 50 mg tablets
1.31 – 1.36	2 tablets/day x 2; 1½ tablets/day x 5 (575 mg/week)	Take 100 mg (2 tablets) once daily on Thursdays and Sundays and 75 mg (1 & 1/2 tablets) once daily on Mondays, Tuesdays, Wednesdays, Fridays, and Saturdays Qty: 23 x 50 mg tablets
1.37 – 1.43	2 tablets/day x 3; 1½ tablets/day x 4 (600 mg/week)	Take 100 mg (2 tablets) once daily on Mondays, Wednesdays, and Fridays and 75 mg (1 & 1/2 tablets) once daily on Tuesdays, Thursdays, Saturdays, and Sundays Qty: 24 x 50 mg tablets
1.44 – 1.49	2 tablets/day x 4; 1½ tablets/day x 3 (625 mg/week)	Take 75 mg (1 & 1/2 tablets) once daily on Mondays, Wednesdays, and Fridays and 100 mg (2 tablets) once daily on Tuesdays, Thursdays, Saturdays, and Sundays Qty: 25 x 50 mg tablets
1.5 – 1.55	2 tablets/day x 5; 1½ tablets/day x 2 (650 mg/week)	Take 75 mg (1 & 1/2 tablets) once daily on Thursdays and Sundays and 100 mg (2 tablets) once daily on Mondays, Tuesdays, Wednesdays, Fridays, and Saturdays Qty: 26 x 50 mg tablets
1.56 – 1.61	2 tablets/day x 6; 1½ tablets/day x 1 (675 mg/week)	Take 75 mg (1 & 1/2 tablets) once daily on Thursdays and 100 mg (2 tablets) once daily on Mondays, Tuesdays, Wednesdays, Fridays, Saturdays, and Sundays Qty: 27 x 50 mg tablets
1.62 – 1.67	2 tablets/day x 7 (700 mg/week)	Take 100 mg (2 tablets) orally once daily Qty: 28 x 50 mg tablets
1.68 – 1.73	2½ tablets/day x 1 2 tablets/day x 6; (725 mg/week)	Take 125 mg (2 & 1/2 tablets) once daily on Thursdays and 100 mg (2 tablets) once daily on Mondays, Tuesdays, Wednesdays, Fridays, Saturdays and Sundays Qty: 29 x 50 mg tablets
1.74 – 1.79	2½ tablets/day x 2; 2 tablets/day x 5 (750 mg/week)	Take 125 mg (2 & 1/2 tablets) once daily on Thursdays and Sundays and 100 mg (2 tablets) once daily on Mondays, Tuesdays, Wednesdays, Fridays, and Saturdays Qty: 30 x 50 mg tablets

1.8 – 1.85	2½ tablets/day x 3; 2 tablets/day x 4 (775 mg/week)	Take 125 mg (2 & 1/2 tablets) once daily on Mondays, Wednesdays, and Fridays and 100 mg (2 tablets) once daily on Tuesdays, Thursdays, Saturdays and Sundays Qty: 31 x 50 mg tablets
1.86 – 1.91	2½ tablets/day x 4; 2 tablets/day x 3 (800 mg/week)	Take 100 mg (2 tablets) once daily on Mondays, Wednesdays, and Fridays and 125 mg (2 & 1/2 tablets) once daily on Tuesdays, Thursdays, Saturdays and Sundays Qty: 32 x 50 mg tablets
1.92 – 1.97	2½ tablets/day x 5; 2 tablets/day x 2 (825 mg/week)	Take 100 mg (2 tablets) once daily on Thursdays and Sundays and 125 mg (2 & 1/2 tablets) once daily on Mondays, Tuesdays, Wednesdays, Fridays and Saturdays Qty: 33 x 50 mg tablets
1.98 – 2.03	2½ tablets/day x 6; 2 tablets/day x 1 (850 mg/week)	Take 100 mg (2 tablets) once daily on Thursdays and 125 mg (2 & 1/2 tablets) once daily on Mondays, Tuesdays, Wednesdays, Fridays, Saturdays and Sundays Qty: 34 x 50 mg tablets
<p>* The 7-day daily dose refers to the weekly dose to attain the weekly target dose of 420 mg/m²</p> <p>** Dispensing Instructions for Day 1 and Day 29 can be used for the administration instruction field of the ARIA prescription for the relevant BSA. Required days of the week and dispensing quantities are included in the instructions. Due to limitations in ARIA the prescription for mercaptopurine has a default dose of 1 mg/m². When prescribing it is advised to modify the prescription from “Complex” to “Take as Directed” and to populate the Admin Instructions with the relevant instructions from this table (Dosing Instructions for Days 1 to 14 and Days 29 to 42).</p> <p>Patients with thiopurine methyltransferase (TPMT) deficiency require dose reductions during therapy. Please refer to original protocol for details. (When myelosuppression has led to significant delays in therapy (greater than 2 weeks) or is disproportionate to the therapy, thiopurine methyltransferase testing should be performed).</p>		

Appendix B**Intrathecal Therapy (IT) – LEUK - [CALGB 10403(Cons) IT]**

Proceed with treatment if:

- *Platelets equal to or greater than $50 \times 10^9/L$*

Days 1, 8, 15 and 22 [omit dose on Days 15 and 22 for CNS3 patients]

Drug	Dose	CCMB Administration Guideline
methotrexate	15 mg	Intrathecal in 6 mL preservative free normal saline administered in L/BMT Clinic

IT is ordered as a separate support regimen to start on Day 1 of CALGB 10403 (Remission Consolidation)