Regimen Reference Order – LEUK – blinatumomab (MRD positive)

ARIA: LEUK - [blinatumomab MRD+]

Planned Course: **Induction (Cycle 1) and Consolidation (Cycles 2, 3 and 4): 28 days of treatment (continuous infusion), followed by 14 days with no therapy**

(1 cycle = 42 days)

Note: Initial CCMB Outpatient blinatumomab infusion bag change is variable depending on when patient is discharged from hospital.

Treatment appointments for blinatumomab must be scheduled at 1130H to ensure coordination between treatment room and Pharmacy. blinatumomab bags are changed at CCMB at 1130H regardless of any residual volume remaining in the bag (as each bag is prepared with overfill).

This RRO outlines initial CCMB Outpatient blinatumomab infusion bag on Day 5 of Cycles 1 and 2. Refer to Appendix A (page 6) for variations to dose and pump infusion times if patient has a different start day.

See regimen Dosing Schema (page 5)

Indication for Use: **Acute Lymphoblastic Leukemia, Minimal Residual Disease (MRD) positive**

Drug Alert: T-Cell Engager

Alert: Protocol is restricted to adult patients greater than or equal to 45 kg

CVAD: Required (Ambulatory Pump) – PICC Preferred

Proceed with treatment if:

- ***AST/ALT is less than 5 times the upper limit of normal***
- ***Total bilirubin is less than 3 times the upper of limit of normal***
- ***Creatinine clearance is greater than 30 mL/minute***

Proceed regardless of platelet or ANC

- **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 – blinatumomab (MRD positive)

Drug	Dose	CCMB Administration Guideline
Cycle 1 Induction and Cycle 2 Consolidation		
Days 1 to 4		
Patients will be admitted to hospital for treatment for the first 3 days of Cycles 1 and 2. Follow inpatient orders Note: Day 3 is ordered as a 48-hour infusion via ambulatory infusion starting at 1130H		
Days 5, 9, 13, 17, 21 and 25		
blinatumomab	112 mcg (28 mcg/day)	IV in normal saline continuously over 96 hours by ambulatory infusion device to start at 1130H *CADD SOLIS VIP settings:* ***Infusion rate = 2.5 mL/hour*** *Reservoir Volume = 240 mL* *Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Nursing Alert: IV tubing is primed with blinatumomab* **Nursing Alert: Change bag exactly every 96 hours. Discard remainder of solution in IV bag and IV line at every bag change and on Day 29 at 1130H* **Nursing Alert: Withdraw 2 mL of blood prior to flushing as a bolus of blinatumomab can be harmful to patient* ***Note: If patient requires an initial CCMB Outpatient blinatumomab bag change on a different start day (i.e. not on Day 5, 9, 13, 17, 21 or 25), patient will receive a one-time only initial 48-hour infusion pump, then switch to every 96-hour bag changes. Refer to Appendix A***
Cycles 3 and 4 Consolidation		
Day 1		
cetirizine	10 mg	Orally 30 minutes prior to blinatumomab
acetaminophen	650 mg	Orally 30 minutes prior to blinatumomab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to blinatumomab **Nursing Alert: blinatumomab starts **1 hour after completion** of dexamethasone infusion*
Wait 1 hour after completion of IV pre-medication(s) before starting blinatumomab		
blinatumomab	112 mcg (28 mcg/day)	IV in normal saline continuously over 96 hours by ambulatory infusion device to start at 1130H *CADD SOLIS VIP settings:* ***Infusion rate = 2.5 mL/hour*** *Reservoir Volume = 240 mL* *Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Nursing Alert: IV tubing is primed with blinatumomab* **Nursing Alert: Withdraw 2 mL of blood prior to flushing as a bolus of blinatumomab can be harmful to patient*

Days 5, 9, 13, 17, 21 and 25		
blinatumomab	112 mcg (28 mcg/day)	IV in normal saline continuously over 96 hours by ambulatory infusion device to start at 1130H *CADD SOLIS VIP settings:* ***Infusion rate = 2.5 mL/hour*** *Reservoir Volume = 240 mL* *Use non-DEHP bags and non-DEHP administration sets with 0.2 or 0.22 micron filter* **Nursing Alert:* *IV tubing is primed with blinatumomab* **Nursing Alert*: *Change bag exactly every 96 hours. Discard remainder of solution in IV bag and IV line at every bag change and on Day 29 at 1130H* **Nursing Alert:* *Withdraw 2 mL of blood prior to flushing as a bolus of blinatumomab can be harmful to patient*
If re-initiating therapy after interruption of 4 hours or more, hospitalization or observation is recommended		

Do NOT flush line when drug is running. This may result in an unintended bolus of blinatumomab. If accessing lumen, withdraw 2 mL of blood (containing drug) first, and then flush.

In the event of an infusion-related hypersensitivity reaction, contact Leukemia/BMT physician on call

REQUIRED MONITORING

CRS and ICANS monitoring (Throughout therapy)

- Monitor for signs and symptoms of cytokine release syndrome (CRS). Serious adverse events that may be associated with CRS include: pyrexia, headache, nausea, asthenia, hypotension, and elevations in serum aminotransferases and bilirubin
- Monitor for signs and symptoms of Immune Effector Cell-Associated Neurotoxicity (ICANS). Symptoms may include: trembling, disturbance or loss of movement of parts of the body, speech or coordination disorders, apraxia, dizziness, confusion, disorientation, reversible seizures, encephalopathy, somnolence and agitation

Cycle 1

Each bag change

- CBC with differential, serum creatinine, urea, electrolytes including phosphate and calcium, AST, ALT, Alkaline phosphatase, LDH, GGT, total bilirubin, uric acid and albumin as per Physician Orders
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) as clinically indicated

Twice weekly

- Lipase

Cycle 2 and Onwards

Weekly

- CBC with differential, serum creatinine, urea, electrolytes including phosphate and calcium, AST, ALT, Alkaline phosphatase, LDH, GGT, total bilirubin, uric acid and albumin as per Physician Orders
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) as clinically indicated

Twice weekly

- Lipase

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
None required		

DISCHARGE INSTRUCTIONS

- Advise patient to contact L/BMT physician on call if they encounter problems with ambulatory infusion pump after hours

ADDITIONAL INFORMATION

- T-Cell Engagers can cause CRS and ICANS
- blinatumomab has been associated with Tumor Lysis Syndrome
- This protocol only applies to adult patients greater than or equal to 45 kg
- Site restrictions are in place for blinatumomab. blinatumomab must be administered at CCMB MacCharles in Winnipeg

Dosing Schema - Cycles 1 and 2

Initial CCMB Outpatient blinatumomab infusion bag change on Day 5

Day	5*	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30 to 42
blinatumomab	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	D/C**	
CCMB bag change	▨				▨				▨				▨				▨				▨				D/C**	
Total dose per bag (mcg)	112				112				112				112				112				112					
Infusion rate (mL/hr)	2.5				2.5				2.5				2.5				2.5				2.5					

*48-hour bag dispensed by HSC on Day 3 will be disconnected at CCMB on Day 5 and replaced with a 96-hour bag
**blinatumomab infusion pump is disconnected on Day 29 (D/C= Disconnect)

Key:

■ **Indicates that blinatumomab will be administered on this day**

▨ **Indicates blinatumomab bag change on this day**

APPENDIX A – CYCLES 1 AND 2

Cycles 1 & 2 - Variations to Initial CCMB Outpatient blinatumomab Infusion Bag Change

Day of initial CCMB Outpatient blinatumomab infusion bag change	Dose	CCMB Administration Guidelines
Day 3, 7, 11, 15, 19, 23 or 27*	56 mcg (28 mcg/day)	IV in normal saline continuously **over 48 hours** by ambulatory infusion device to start at 1130H *CADD SOLIS VIP settings:* ***Infusion rate = 5 mL/hour*** *Reservoir Volume = 240 mL*

***Day 27: One-time infusion bag to complete cycle**

Additional Information (Cycles 1 and 2):

- If the patient requires an initial bag change at CCMB on Day 3, 7, 11, 15, 19, 23 or 27 then a 48-hour bag will be ordered for the initial dose only, then patient will switch to every 96-hour bag changes as outlined in RRO
- Note: If the patient requires an initial bag change at CCMB on Day 27, then a 48-hour bag will complete cycle
  - Support protocol under **blinatumomab 48 hr** in the "Leukemia" folder is to be used to order the 48-hour blinatumomab infusion bag when required

Example:* *Initial CCMB Outpatient blinatumomab infusion bag change on Day 7

Day	7*	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30 to 42
blinatumomab	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	D/C**	
CCMB bag change	▨		▨				▨				▨				▨				▨				D/C**	
Total dose per bag (mcg)	56		112				112				112				112				112					
Infusion rate (mL/hr)	5		2.5				2.5				2.5				2.5				2.5					

*48-hour bag dispensed by HSC on Day 5 will be disconnected at CCMB on Day 7 and replaced with a 48-hour bag
**blinatumomab infusion pump is disconnected on Day 29 (D/C = Disconnect)

Key:

■ **Indicates that blinatumomab will be administered on this day**

▨ **Indicates blinatumomab bag change on this day**