CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

GUIDELINES FOR OUTPATIENT BLINATUMOMAB

Section: Nursing
Compliance: N/A
ACHC Standards: N/A
URAC Standards: N/A
TJC Standards: N/A
Policy ID: NUR236
Effective: 6/1/22
Reviewed:
Revised:
Approved by: Kathleen Patrick, President, 6/1/22

I. POLICY

Blinatumomab is a bispecific CD19-directed CD3 T-cell engager. Its mechanism of action mediates the production of cytolytic proteins, release of inflammatory cytokines, and proliferation of T cells, causing lysis of CD19-positive cells. Blinatumomab is used in B-Cell acute lymphoblastic leukemia (ALL) that is Philadelphia chromosome-negative. It can also be used in patients with recurred or refractory acute lymphoblastic leukemia. The following outlines the procedures and protocols for coordination of servicing patients in need of outpatient Blinatumumab home infusions.

II. PATIENT ACCEPTANCE CRITERIA

1. The first and second cycle must be administered in a hospital setting.

2. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon Chartwell Pennsylvania's admission criteria. The following criteria will be evaluated:
    1. Prescriber preference
    2. Allergy profile
    3. Age ≥18 years
    4. Ability to secure contracted nursing for subsequent infusions
    5. Other relevant social and/or medical history

3. Venous access must be adequate for administration

4. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See policy NUR012 (Appendix A).

III. PHARMACOLOGY OVERVIEW

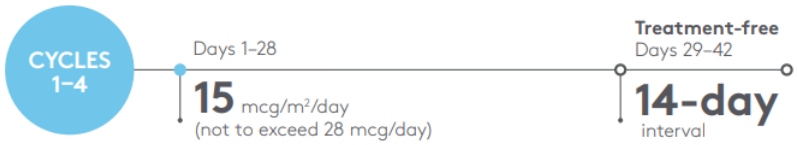
A. Indications
    1. B-cell acute lymphoblastic leukemia, CD19-positive disease in first or second

complete remission with minimal residual disease-positive (0.1% or greater) – **will be referred to as MDR+**

2. Philadelphia chromosome-negative relapsed or refractory B- cell precursor acute lymphoblastic leukemia – **will be referred to as RR**

B. Dosage

1. MDR+
   a. Less than 45 kg
      - Dosing is weight-based using BSA
      - Induction cycle 1: 15 mcg/m(2)/day (maximum daily dose: 28 mcg/day) continuous IV infusion on days 1 through 28 followed by 2 weeks of no treatment.

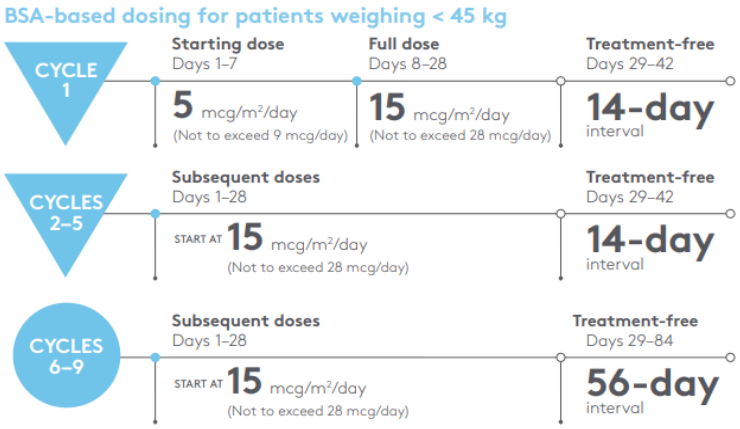


      - Consolidation cycles 2 through 4: 15 mcg/m(2)/day (maximum daily dose: 28 mcg/day) continuous IV infusion on days 1 through 28 followed by 2 weeks of no treatment.

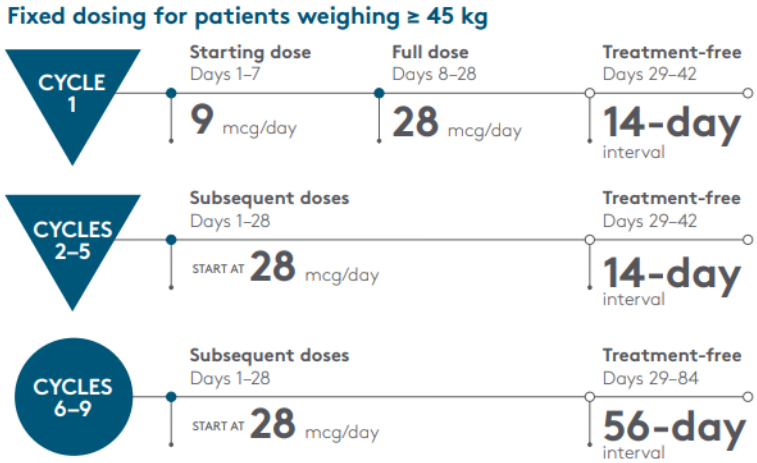
   b. 45 kg or Greater
      - Dosing is fixed-dose
      - Induction cycle 1: 28 mcg/day continuous IV infusion on days 1 through 28 followed by 2 weeks of no treatment.

      - Consolidation cycles 2 through 4: 28 mcg/day continuous IV infusion on days 1 through 28 followed by 2 weeks of no treatment

2. RR
   a. Body weight less than 45 kg
      - Induction cycle 1: 5 mcg/m(2)/day (MAX, 9 mcg/day) continuous IV infusion on days 1 through 7 and 15 mcg/m(2)/day (MAX, 28 mcg/day) continuous infusion on days 8 through 28, followed by 2 weeks of no treatment
      - Cycles 2 through 5: 15 mcg/m(2)/day (MAX, 28 mcg/day) continuous IV infusion on days 1 through 28 followed by 2 weeks of no treatment
      - Continued therapy cycles 6 through 9: 15 mcg/m(2)/day (MAX, 28 mcg/day) continuous infusion on days 1 through 28 followed by 8 weeks of no treatment.



b. Body weight 45 kg or Greater
   - Induction cycle 1: 9 mcg/day continuous IV infusion on days 1 through 7 and 28 mcg/day continuous IV infusion on days 8 through 28, followed by 2 weeks of no treatment
   - Cycle 2 through 5: 28 mcg/day continuous IV infusion on days 1 through 28 followed by 2 weeks of no treatment
   - Continued therapy cycles 6 through 9: 28 mcg/day continuous IV



C. Contraindications

1. Blinatumomab is contraindicated in patients with known hypersensitivity to Blinatumomab or to any component of the product formulation

D. Warnings and Precautions

1. Cytokine Release Syndrome (CRS)
   a. Median onset is 2 days after start of the infusion
   b. Manifestations include fever, headache, nausea, asthenia, hypotension, increased alanine aminotransferase, increased aspartate aminotransferase, increased total bilirubin, and disseminated intravascular coagulation (DIC)

2. Neurotoxicity
    a. Approximately 50% of patients receiving Blinatumomab in clinical trials experienced neurological toxicities
    b. Severe, life-threatening, or fatal neurological toxicities occurred in approximately 15% of patients

3. Infections
    a. Approximately 25% of patients receiving Blinatumomab experienced serious infections
    b. Administer prophylactic antibiotics and employ surveillance testing as appropriate during treatment
    c. If an infection occurs, treat appropriately, including interruption or discontinuation of Blinatumomab if needed

4. Life-threatening or fatal Tumor Lysis Syndrome (TLS)
    a. Preventive measures, such as pretreatment nontoxic cytoreduction and hydration should be used during Blinatumomab treatment
    b. Discontinue Blinatumomab as needed

5. Avoid driving and using machineries
    a. Due to the possibility of neurological events including seizures, patients receiving Blinatumomab are at risk for loss of consciousness, and should not be driving and engaging in hazardous occupations or activities such as operating heavy or potentially dangerous machinery while Blinatumomab is being administered.

6. Hepatotoxicity
    a. Observed in the setting of CRS with a median onset of 15 days
    b. Grade 3 or greater elevations in liver enzymes occurred in 6% of patients outside the setting of CRS and resulted in treatment discontinuation in less than 1% of patients
    c. Blinatumomab treatment should be interrupted if transaminases rise to > 5 times the upper limit of normal (ULN) or if total bilirubin rises to > 3 times ULN.

7. Leukoencephalopathy
    a. Cranial magnetic resonance imaging (MRI) changes showing leukoencephalopathy have been observed in patients receiving Blinatumomab, especially in patients previously treated with cranial irradiation and anti-leukemic chemotherapy

8. Bone marrow suppression
    a. Neutropenia and neutropenic fever, including life-threatening episodes, have been reported

9. Pancreatitis
    a. Fatal cases of pancreatitis in patients receiving Blinatumomab plus dexamethasone have been reported in the post marketing setting

10. Preparation and administration errors have occurred
    a. Follow instructions for preparation and administration strictly to minimize medication errors (including under dose and overdose)

11. Due to the addition of bacteriostatic saline, 7-day bags of Blinatumomab solution for infusion with preservative contain benzyl alcohol and are not recommended for use in any patients weighing less than 22 kg

12. Pregnancy Category: C

E. Pharmacokinetics

1. The mean half-life is ~ 2 hours
2. The metabolic pathway of blinatumomab has not been characterized

F. Adverse Reactions

1. >10%
    a. Cardiovascular
        - arrhythmia, edema, hyper/hypotension
    b. Dermatologic
        - Rash
    c. Endocrine & metabolic
        - Weight gain
    d. Hematologic & oncologic
        - Anemia, decreased absolute lymphocyte count, decreased serum immunoglobulins, leukopenia, neutropenia, thrombocytopenia
    e. Hepatic
        - Increased serum transaminases
    f. Hypersensitivity
        - Cytokine release syndrome-highest elevation of cytokines was observed in the first 2 days following start of Blinatumomab infusion
    g. Infection
        - bacterial, fungal infection, opportunistic infection
    h. Nervous system
        - Aphasia, chills, headache, insomnia, neurotoxicity
    i. Neuromuscular & skeletal
        - Back pain, tremor
    j. Respiratory
        - Cough
    k. Miscellaneous
        - Fever, infusion related reaction

2. <10%
    a. Cardiovascular
        - Septic shock
    b. Hematologic & oncologic
        - Febrile neutropenia, lymphocytopenia
    c. Immunologic
        - Antibody development
    d. Nervous system
        - Dizziness, encephalopathy, seizure

G. Drug Interactions

1. CYP450 substrates such as Busulfan:

a. Blinatumomab causes a transient elevation of cytokines which may suppress CYP450 enzyme activities and result in increased exposure of CYP450 substrates, especially those with a narrow therapeutic index
b. Risk of interaction is increased during the first 9 days of the first cycle of Blinatumomab and the first 2 days of the second cycle
c. Monitor for toxicity and/or drug concentrations
    - Adjust the dose of the concomitant drug as needed

2. Vaccines (Inactivated):
    a. Vaccine efficacy may be reduced
    b. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant
    c. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation

3. Vaccines (Live):

4. Vaccination with live virus vaccines is not recommended for at least 2 weeks prior to Blinatumomab initiation, during treatment, and until immune system recovery following the last cycle of therapy

IV. ADMINISTRATIVE GUIDELINES

A. Administration

1. MDR+
    a. Hospitalization is recommended for the first 3 days of cycle 1, and the first 2 days of cycle 2.
    b. **Do not flush infusion line, particularly when changing infusion bags or at completion of infusion; may result in overdose**
    c. Premedication
        - Adults: 100 mg prednisone intravenously or equivalent (eg, dexamethasone 16 mg) 1 hour prior to the first dose of each Blinatumomab cycle
        - Pediatrics: 5 mg/m2 of dexamethasone, to a maximum dose of 20 mg prior to the first dose of Blinatumomab in the first cycle and when restarting an infusion after an interruption of 4 or more hours in the first cycle
2. RR
    a. Hospitalization is recommended for the first 9 days of the first cycle and the first 2 days of the second cycle
    b. **Do not flush infusion line, particularly when changing infusion bags or at completion of infusion; may result in overdose**
    c. Premedication
        - Adults: 20 mg dexamethasone 1 hour prior to the first dose of Blinatumomab of each cycle, prior to a step dose (such as cycle 1 day 8), and when restarting infusion after an interruption of 4 or more hours
        - Pediatrics: 5 mg/m2 of dexamethasone, to a maximum dose of 20 mg prior to the first dose of Blinatumomab in the first cycle, prior to a step dose (such as cycle 1 day 8), and when restarting an infusion after an interruption of 4 or more hours in the first cycle.

3. Requires a continuous intravenous (IV) infusion at a constant flow rate using an infusion pump that is programmable, lockable, non-elastomeric, and has an alarm

4. The final volume of infusion solution is more than the volume administered to the patient to account for the priming of the IV tubing and to ensure that the patient will receive the full dose of Blinatumomab.

5. The Blinatumomab solution must be administered using IV tubing that contains a sterile, nonpyrogenic, low protein-binding, 0.2 micron in-line filter with the exception of the 7-day bag which DOES NOT require a filter.

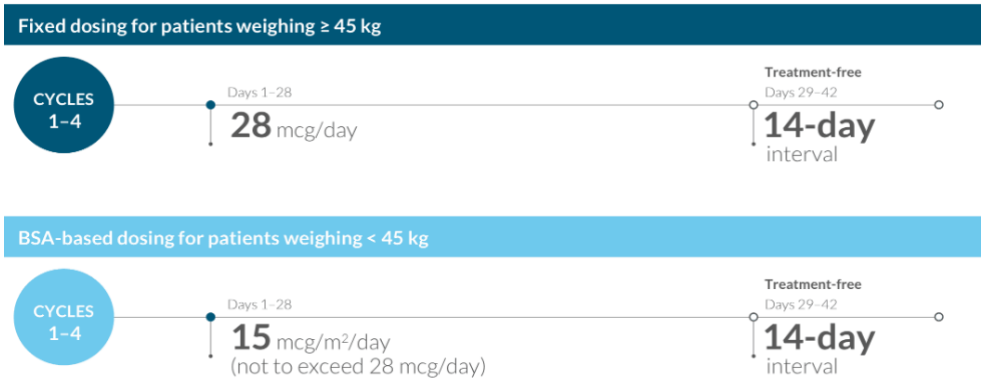
6. Only use polyolefin, PVC non-diethylhexylphthalate (non-DEHP), or ethyl vinyl acetate (EVA) infusion bags, pump cassettes and IV tubing
    a. IV tubing should be primed with prepared infusion solution, not NSS

7. Infusion Options
    a. 24- or 48-hour infusions
        - Infuse 240 mL Blinatumomab solution following constant infusion rates of 10mL/h for a duration of 24 hours OR 5mL/h for a duration of 48 hours
    b. 7-day infusion
        - 0.6 mL for a duration of 7 days

8. IV infusions should be given immediately after reconstitution and dilution. Use within 1 hour of preparation per current USP Immediate-Use Guidelines

B. Duration

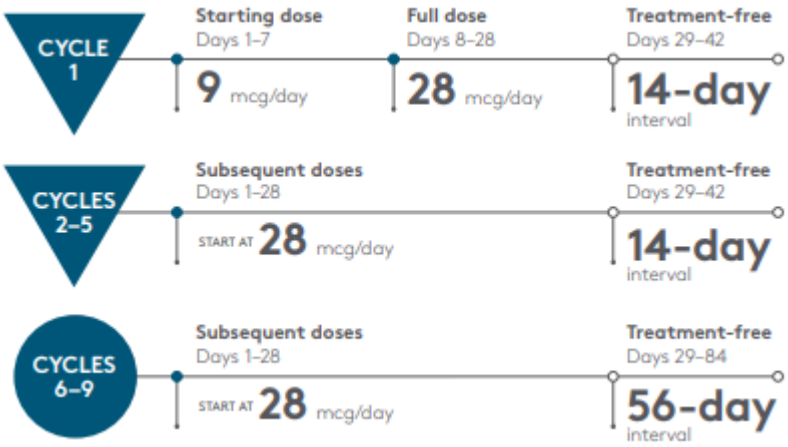
1. MDR+
    a. Treatment Cycles
        - A single cycle of treatment of Blinatumomab induction or consolidation consists of 28 days of continuous intravenous infusion followed by a 14-day treatment-free interval (42 days total).
        - A treatment course consists of 1 cycle for induction followed by up to 3 additional cycles for consolidation.



2. RR
    a. Treatment Cycles
        - A single induction or consolidation treatment cycle consists of 28 days of continuous IV infusion followed by 14 days of no treatment, for a total of 42

days.

- A treatment course consists of up to 2 induction cycles followed by 3 additional consolidation cycles (up to a total of 5 cycles) Continued therapy of up to 4 additional cycles may be given following consolidation treatment (total of up to cycles)
- A single cycle of continued therapy consists of 28 days of continuous IV infusion followed by 56 days of no treatment, for a total of 84 days



C. Dose Adjustment

1. Dosage Adjustment in Renal Failure
    a. None

2. Dosage Adjustment in Hepatic Insufficiency
    a. None initially however if transaminases are >5 times ULN or if bilirubin is >3 times ULN, may need to interrupt therapy according to the Grade of Severity (see Table 1)

3. Dosage Adjustments when managing adverse effects please see Table 1
    a. If interruption is >7 days, start a new cycle of Blinatumomab

D. Patient Monitoring

1. Liver function tests: ALT, AST, gamma-glutamyl transferase, and total bilirubin at baseline and throughout therapy.
2. Cytokine release syndrome
3. Neurotoxicity
4. Signs and symptoms of Infection
5. Tumor lysis syndrome
6. Local reactions at injection sites
7. Monitor CBC with differential

V. NURSING PROCEDURE

A. Supplies

1. Alcohol swabs
2. Gloves
3. Tape
4. Peripheral start kit
5. Peripheral IV catheter
6. Central IV line kit if patient has a central line with corresponding port access needles
7. 8" extension set
8. IV injection cap
9. Luer lock Syringes ranging from 5mL-60mL depending on volume of drug needed
10. 18 gauge x 1" needles
11. Ambulatory pump tubing with 0.22 micron filter (**24 and 48 hour bags requires filter**)
12. Ambulatory pump
13. Batteries for ambulatory pump (Ex: 9 Volt Duracell battery or 4 Double A batteries)
14. Battery change procedure teaching sheet
15. Continuous delivery mode teaching sheet
16. Pump return box
17. IV pole
18. Approprite number of Blinatumomab vials for preparation
19. Preservative-free, Sterile Water for Injection
20. 250 mL 0.9% Sodium Chloride IV bag
21. Use only polyolefin, PVC non-diethylhexylphthalate (non-DEHP), or ethylvinylacetate (EVA) infusion bags/pump cassettes.
22. Polyolefin, PVC non-DEHP, or EVA IV tubing with a sterile, non-pyrogenic, low protein-binding 0.2 micron in-line filter
23. Supplies to make a 270 mL 0.9% Sodium Chloride IV bag
    a. An empty IV bag (use only polyvinyl chloride [PVC] di-ethylhexylphthalate-free [DEHP-free], polyolefin, or ethyl vinyl acetate [EVA] infusion bags/pump cassettes)
    b. 0.9% Sodium Chloride Injection, USP (eg, 1000 mL) • Preservative-free Sterile Water for Injection, USP
    c. PVC DEHP-free, polyolefin, or EVA IV tubing with a sterile, non-pyrogenic, low-protein-binding 0.2 micron in-line filter

B. Procedures - Preparation of product, Infusion rates, post infusion monitoring time

1. Preparation
    a. Explain the reasoning for visit and use Blintumomab
    b. Don gloves
    c. Establish venous access prior to preparation of drug
    d. Counsel patient on warnings, precautions, and potential side effects
    e. 1 package Blintumomab includes 1 vial of Blintumomab and 1 vial of IV Solution Stabilizer
        - IV Solution Stabilizer is provided with the Blintumomab package and is used to coat the IV bag prior to addition of reconstituted Blintumomab to prevent adhesion of Blintumomab to IV bags and IV tubing
        - More than 1 package of Blintumomab may be needed to prepare some of the prescribed doses
    f. Reconstitute each Blintumomab vial with 3 mL of preservative-free Sterile Water for Injection, USP by directing the water along the walls of the Blintumomab vial and not directly on the lyophilized powder (resulting in a final Blintumomab concentration of 12.5 mcg/mL)
    g. Do not reconstitute Blintumomab with IVSS

h. Gently swirl the contents to avoid excess foaming. Do not shake.
i. Visually inspect the reconstituted solution for particulate matter and discoloration during reconstitution and prior to infusion. The resulting solution should be clear to slightly opalescent, colorless to slightly yellow. Do not use if solution is cloudy or has precipitated.
j. Verify the prescribed dose and infusion duration for each Blintumomab infusion bag
    - To minimize errors, use the specific volumes described in Tables 2 to 4 to prepare the Blintumomab infusion bag
    - Table 2 for patients weighing greater than or equal to 45 kg
    - Tables 3 and 4 for patients weighing less than 45 kg

k. Preparation is now different depending on the infusion time:

24 or 48 hour infusion

1) Aseptically add 270 mL of 0.9% Sodium Chloride Injection, USP to the empty IV bag.
2) Aseptically transfer 5.5 mL of IVSS to the IV bag containing 0.9% Sodium Chloride Injection, USP.
3) Aseptically transfer the required volume of reconstituted Blintumomab to obtain ordered dose into the IV bag containing 0.9% Sodium Chloride Injection and IVSS. Gently mix the contents of the bag to avoid foaming. Discard any remaining IVSS or Blintumomab.
4) Under aseptic conditions, attach the IV tubing to the IV bag with the sterile 0.2 micron in-line filter (PVC DEHP-free, polyolefin, or EVA IV tubing).
5) Ensure that the IV tubing is compatible with the infusion pump
6) Remove air from the IV bag. This is particularly important for use with an ambulatory infusion pump.
7) Prime the IV tubing only with the solution in the bag containing the FINAL prepared Blintumomab solution for infusion
8) Do not prime with 0.9% Sodium Chloride Injection, USP
9) Visually inspect the reconstituted solution for particulate matter and discoloration during reconstitution and prior to infusion. The resulting solution should be clear to slightly opalescent, colorless to slightly yellow. Do not use if solution is cloudy or has precipitated.
10) Store at 2°C to 8°C (36°F to 46°F) if not used immediately

7-Day Infusion

1) Aseptically add 90 mL Bacteriostatic 0.9% Sodium Chloride Injection, USP to the empty IV bag.
2) Aseptically transfer 2.2 mL IV Solution Stabilizer to the IV bag containing the saline solution. Gently mix the contents of the bag to avoid foaming. Discard the vial containing the unused IV Solution Stabilizer.
3) Aseptically transfer required amount of reconstituted Blintumomab into the IV bag containing the saline solution and IV Solution Stabilizer. Gently mix the contents of the bag to avoid foaming. Refer to Table 5 for the specific volume of reconstituted Blintumomab.
4) Aseptically add 0.9% Sodium Chloride Injection, USP to the IV bag to a final volume of 110 mL resulting in 0.74% benzyl alcohol. Gently mix the contents of the bag to avoid foaming. Refer to Table 5 for the specific volume

of 0.9% Sodium Chloride Injection, USP.

5) Under aseptic conditions, attach the IV tubing to the IV bag. An in-line filter is not required for a 7-day bag. Ensure that the IV tubing is compatible with the infusion pump.
6) Remove air from the IV bag. This is particularly important for use with an ambulatory infusion pump. Prime the IV tubing only with the prepared solution for infusion. Do not prime with 0.9% Sodium Chloride Injection, USP. Store at 2°C to 8°C if not used immediately.
7) The final volume of infusion solution (110 mL) will be more than the volume administered to the patient (100 mL) to account for the priming of the IV tubing and to ensure that the patient will receive the full dose of Blintumomab.
8) Infuse Blintumomab solution according to the instructions on the pharmacy label on the prepared bag at an infusion rate of 0.6 mL/hour for a duration of 7 days.

l. Administer Blintumomab as a continuous intravenous infusion at a constant flow rate using an infusion pump.
m. The pump should be programmable, lockable, non-elastomeric, and have an alarm.
n. When administering via a multi-lumen venous catheter, blintumomab should be infused through a dedicated lumen.
o. At the end of the infusion, any unused blintumomab solution in the IV bag and IV tubing should be disposed of in accordance with local requirements.

C. How Supplied

1. Blinatumomab is supplied in a single-dose vial as a sterile, preservative-free, white to off-white lyophilized powder for intravenous administration.
2. A Blinatumomab package contains:
    a. One Blinatumomab 35 mcg single-use vial containing a sterile, preservative-free, white to off-white lyophilized powder
    b. One IV Solution Stabilizer 10 mL single-use glass vial containing a sterile, preservative-free, colorless to slightly yellow, clear solution. **Do not use this IV Solution Stabilizer to reconstitute Blinatumomab.**

D. Storage and Handling

1. Store blinatumomab and IV Solution Stabilizer vials in the original package refrigerated at 2°C to 8°C (36°F to 46°F) and protect from light until time of use
2. Do not freeze and do not use product that has been frozen
3. Store and transport the prepared IV bag containing blinatumomab solution for infusion at 2°C to 8°C (36°F to 46°F) conditions
4. The prepared IV bag can remain at room temperature up to 48 hours (without preservative) or 7 days (with preservative), including infusion time
    a. If the prepared IV bag is not administered within the time frames and temperatures indicated, it must be discarded; it should not be refrigerated again

E. Compatibility
1. Compatible with normal saline

F. Procedures: Preparation of product, Infusion rates, post infusion monitoring time.
1. Explain the reasoning for visit and use of anifrolumab-fnia.
2. Don gloves.

3. Establish venous access prior to preparation of drug.
4. Counsel patient on warnings, precautions, and potential side effects including but not limited to those listed below under Clinical Monitoring and Table 1.
5. Prepare Product
6. At the end of the infusion, any unused Blinatumomab solution in the IV bag and IV lines should be disposed of in accordance with local requirements.

VI. CLINICAL MONITORING

A. Liver function tests: ALT, AST, gamma-glutamyl transferase, and total bilirubin at baseline and throughout therapy.

B. Cytokine release syndrome: Signs/symptoms include fever, fatigue, dizziness, headache, hypotension, nausea, vomiting, chills, face swelling, wheezing/shortness of breath, skin rash, disseminated intravascular coagulation (DIC), capillary leak syndrome (CLS), and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS)

C. Neurotoxicity: Signs/symptoms include seizures, difficulty in speaking or slurred speech, loss of consciousness, confusion and disorientation, loss of balance

D. Signs and symptoms of infection

E. Tumor lysis syndrome

F. Local reactions at injection sites

G. Monitor CBC with differential for neutropenia, anemia, or thrombocytopenia

VII. REFERENCES:

Onyx Pharmaceuticals. Blincyto (Blinatumomab) full prescribing information (online). Available from URL: http://www.onyx.com/file.cfm/723/docs/blincyto_pi_hcp_english.pdf. Accessed 2015 May 15.

Amgen Inc., Blincyto (Blinatumomab) Risk Evaluation and Mitigation Strategy (online). Available from URL: http://www.blincytorems.com/HCP.pdf. Accessed 2015 May 15.

Blinatumomab. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Hudson, OH. Available from URL: http://online.lexi.com. Accessed 2015 May 15.

Table 1: Managing Adverse Effects

Adverse Reaction	Grade	Patients Weighing ≥ 45 kg	Patients Weighing <45 kg
Cytokine Release Syndrome (CRS)	3	**Interrupt Blincyto.** Administer Dexamethasone 8 mg every 8 hours IV or orally for up to 3 days, and taper over 4 days. When CRS is resolved, restart Blincyto at 9 mcg/day, and escalate to 28 mcg/day after 7 days if adverse reaction does not occur	**Interrupt Blincyto.** Administer dexamethasone 5 mg/m² (maximum of 8 mg) every 8 hours IV or orally for up to 3 days, and taper thereafter over 4 days. When CRS is resolved, restart Blincyto at 5 mcg/m²/day, and escalate to 15 mcg/m²/day after 7 days if adverse reaction does not recur.
	4	**Discontinue Blincyto permanently.** Administer dexamethasone as instructed for Grade 3 CRS	
Neurological Toxicity	Seizure	**Discontinue Blincyto permanently if more than one seizure occurs.**	
	Grade 3	**Interrupt Blincyto** until no more than Grade 1 (mild) and for at least 3 days, then restart Blincyto at 9 mcg/day. Escalate to 28 mcg/day after 7 days if the adverse reaction does not recur. If adverse reaction occurred at 9 mcg/day, or if the adverse reaction takes more than 7 days to resolve discontinue Blincyto permanently.	**Interrupt Blincyto** until no more than Grade 1 (mild) and for at least 3 days, then restart Blincyto at 5 mcg/m²/day. Escalate to 15 mcg/m²/day after 7 days if the adverse reaction does not recur. If adverse reaction occurred at 5 mcg/m²/day, or if the adverse reaction takes more than 7 days to resolve discontinue Blincyto permanently.
	Grade 4	**Discontinue Blicyto permanently.**	
Other Clinically Relevant Adverse Side Effects	Grade 3	**Interrupt Blincyto** until no more than Grade 1 (mild), then restart Blincyto at 9 mcg/day. Escalate to 28 mcg/day after 7 days if the adverse reaction does not recur. If adverse reaction takes more than 14 days to resolve discontinue Blincyto permanently.	**Interrupt Blincyto** until no more than Grade 1 (mild), then restart Blincyto at 5 mcg/m²/day. Escalate to 15 mcg/m²/day after 7 days if the adverse reaction does not recur. If adverse reaction takes more than 14 days to resolve discontinue Blincyto permanently.
	Grade 4	***Consider discontinuing*** **Blincyto permanently**	

Table 2: For Patients Weighing Greater Than or Equal to 45 kg: Volumes to Add to IV Bag

0.9% Sodium Chloride Injection, USP (starting volume)			270 mL
IV Solution Stabilizer			5.5 mL
Dose	**Infusion Duration**	**Infusion Rate**	**Reconstituted BLINCYTO**
9 mcg/day	24 hours	10 mL/hour	0.83 mL
	48 hours	5 mL/hour	1.7 mL
28 mcg/day	24 hours	10 mL/hour	2.6 mL
	48 hours	5 mL/hour	5.2 mL*

* 2 packages of BLINCYTO are needed for preparation of 28 mcg/day dose infused over 48 hours at a rate of 5 mL/hour.

Table 3: For Patients Weighing Less Than 45 kg: Volumes to Add to IV Bag for 5 mcg/m2 /day Dose

0.9% Sodium Chloride Injection, USP (starting volume)				270 mL
IV Solution Stabilizer				5.5 mL
Dose	**Infusion Duration**	**Infusion Rate**	**BSA (m^2)**	**Reconstituted BLINCYTO**
5 mcg/m^2/day	24 hours	10 mL/hour	1.5 – 1.59	0.7 mL
			1.4 – 1.49	0.66 mL
			1.3 – 1.39	0.61 mL
			1.2 – 1.29	0.56 mL
			1.1 – 1.19	0.52 mL
			1 – 1.09	0.47 mL
			0.9 – 0.99	0.43 mL
			0.8 – 0.89	0.38 mL
			0.7 – 0.79	0.33 mL
			0.6 – 0.69	0.29 mL
			0.5 – 0.59	0.24 mL
			0.4 – 0.49	0.2 mL
5 mcg/m^2/day	48 hours	5 mL/hour	1.5 – 1.59	1.4 mL
			1.4 – 1.49	1.3 mL
			1.3 – 1.39	1.2 mL
			1.2 – 1.29	1.1 mL
			1.1 – 1.19	1 mL
			1 – 1.09	0.94 mL
			0.9 – 0.99	0.85 mL
			0.8 – 0.89	0.76 mL
			0.7 – 0.79	0.67 mL
			0.6 – 0.69	0.57 mL
			0.5 – 0.59	0.48 mL
			0.4 – 0.49	0.39 mL

Table 4 : For Patients Weighing Less Than 45 kg: Volumes to Add to IV Bag for 15 mcg/m2 /day Dose

0.9% Sodium Chloride Injection, USP (starting volume)				270 mL
IV Solution Stabilizer				5.5 mL
Dose	**Infusion Duration**	**Infusion Rate**	**BSA (m^2)**	**Reconstituted BLINCYTO**
15 mcg/m^2/day	24 hours	10 mL/hour	1.5 – 1.59	2.1 mL
			1.4 – 1.49	2 mL
			1.3 – 1.39	1.8 mL
			1.2 – 1.29	1.7 mL
			1.1 – 1.19	1.6 mL
			1 – 1.09	1.4 mL
			0.9 – 0.99	1.3 mL
			0.8 – 0.89	1.1 mL
			0.7 – 0.79	1 mL
			0.6 – 0.69	0.86 mL
			0.5 – 0.59	0.72 mL
			0.4 – 0.49	0.59 mL
15 mcg/m^2/day	48 hours	5 mL/hour	1.5 – 1.59	4.2 mL*
			1.4 – 1.49	3.9 mL*
			1.3 – 1.39	3.7 mL*
			1.2 – 1.29	3.4 mL*
			1.1 – 1.19	3.1 mL*
			1 – 1.09	2.8 mL
			0.9 – 0.99	2.6 mL
			0.8 – 0.89	2.3 mL
			0.7 – 0.79	2 mL
			0.6 – 0.69	1.7 mL
			0.5 – 0.59	1.4 mL
			0.4 – 0.49	1.2 mL

* 2 packages of BLINCYTO are needed for preparation of 15 mcg/m^2/day dose infused over 48 hours at a rate of 5 mL/hour for patients with a BSA greater than 1.09 m^2.

Table 5: For 7-Day Infusion: Volumes to Add to IV Bag for 28 mcg/day and 15 mcg/m2 /day; Not Recommended for Patients Less Than 22 kg

Bacteriostatic 0.9% Sodium Chloride Injection, USP (starting volume)	90 mL
IV Solution Stabilizer	2.2 mL
Reconstituted BLINCYTO	Specific volume listed below in table
Quantity Sufficient (qs) with 0.9% Sodium Chloride Injection, USP to a Final Volume of 110 mL	
Infusion Duration	7 days
Infusion Rate	0.6 mL/hour

Patient Weight	**Dose**	**BSA (m^2)**	**Number of BLINCYTO Packages**	**Reconstituted BLINCYTO**	**0.9% Sodium Chloride Injection, USP to qs to a Final Volume of 110 mL**
Greater than or equal to 45 kg *(fixed-dose)*	28 mcg/day		6	16.8 mL	1 mL
22-45 kg *(BSA-based dose)*	15 mcg/m^2/day	1.5 – 1.59	5	14 mL	3.8 mL
		1.4 – 1.49	5	13.1 mL	4.7 mL
		1.30 – 1.39	5	12.2 mL	5.6 mL
		1.20 – 1.29	5	11.3 mL	6.5 mL
		1.10 – 1.19	4	10.4 mL	7.4 mL
		1 – 1.09	4	9.5 mL	8.3 mL
		0.9 – 0.99	4	8.6 mL	9.2 mL

APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS

Emergency Medication After Your Infusion

Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.
The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.

Start with a clean work surface and clean hands.

Open the supply bag labeled Anaphylaxis Kit Contents.

You will need:

1. **Bag containing Pills** (2 Acetaminophen and 2 Diphenhydramine)
2. **Bag containing Alcohol Prep Pads**
3. **Bag labeled IM Epinephrine**

All other contents will not be needed.

Open the IM Epinephrine Bag

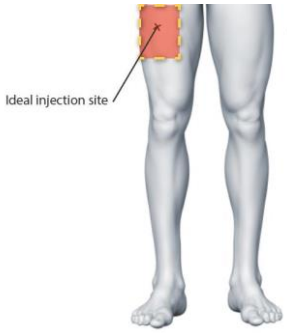
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampul use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampul of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

1. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
2. Using an **alcohol swab, wipe the neck of the epinephrine ampul.**
3. Holding the ampul upright, **swirl and flick the ampul until all fluid flows to the bottom chamber** (the top chamber should be empty).
4. Using a new alcohol wipe, grasp the neck of the ampul and with your other hand grasp the bottom chamber of the ampul. **Quickly snap the top of the ampul off, directing the snap way from you.**
5. **Place the tip of the brown filter needle inside the ampul**. Tilting the ampul, **withdraw dose of medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampul and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**

7. **Push the air out of the syringe by gently pushing on the plunger**.
8. Replace the cap on the brown filter needle. Discard remainder in ampul.
9. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



1. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
2. **Push the needle into your leg muscle straight** in at a 90-degree angle.
3. **Inject the medication** by depressing the plunger in a slow and steady motion.
4. **Remove the needle** and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (**maximum 3 doses**) if ordered per protocol.

Take the pills by mouth.

a. 2 – Acetaminophen
b. 2 – Diphenhydramine

Place all trash in the bag the pills came in and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.
Call 911 or have someone drive you to the emergency department.