BLINCYTO®▼ (blinatumomab)

Important Risk Minimisation Information for Pharmacists

This educational brochure contains important information regarding the reconstitution and preparation procedures for blinatumomab. To ensure the safe and effective use of the medicinal product and appropriate management of the important selected risks, please carefully read this material before preparing the medicinal product.

If you have any questions about the reconstitution and preparation of blinatumomab please refer to the Summary of Product Characteristics (SmPC), which is provided on the European Medicines Agency website under following link:
https://www.ema.europa.eu/en/medicines/human/EPAR/blincyto#product-information-section

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions to the Medicines Authority by post or e-mail: ADR reporting/ Sir Temi Zammit Building, Malta Life Sciences Park, San Gwann or on www.medicinesauthority.gov.mt/adrportal

Important information about the preparation of BLINCYTO intravenous administration

Specific reconstitution and dilution instructions are provided for each dose and infusion time. Verify the prescribed dose and infusion time of BLINCYTO and identify the appropriate dosing preparation requirements below.

- **For patients <u>weighing greater than or equal to 45kg</u> use Table 1 and Guide 1.**
  Note: For patients <u>weighing less than 45 kg</u> please use Tables 2 to 5 and Guide 2.

Table 1. Preparation of BLINCYTO infusion solution for patients <u>weighing greater than or equal to 45 kg</u>: volumes of sodium chloride 9 mg/mL (0.9%) solution for injection, solution (stabiliser), and reconstituted BLINCYTO to add to infusion bag

Dose	Infusion duration	Normal Saline (250-ml bag)[a]	Solution (Stabiliser) Volume (mL)	Required Number of BLINCYTO vials	Reconstituted BLINCYTO solution (mL)	Infusion rate (mL/hr)
9 mcg/day	24 hours	1	5.5	1	0.83	10
	48 hours	1	5.5	1	1.7	5
	72 hours	1	5.5	1	2.5	3.3
	96 hours	1	5.5	2	3.3	2.5
28 mcg/day	24 hours	1	5.5	1	2.6	10
	48 hours	1	5.5	2	5.2	5
	72 hours	1	5.5	3	8	3.3
	96 hours	1	5.5	4	10.7	2.5

[a]Normal saline (0.9% Sodium Chloride)

Use only polyolefin, PVC non-di-ethylhexylphthalate (non-DEHP), or ethyl vinyl acetate (EVA) infusion bags/pump cassettes and polyolefin, PVC non-DEHP, or EVA intravenous tubing with a sterile, non-pyrogenic, low protein-binding 0.2 µm in-line filter

Guide 1: Steps to prepare BLINCYTO infusion solution under aseptic conditions using aseptic techniques

Step 1	• Before preparation, consult the dosing tables and assemble the correct number of vials and other excipients
Step 2	• Transfer appropriate amount of Solution (stabiliser) to the Normal Saline (0.9% Sodium Chloride) infusion bag • Gently mix the contents of the bag to avoid foaming • Discard remaining Solution (stabiliser) vial if applicable
Step 3	• Reconstitute BLINCYTO powder for concentrate with 3 mL of Water for Injection • Do not reconstitute BLINCYTO with the Solution (stabiliser) • Do not shake • Gently swirl contents to avoid excess foaming • Reconstitute the required number of BLINCYTO vials (see Table 1). 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 Normal Saline (0.9% Sodium Chloride) infusion bag • Gently mix the contents of the bag to avoid foaming
Step 5	• Attach the intravenous tubing to the prepared BLINCYTO infusion solution bag with the sterile 0.2 µm in-line filter
Step 6	• Remove air from the prepared BLINCYTO infusion solution bag
Step 7	• Prime the intravenous infusion line with the prepared BLINCYTO infusion solution • Do not prime the intravenous infusion line with Normal Saline (0.9% Sodium Chloride) solution for injection
Step 8	• Store the prepared BLINCYTO infusion solution bag at 2°C to 8°C for a maximum of 10 days if not immediately used (for further information, please see section 6.3 of the SmPC)

Important information about the preparation of BLINCYTO intravenous administration

- **For patients weighing less than 45 kg please use Tables 2 to 5 and Guide 2.**
  Note: For patients weighing greater than or equal to 45 kg use Table 1 and Guide 1.

Table 2. Preparation of BLINCYTO infusion solution for patients weighing less than 45 kg: Volumes of sodium chloride 9 mg/mL (0.9%) solution for injection, solution (stabiliser), and reconstituted BLINCYTO to add to infusion bag for 5 mcg/m^2/day dose for 24 and 48 Hours infusion

Dose	Infusion duration	Normal Saline (250-ml bag)[a]	Solution (Stabiliser) Volume (mL)	Required Number of BLINCYTO vials	Body Surface Area (m^2)	Reconstituted BLINCYTO solution (mL)	Infusion rate (mL/hr)
5 mcg/m²/day	24 hours	1	5.5	1	1.50 – 1.59	0.70 mL	10
					1.40 – 1.49	0.66 mL	
					1.30 – 1.39	0.61 mL	
					1.20 – 1.29	0.56 mL	
					1.10 – 1.19	0.52 mL	
					1.00 – 1.09	0.47 mL	
					0.90 – 0.99	0.43 mL	
					0.80 – 0.89	0.38 mL	
					0.70 – 0.79	0.33 mL	
					0.60 – 0.69	0.29 mL	
					0.50 – 0.59	0.24 mL	
					0.40 – 0.49	0.20 mL	
5 mcg/m²/day	48 hours	1	5.5	1	1.50 – 1.59	1.4 mL	5
					1.40 – 1.49	1.3 mL	
					1.30 – 1.39	1.2 mL	
					1.20 – 1.29	1.1 mL	
					1.10 – 1.19	1.0 mL	
					1.00 – 1.09	0.94 mL	
					0.90 – 0.99	0.85 mL	
					0.80 – 0.89	0.76 mL	
					0.70 – 0.79	0.67 mL	
					0.60 – 0.69	0.57 mL	
					0.50 – 0.59	0.48 mL	
					0.40 – 0.49	0.39 mL	

[a]Normal saline (0.9% Sodium Chloride)

Use only polyolefin, PVC non-di-ethylhexylphthalate (non-DEHP), or ethyl vinyl acetate (EVA) infusion bags/pump cassettes and polyolefin, PVC non-DEHP, or EVA intravenous tubing with a sterile, non-pyrogenic, low protein-binding 0.2 µm in-line filter

Table 3. Preparation of BLINCYTO infusion solution for patients weighing less than 45 kg: Volumes of sodium chloride 9 mg/mL (0.9%) solution for injection, solution (stabiliser), and reconstituted BLINCYTO to add to infusion bag for 5 mcg/m^2/day dose for 72 and 96 Hours infusion

Dose	Infusion duration	Normal Saline (250-ml bag)[a]	Solution (Stabiliser) Volume (mL)	Required Number of BLINCYTO vials	Body Surface Area (m^2)	Reconstituted BLINCYTO solution (mL)	Infusion rate (mL/hr)
5 mcg/m²/day	72 hours	1	5.5	1	1.50 – 1.59	2.1 mL	3.3
					1.40 – 1.49	2.0 mL	
					1.30 – 1.39	1.8 mL	
					1.20 – 1.29	1.7 mL	
					1.10 – 1.19	1.6 mL	
					1.00 – 1.09	1.4 mL	
					0.90 – 0.99	1.3 mL	
					0.80 – 0.89	1.1 mL	
					0.70 – 0.79	1 mL	
					0.60 – 0.69	0.86 mL	
					0.50 – 0.59	0.72 mL	
					0.40 – 0.49	0.59 mL	
5 mcg/m²/day	96 hours	1	5.5	1	1.50 – 1.59	2.8 mL	2.5
					1.40 – 1.49	2.6 mL	
					1.30 – 1.39	2.4 mL	
					1.20 – 1.29	2.3 mL	
					1.10 – 1.19	2.1 mL	
					1.00 – 1.09	1.9 mL	
					0.90 – 0.99	1.7 mL	
					0.80 – 0.89	1.5 mL	
					0.70 – 0.79	1.3 mL	
					0.60 – 0.69	1.2 mL	
					0.50 – 0.59	0.97 mL	
					0.40 – 0.49	0.78 mL	

[a]Normal saline (0.9% Sodium Chloride)

Use only polyolefin, PVC non-di-ethylhexylphthalate (non-DEHP), or ethyl vinyl acetate (EVA) infusion bags/pump cassettes and polyolefin, PVC non-DEHP, or EVA intravenous tubing with a sterile, non-pyrogenic, low protein-binding 0.2 µm in-line filter

Table 4. Preparation of BLINCYTO infusion solution for patients weighing less than 45 kg: volumes of sodium chloride 9 mg/mL (0.9%) solution for injection, solution (stabiliser), and reconstituted BLINCYTO to add to infusion bag for 15 mcg/m^2/day dose for 24 and 48 Hours infusion

Dose	Infusion duration	Normal Saline (250-ml bag)[a]	Solution (Stabiliser) Volume (mL)	Required Number of BLINCYTO vials	Body Surface Area (m^2)	Reconstituted BLINCYTO solution (mL)	Infusion rate (mL/hr)
15 mcg/m²/day	**24 hours**	1	5.5	1	1.50 – 1.59	2.1 mL	10
				1	1.40 – 1.49	2.0 mL	
				1	1.30 – 1.39	1.8 mL	
				1	1.20 – 1.29	1.7 mL	
				1	1.10 – 1.19	1.6 mL	
				1	1.00 – 1.09	1.4 mL	
				1	0.90 – 0.99	1.3 mL	
				1	0.80 – 0.89	1.1 mL	
				1	0.70 – 0.79	1.00 mL	
				1	0.60 – 0.69	0.86 mL	
				1	0.50 – 0.59	0.72 mL	
				1	0.40 – 0.49	0.59 mL	
15 mcg/m²/day	**48 hours**	1	5.5	2	1.50 – 1.59	4.2 mL	5
				2	1.40 – 1.49	3.9 mL	
				2	1.30 – 1.39	3.7 mL	
				2	1.20 – 1.29	3.4 mL	
				2	1.10 – 1.19	3.1 mL	
				1	1.00 – 1.09	2.8 mL	
				1	0.90 – 0.99	2.6 mL	
				1	0.80 – 0.89	2.3 mL	
				1	0.70 – 0.79	2.0 mL	
				1	0.60 – 0.69	1.7 mL	
				1	0.50 – 0.59	1.4 mL	
				1	0.40 – 0.49	1.2 mL	

[a]Normal saline (0.9% Sodium Chloride)

Use only polyolefin, PVC non-di-ethylhexylphthalate (non-DEHP), or ethyl vinyl acetate (EVA) infusion bags/pump cassettes and polyolefin, PVC non-DEHP, or EVA intravenous tubing with a sterile, non-pyrogenic, low protein-binding 0.2 µm in-line filter

Table 5. Preparation of BLINCYTO infusion solution for patients <u>weighing less than 45 kg</u>: volumes of sodium chloride 9 mg/mL (0.9%) solution for injection, solution (stabiliser), and reconstituted BLINCYTO to add to infusion bag for <u>15 mcg/m^2/day dose for 72 and 96 Hours infusion.</u>

Dose	Infusion duration	Normal Saline (250-ml bag)[a]	Solution (Stabiliser) Volume (mL)	Required Number of BLINCYTO vials	Body Surface Area (m^2)	Reconstituted BLINCYTO solution (mL)	Infusion rate (mL/hr)
15 mcg/m²/day	**72 hours**	1	5.5	3	1.50 – 1.59	6.3 mL	3.3
				3	1.40 – 1.49	5.9 mL	
				2	1.30 – 1.39	5.5 mL	
				2	1.20 – 1.29	5.1 mL	
				2	1.10 – 1.19	4.7 mL	
				2	1.00 – 1.09	4.2 mL	
				2	0.90 – 0.99	3.8 mL	
				2	0.80 – 0.89	3.4 mL	
				2	0.70 – 0.79	3.0 mL	
				1	0.60 – 0.69	2.6 mL	
				1	0.50 – 0.59	2.2 mL	
				1	0.40 – 0.49	1.8 mL	
15 mcg/m²/day	**96 hours**	1	5.5	3	1.50 – 1.59	8.4 mL	2.5
				3	1.40 – 1.49	7.9 mL	
				3	1.30 – 1.39	7.3 mL	
				3	1.20 – 1.29	6.8 mL	
				3	1.10 – 1.19	6.2 mL	
				3	1.00 – 1.09	5.7 mL	
				2	0.90 – 0.99	5.1 mL	
				2	0.80 – 0.89	4.6 mL	
				2	0.70 – 0.79	4.0 mL	
				2	0.60 – 0.69	3.4 mL	
				2	0.50 – 0.59	2.9 mL	
				1	0.40 – 0.49	2.3 mL	

[a]Normal saline (0.9% Sodium Chloride)

Use only polyolefin, PVC non-di-ethylhexylphthalate (non-DEHP), or ethyl vinyl acetate (EVA) infusion bags/pump cassettes and polyolefin, PVC non-DEHP, or EVA intravenous tubing with a sterile, non-pyrogenic, low protein-binding 0.2 µm in-line filter

Guide 2: Steps to prepare BLINCYTO infusion solution under aseptic conditions using aseptic techniques

Step 1	• Before preparation, consult the dosing tables and assemble the correct number of vials and other excipients
Step 2	• Transfer appropriate amount of Solution (stabiliser) to the Normal Saline (0.9% Sodium Chloride) infusion bag • Gently mix the contents of the bag to avoid foaming • Discard remaining Solution (stabiliser) vial if applicable
Step 3	• Reconstitute BLINCYTO powder for concentrate with 3 mL of Water for Injection • Do not reconstitute BLINCYTO with the Solution (stabiliser) • Do not shake • Gently swirl contents to avoid excess foaming • Reconstitute the required number of BLINCYTO vials (see pages 3 to 6 and select the table which matches the required dose and infusion time). 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 Normal Saline (0.9% Sodium Chloride) infusion bag • Gently mix the contents of the bag to avoid foaming
Step 5	• Attach the intravenous tubing to the prepared BLINCYTO infusion solution bag with the sterile 0.2 µm in-line filter
Step 6	• Remove air from the prepared BLINCYTO infusion solution bag
Step 7	• Prime the intravenous infusion line with the prepared BLINCYTO infusion solution • Do not prime the intravenous infusion line with Normal Saline (0.9% Sodium Chloride) solution for injection
Step 8	• Store the prepared BLINCYTO infusion solution bag at 2^{o}C to 8^{o}C for a maximum of 10 days if not immediately used (for further information, please see section 6.3 of the SmPC)