DOSAGE AND ADMINISTRATION

INFUSION PROCESS[1]

Because of its short half life (<3 hours) BLINCYTO® must be administered as a cIV infusion delivered at a constant flow rate using an infusion pump.[1]

BLINCYTO® may be administered either from an IV bag or from a cassette.[1]

Infusion bags are prepared to infuse over 24, 48, 72 or 96 hours and each duration has a specific constant infusion rate to ensure the correct dose of BLINCYTO® is administered.[1]

Different infusion durations are designed to help treatment fit around the schedules of the care team and patient.

Clearly label the prepared IV infusion bag or cassette with the dose, infusion rate and duration of infusion.[1]

IV LINE

IMPORTANT NOTE: Do not flush infusion lines into the patient, as it will cause an inadvertent bolus of drug to be administered. BLINCYTO® should be infused through a dedicated lumen.[1]

The BLINCYTO® solution for infusion must be administered using IV tubing that contains a sterile, non-pyrogenic, low protein-binding 0.2 micron in-line filter.[1]

BLINCYTO® is compatible with polyolefin, PVC non-di-ethylhexylphthalate (non-DEHP), or ethyl vinyl acetate (EVA) infusion bags/pump cassettes.[1]

CHANGE OF IV BAG OR CASSETTE

The IV bag or cassette must be changed at least every 96 hours by a healthcare professional for sterility reasons.[1]

If using IV bags, to minimise the number of aseptic transfers, it is recommended to use a 250 mL-prefilled IV bag.[1] 250 mL prefilled IV bags typically contain overfill with a total volume of 265 mL to 275 mL.[1] **BLINCYTO® dose calculations are based on a starting volume of 265 mL to 275 mL 0.9% sodium chloride.**[1]

PUMP SPECIFICATIONS

The infusion pump should be:[1]

- **Programmable:** to set infusion rate and duration
- **Lockable:** to avoid patients accidentally changing settings
- **Non-elastomeric:** to provide a constant infusion rate
- **Fitted with an alarm:** to alert patients and care team to problems with the pump

Reference: 1. BLINCYTO® (blinatumomab) Product Information. www.amgen.com.au/Blincyto.PI.

DOSAGE AND ADMINISTRATION

IMPORTANT CONSIDERATIONS WHEN USING BLINCYTO®

Use aseptic technique[1]

To prevent **accidental contamination**, prepare BLINCYTO® according to aseptic standards (see Product Information for more information)

Follow instructions carefully[1]

It is very important that the instructions for preparation (including reconstitution and dilution) and administration are strictly followed to **minimise medication errors** (including underdose and overdose)

Do not flush the infusion line[1]

Do not flush the BLINCYTO® IV catheter, especially when changing infusion bags. Flushing when changing bags or at completion of infusion can result in excess dosage and complications thereof

Patients should not adjust the pump setting[2]

Inform patients that any changes to pump function may result in **dosing errors**. If there is a problem with the infusion pump or the pump alarms, patients should **contact their doctor or nurse immediately**

In the event of overdose:[1]

- **Temporarily interrupt** the infusion
- **Monitor** the patient

Consider re-initiation of BLINCYTO® at the correct therapeutic dose

Medication errors have been observed with BLINCYTO® treatment. It is very important that the instructions for preparation (including reconstitution and dilution) and administration are strictly followed to minimise medication errors (including underdose and overdose).[1]

References: 1. BLINCYTO® (blinatumomab) Product Information. www.amgen.com.au/Blincyto.PI
2. BLINCYTO® (blinatumomab) Consumer Medicine Information. www.amgen.com.au/Blincyto.CMI

DOSAGE AND ADMINISTRATION

BLINCYTO® INFUSION CHECKLIST[1]

INFUSION CHECKLIST[1]

- ✓ The patient has received appropriate dexamethasone premedication if starting a new cycle
- ✓ The infusion will take place through a dedicated lumen
- ✓ The BLINCYTO® solution has been prepared at a concentration of 9 mcg/day (starting dose) or 28 mcg/day (full dose), as appropriate for patients weighing ≥45 kg and 5 mcg/m^2/day (starting dose; not to exceed 9 mcg/day) or 15 mcg/m^2/day (full dose; not to exceed 28 mcg/day), as appropriate, for patients weighing <45 kg
- ✓ The IV tubing is attached to the bag along with an in-line, sterile, non-pyrogenic, low protein binding 0.2 micron in-line filter
- ✓ Excess air has been removed (particularly important for use with an ambulatory infusion pump)
- ✓ The IV line has been primed with the prepared solution for infusion
- ✓ The infusion bag size is correct (250 mL with usual overfill volume of 265 to 275 mL)
- ✓ The duration of infusion has been confirmed (24, 48, 72, or 96 h)
- ✓ The infusion rate has been verified
- ✓ The pump has been correctly programmed and the tubing and filter are properly set up

THERAPY INTERRUPTION

- Healthcare professional supervision or hospitalisation is recommended in instances where treatment is being re-initiated following an interruption of ≥4 hours[1]

Medication errors have been observed with BLINCYTO® treatment. It is very important that the instructions for preparation (including reconstitution and dilution) and administration are strictly followed to minimise medication errors (including underdose and overdose).[1]

MEDICATION OVERDOSE

Stop the infusion immediately	**Consult the treating physician**	**Assess for treatment-related adverse events**	**If none, consider, with the treating physician, resuming therapy at the correct dose**	**If the overdose results in an adverse event, monitor the patient until all signs of toxicity are resolved**

Reference: 1. BLINCYTO® (blinatumomab) Product Information. www.amgen.com.au/Blincyto.PI.

DOSAGE AND ADMINISTRATION

BLINCYTO® IV PREPARATION[1]

STEPS TO PREPARE BLINCYTO® IV SOLUTION UNDER CONDITIONS USING ASEPTIC TECHNIQUES[1]

Step 1	• Transfer appropriate amount of BLINCYTO® IV solution stabiliser to the 0.9% Sodium Chloride infusion bag • Gently mix the contents of the bag to avoid foaming • Discard remaining BLINCYTO® IV solution stabiliser vial if applicable
Step 2	• Reconstitute BLINCYTO® lyophilised powder vial with 3 mL of Preservative Free Sterile Water for injection • Do not reconstitute BLINCYTO® with BLINCYTO® IV solution stabiliser • Do not shake • Gently swirl contents to avoid excess foaming • Reconstitute the required number of BLINCYTO® vials • Visually inspect the reconstituted solution for particulate matter and to confirm colour. The solution should be clear to slightly opalescent, colourless to slightly yellow
Step 3	• Transfer appropriate amount of reconstituted BLINCYTO® solution into the 0.9% Sodium Chloride infusion bag containing IV solution stabilser • Gently mix the contents of the bag to avoid foaming
Step 4	• Attach the IV tubing with the sterile 0.2 micron in-line filter to the prepared infusion bag
Step 5	• Remove air from the prepared BLINCYTO® infusion solution bag
Step 6	• Prime the IV tubing with the prepared BLINCYTO® infusion solution • Do not prime the IV tubing with 0.9% Sodium Chloride solution for injection
Step 7	• Store the prepared BLINCYTO® infusion solution bags at 2^0C to 8^0C for a maximum of 10 days if not immediately used • Clearly label the prepared IV infusion bag with the dose, infusion rate and duration of infusion

Note: for comprehensive preparation instructions, please refer to the BLINCYTO® Product Information.

Reference: 1. BLINCYTO® (blinatumomab) Product Information. www.amgen.com.au/Blincyto.PI.

DOSAGE AND ADMINISTRATION

BLINCYTO® CASSETTE PREPARATION[1]

STEPS TO PREPARE BLINCYTO® CASSETTE UNDER CONDITIONS USING ASEPTIC TECHNIQUES[1]

Step 1	• Transfer appropriate amount of 0.9% Sodium Chloride solution to the cassette
Step 2	• Transfer appropriate amount of BLINCYTO® IV solution stabiliser to the cassette • Gently mix the contents of the cassette to avoid foaming • Discard remaining BLINCYTO® IV solution stabiliser vial if applicable
Step 3	• Reconstitute BLINCYTO® lyophilised powder vial with 3 mL of Preservative Free Sterile Water for injection • Do not reconstitute BLINCYTO® with BLINCYTO® IV solution stabiliser • Do not shake • Gently swirl contents to avoid excess foaming • Reconstitute the required number of BLINCYTO® vials as needed • Visually inspect the reconstituted solution for particulate matter and to confirm colour. The solution should be clear to slightly opalescent, colourless to slightly yellow
Step 4	• Transfer appropriate amount of reconstituted BLINCYTO® solution into the cassette • Gently mix the contents of the cassette to avoid foaming • Redraw approximately 10 mL of fluid from the cassette and inject back to ensure no BLINCYTO® remains in the cassette line. Gently mix again
Step 5	• Remove air from the cassette using a syringe
Step 6	• Attach the IV tubing with the sterile 0.2 micron in-line filter to the cassette using a syringe
Step 7	• Prime the IV tubing with the prepared BLINCYTO® solution for infusion • Do not prime the IV tubing with 0.9% Sodium Chloride solution for injection
Step 8	• Store at 2°C to 8°C for a maximum of 10 days if not used immediately • Clearly label the prepared cassette with the dose, infusion rate and duration of infusion

Note: for comprehensive preparation instructions, please refer to the BLINCYTO® Product Information.

Reference: 1. BLINCYTO® (blinatumomab) Product Information. www.amgen.com.au/Blincyto.PI.

DOSAGE AND ADMINISTRATION

DEFINING A BLINCYTO® SCHEDULE[1]

It is recommended that the multidisciplinary care team, including prescribing physician, pharmacist and nurse, work with the patient to define a schedule for infusion bag changes.

Below is part of an EXAMPLE schedule for a **adult patient with relapsed or refractory B-ALL weighing ≥45 kg** starting treatment. Please note it is NOT a recommendation of how patients should receive BLINCYTO®; individual hospital regulations and processes as well as each patient's situation need to be taken into consideration.[1]

Day			Treatment setting	Bag prepared by pharmacist	Bag changed by HCP
1	Tuesday	AM	Hospitalisation for 9 days	72-hour bag	
		PM			72-hour bag
2	Wednesday	AM			
		PM			
3	Thursday	AM			
		PM			
4	Friday	AM		96-hour bag	
		PM			96-hour bag
5	Saturday	AM			
		PM			
6	Sunday	AM			
		PM			
7	Monday	AM			
		PM			
8	Tuesday	AM		72-hour bag	
		PM			72-hour bag
9	Wednesday	AM			
		PM			
10	Thursday	AM	Patient returns home		
		PM			
11	Friday	AM	Outpatient visit	96-hour bag	
		PM			96-hour bag
12	Saturday	AM			
		PM			
13	Sunday	AM			
		PM			
14	Monday	AM			
		PM			
15	Tuesday	AM	Outpatient visit	72-hour bag	
		PM			72-hour bag
16	Wednesday	AM			
		PM			
17	Thursday	AM			
		PM			
18	Friday	AM	Outpatient visit	96-hour bag	
		PM			96-hour bag
19	Saturday	AM			
		PM			
20	Sunday	AM			
		PM			
21	Monday	AM			
		PM			
22	Tuesday	AM	Outpatient visit	72-hour bag	
		PM			72-hour bag
23	Wednesday	AM			
		PM			
24	Thursday	AM			
		PM			
25	Friday	AM	Outpatient visit	96-hour bag	
		PM			96-hour bag
26	Saturday	AM			
		PM			
27	Sunday	AM			
		PM			
28	Monday	AM	End of cycle visit		
		PM			
2-week treatment-free interval					

Reference: 1. BLINCYTO® (blinatumomab) Product Information. www.amgen.com.au/Blincyto.PI.

DOSAGE AND ADMINISTRATION

AFTER RECONSTITUTION AND DILUTION[1]

Storage requirements for reconstituted BLINCYTO® and prepared IV bag or cassettes[1]

Maximum storage time of reconstituted BLINCYTO®* solution		Maximum combined storage and infusion time of diluted BLINCYTO®* solution in IV bags or cassette	
Room Temperature (Below 25ºC**)	Refrigerated (2ºC to 8ºC)	Room Temperature (Below 25ºC**)	Refrigerated (2ºC to 8ºC)
4 hours	24 hours	96 hours***	10 days***

*While stored, protect reconstituted BLINCYTO® from light. **Do not freeze. ***If IV bag or cassette containing BLINCYTO® solution for infusion is not administered within the timeframes and temperatures indicated, it must be discarded; it should not be refrigerated again.

The maximum storage time of the prepared IV bag at room temperature should not be longer than 6 hours prior to the start of infusion.[1]

Store and transport the prepared IV bag or cassette containing BLINCYTO® solution at 2ºC to 8ºC (Refrigerate. Do not freeze).[1]

DISPOSAL

At the end of the infusion, any unused BLINCYTO® solution in the IV bag and IV lines should be disposed of in accordance with local requirements.[1]

SPILLAGE

BLINCYTO® is not a cytotoxic chemotherapy.[2] In case of spillage, please follow your hospital or facility's protocol for immunotherapies or biological medicines.

References: 1. BLINCYTO® (blinatumomab) Product Information. www.amgen.com.au/Blincyto.PI. **2.** Amgen Data on File.

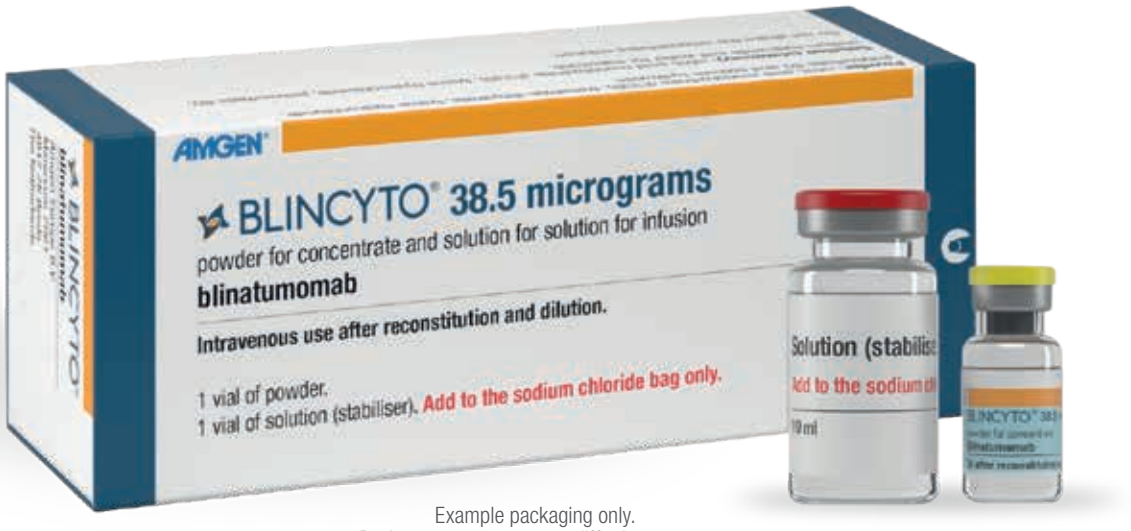
DOSAGE AND ADMINISTRATION

BLINCYTO® PRESENTATION AND STORAGE[1]

Pack size: 1 vial BLINCYTO® and 1 vial IV solution stabiliser for BLINCYTO® supplied in a composite pack.[1]

Each BLINCYTO® pack contains:[1]

- BLINCYTO® supplied in a single-use glass vial as a sterile, preservative-free, white to off-white lyophilised powder (38.5 mcg/vial); and
- IV solution stabiliser supplied in a 10 mL single-use glass vial as a sterile, preservative-free, colourless to slightly yellow, clear solution. **Do not use the IV solution stabiliser to reconstitute BLINCYTO®**



Example packaging only.
Package appearance may differ by country.

It is recommended to store unopened BLINCYTO® and solution stabiliser for BLINCYTO® vials in a refrigerator at 2°C to 8°C in the original carton. Do not freeze. Protect from direct light.[1]

Once removed from the refrigerator, unopened BLINCYTO® and solution stabiliser for BLINCYTO® vials may be stored at or below 25°C for up to 8 hours in the original container (do not freeze).[1]

Reference: 1. BLINCYTO® (blinatumomab) Product Information. www.amgen.com.au/Blincyto.PI.

BLINCYTO®
(blinatumomab)

For more information on BLINCYTO® or to report any adverse events or product complaints involving BLINCYTO® please contact Australia Medical Information on 1800 803 638

PBS Information: Section 100 listed. Authority required.
Refer to PBS Schedule for full Authority listing.

***WARNING*:** *The following have occurred in patients receiving BLINCYTO®:*
• Cytokine Release Syndrome, which may be life-threatening or fatal • Neurological toxicities, which may be severe, life-threatening, or fatal • Reactivation of JC viral infection
Interrupt or discontinue BLINCYTO® as recommended if any of these adverse events occur
(See Section 4.4 Special warnings and precautions for use and Section 4.2 Dose and method of administration).

REFER TO FULL PRODUCT INFORMATION BEFORE PRESCRIBING; AVAILABLE FROM AMGEN AUSTRALIA PTY LTD, PH: 1800 803 638 OR AT WWW.AMGEN.COM.AU/BLINCYTO.PI

For more information about BLINCYTO® or to report an adverse event or product complaints about BLINCYTO®, please contact Amgen Medical Information on 1800 803 638.

BLINCYTO® Minimum Product Information: Indication: treatment of relapsed or refractory (R/R) B-cell precursor acute lymphoblastic leukaemia (ALL); treatment of minimal residual disease (MRD) positive ALL in patients in complete haematological remission. **Contraindications:** hypersensitivity to blinatumomab, CHO-derived proteins or any excipient. **Precautions:** neurologic events; increased risk for serious infections; cytokine release syndrome; infusion reactions; tumour lysis syndrome, pancreatitis. Management of these adverse reactions may require interruption or discontinuation of treatment. Neutropenia and febrile neutropenia; elevated liver enzymes; leukoencephalopathy; medication errors – strictly follow preparation and administration instructions. Pregnancy Category: C. Use contraception during and for 48 hours after treatment. Discontinue breast-feeding during and for at least 48 hours after treatment. Do not use recommended adult fixed dose in paediatric patients. No data in patients aged less than 28 days. **Interactions:** low potential of clinically meaningful drug interaction with BLINCYTO® mediated cytokine elevation. Vaccination with live viral vaccines not recommended 2 weeks prior to or during treatment, and until recovery of B lymphocytes to normal range following last treatment cycle. **Adverse Reactions:** Common: infections, pyrexia, infusion-related reactions, headache, anaemia, febrile neutropenia, neutropenia, thrombocytopenia, oedema, increased liver enzymes, fatigue, nausea, tremor, hypokalaemia, diarrhoea, chills. See also Precautions for serious adverse reactions. **Dosage & Administration:** R/R ALL: Single cycle is 4 weeks continuous intravenous (cIV) infusion then 2 week treatment free interval. *For patients greater than or equal to 45 kg (fixed dose)*: Cycle 1 – starting dose 9 micrograms/day for days 1-7, then 28 micrograms/day for days 8-28. All other cycles 28 micrograms/day for 4 weeks. For patients less than 45 kg (body surface area based dose): Cycle 1 – starting dose 5 micrograms/m^2/day for days 1-7 (do not exceed 9 micrograms/day), then 15 micrograms/m^2/day (do not exceed 28 micrograms/day); all other cycles, 15 micrograms/m^2/day (do not exceed 28 micrograms/day). For maintenance, 28 day cIV infusion, then 56 days treatment free. Hospitalise at least first 9 days of Cycle 1 and first 2 days of Cycle 2. Supervision or hospitalisation for other cycle starts and reinitiation. Adults: premedicate with 20 mg IV dexamethasone prior to initiation of each cycle. Intrathecal chemotherapy prophylaxis recommended before and during therapy. Treat with dexamethasone (≤ 24 mg/day) if high tumour burden. Paediatrics: premedicate with dexamethasone 10 mg/m2 (not to exceed 20 mg) oral or IV 6 to 12 hours prior to start of BLINCYTO® (Cycle 1 day 1), followed by premedication with dexamethasone 5 mg/m^2 oral or IV within 30 minutes of start of BLINCYTO® (Cycle 1 day 1). **MRD+ ALL:** 28 day cIV infusion then 14 days treatment free, for up to 4 cycles; premedicate with prednisone 100 mg IV or equivalent 1 hour prior to start of BLINCYTO® each cycle; hospitalise first 3 days Cycle 1 and first 2 days Cycle 2, supervise/hospital for subsequent cycle starts and reinitiation – see full PI. R/R & MRD+ ALL – Interrupt BLINCYTO® if grade 3 neurological events, Cytokine Release Syndrome or other clinically relevant adverse reactions occur see full PI.

BLINCYTO®
(blinatumomab)

AMGEN®