



NCIS GUIDE Blinatumomab

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1. Background

Blinatumomab is an anticancer drug used in the treatment of Acute Lymphoblastic Leukaemia (ALL) in both adults and children. The prescribing, preparation and administration of blinatumomab is unique and complex.

This guide has been created to support the prescribing, preparation and administration of blinatumomab in the NCIS System for <u>adults</u> in line with the relevant NCCP blinatumomab Regimen.

This guide was developed through consultation with sites and in conjunction with the following references

References

- 1. SmPC for Blincyto accessed on <u>www.ema.europa.eu</u> on 17.06.2024 at https://www.ema.europa.eu/en/medicines/human/EPAR/blincyto#product-info
- 2. NCCP regimens for blinatumomab therapy available at <u>https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/leukemia-bmt/protocols%20leukaemia.html</u>
- 3. Cirino, M., Provasi, R., Cebulec, I., Palmieri, C., Schincariol, P., & Zanon, D. (2020). Pediatric blinatumomab preparation: Risk assessment on SmPC for software compliance. Journal of Oncology Pharmacy Practice, 27(7), 1674–1683. <u>https://doi.org/10.1177/1078155220966394</u>

2. Prescribing of blinatumomab

Blinatumomab is dosed as either 9mcg/day or 28 mcg/day ranging from 7 days to 28 days duration. It is delivered through continuous IV infusion in NaCl 0.9% bags that must be changed at least every 96 hours.

Note µg = mcg = micrograms dosing for blinatumomab

In order to correctly prepare blinatumomab it is necessary to prescribe and prepare an excess dose so that the actual daily dose will be present in 240ml volume administered.

Note the infusion rate in NCIS will not match the intended infusion rate due to the excess dose calculation

The following table has been used to calculate the excess dose in line with the manufacturer's recommendations.

Table 1: Blinatumomab adult doses to be manufactured and equivalent doses to be administered¹

Dose	9 mcg per day				28 mcg per day			
Infusion	24 hours	48 hours	72 hours	96 hours	24 hours	48 hours	72 hours	96 hours
Infusion Pato	10ml /br	5ml /br	2 2ml /hr	2 Eml /br	10ml /br	5ml /br	2 2ml /hr	2 5ml /br
Volumo to bo	240ml over	240ml	3.5111L/111	2.5IIIL/III	240ml	240ml	3.5111L/111	2.5IIIL/III
administered	240mL Over	24011L over 18	24011L over 72	240mL	24011L over 24	24011L over /18	24011L over 72	96 hours -
and	9 mcg in 24	bours - 18	hours -27	bours - 36	hours $= 28$	bours -	hours $-8/$	112 mcg in
Blinatumomab	hours	mcg in 48	mcg in 72	mcg in 96	mcg in 24	56 mcg	mcg in 72	96 hours
equivalent	nours	hours	hours	hours	hours	in 48	hours	50 110015
dose		nours	nours	nours	nours	hours	nours	
Volume of	0.83 mL (1)	1.7mL (1)	2.5mL (1)	3.3 mL (2)	2.6 mL (1)	5.2mL (2)	8mL (3)	10.7mL (4)
reconstituted				. ,	. ,	. ,		. ,
blinatumomab								
required								
(Number of								
Vials)								
Plinatumomah				12 Em				
reconstituted				12.5111	cg/IIIL			
vial								
Concentration								
Total dose to	10.38 mcg*	21.25 mcg	31.25 mcg	41.25 mcg	32.5 mcg	65 mcg	100 mcg	133.75 mcg
be prescribed	Rounded to 2	0	0	0	0	Ū	0	5
and prepared	decimal places							
(including								
excess).								
(Blinatumomab								
reconstituted vial								
Volume of								
reconstituted								
blinatumomab								
Final volume		25	0 mL (usual ov	verfill volume o	of 265 to 275 r	nL) infusion	bag	1
							2	
			+	Volume of sta	biliser (5.5mL)		
			+ Volume o	freconstituted	l blinatumoma	ab required		

¹ SmPC for Blincyto accessed 17.06.2024 at <u>https://www.ema.europa.eu/en/medicines/human/EPAR/blincyto#product-info</u>

Regimens in NCIS has been built with alternating 72 hour and 96 hour infusion durations for blinatumomab in line with the appropriate excess dose. Drug comments have been added to indicate the infusion duration, the dose (9mcg/day or 28mcg/day), the volume to be infused and the infusion rate. See images below

Image 1: Blinatumomab 9mcg/day for 96 hours

Day 1		[]]]	96 hour infusion for 9mcg/24 hour dose Infuse 240mL only Infusion rate 2.5mL/h over 96 hours		^
	08:00	4d	Blincyto Powder for solution for41.25µg infusion in 250mL NaCl 0.9% • by intravenous infusion	Р	\sim

Image 2: Blinatumomab 9mcg/day for 72 hours

Day 5			72 hour infusion for 9mcg/24 hour dose Infuse 240mL only Infusion rate 3.3mL/h over 72 hours		\sim
	08:00	3d	Blincyto Powder for solution for31.25µg infusion in 250mL NaCl 0.9% • by intravenous infusion	Р	\sim

Image 3: Blinatumomab 28mcg/day for 96 hours



Image 4: Blinatumomab 28mcg/day for 72 hours

Day 5		lli}	72 hour infusion for 28mcg/24 hour dose Infuse 240mL only Infusion rate 3.3mL/h over 72 hours		^
	08:00	3d	Blincyto Powder for solution for100µg infusion in 250mL NaCl 0.9% • by intravenous infusion	Р	\sim

If an alternative infusion duration is required a blinatumomab medication selection can be added by clicking on the cycle banner and selecting medication selection. Then define the appropriate excess dose and infusion duration for the chosen time and date in the cycle as required. Note that anti-emetic medication will also need to be added as required (it is possible to use a medication selection for this purpose).

When the user selects define there is the option to select the appropriate blinatumomab dose as shown below. Note a pop up will appear with further information when the user hovers over each selection.

(Define medication selection							
	Define medication selection							
	Medication selection: Blinatumomab - select required dose (including excess) and duration - Version 1	Medication selection: Blinatumomab - select required dose (including excess) and duration - Version 1						
	Select all							
	Blincyto 12.5 µg/mL Powder for solution for infusion 10.38µg in 250mL NaCl 0.9% by intravenous infusion over 24 h							
	Blincyto 12.5 µg/mL Powder for solution for infusion 21.25µg in 250mL NaCl 0.9% by intravenous infusion over 2 Days							
	Blincyto 12.5 µg/mL Powder for solution for infusion 31.25µg in 250mL NaCl 0.9% by intravenous infusion over 3 Days							
	Blincyto 12.5 µg/mL Powder for solution for infusion 41.25µg in 250mL NaCl 0.9% by intravenous infusion over 4 Days							
	Blincyto 12.5 µg/mL Powder for solution for infusion 32.5µg in 250mL NaCl 0.9% by intravenous infusion over 24 h							
	Blincyto 12.5 µg/mL Powder for solution for infusion 65µg in 250mL NaCl 0.9% by intravenous infusion over 2 Days							
	Blincyto 12.5 µg/mL Powder for solution for infusion 100µg in 250mL NaCl 0.9% by intravenous infusion over 3 Days							
	Blincyto 12.5 µg/mL Powder for solution for infusion 133.75µg in 250mL NaCl 0.9% by intravenous infusion over 4 Days							
	Skip 96 hour infusion for 28mcg/24 hour dose Infuse 240mL only Infusion rate 2.5mL/h over 96 hours	æ						

If the user selected the first option for the 10.38mcg dose over 24 hours the following medication will appear in the therapy plan

	 24 hour infusion for 9mcg/24 hour dose Infuse 240mL only Infusion rate 10mL/h over 24 hours 			^	
08:00	24h X	Blincyto 12.5 µg/mL Powder for solution10.38µg for infusion in 250mL NaCl 0.9% • by intravenous infusion	PLANNED	Р	\sim

The medication can now be physician verified.

3. Preparation of blinatumomab

The pharmacist can select to pharmacist verify and check the details as shown below. The excess dose to be manufactured in the example below is 10.38 mcg using a volume of 0.83mL which is required to prepare the dose of 9 mcg over 24 hours in 240mL.

¢	Pharmacist Verification of a Medication Verified By Physician				x
	Pharmacist Verification of a Medication Verified By Physician				
Γ	Prep. approved 🔻 TRAIN 🗸 🗹 Volumetric only 🗌 Medication dispensed 🗌 To be completed at unit 🗌 Urgent		M	edical result	<u>s</u>
	Active ingredient / Product Usual dose Calculation	Dose	Volume	÷	
	Blincyto Powder for solution for infusion (Blinatumomab) 10.38µg 100% = 10.38µg	10.38µg	0.83mL		
	Active ingredient Product Usual dose	Reference			
	Blinatumomab 🕀 Blincyto Powder for solution for infusion 🕀 10.38 µg ∨ Absolut	2		Û	
	Dose: 10.38µg x 100.00 % = µg 🗸 10.38 µg 🗸				
	Diluent: Water for Injections 🗸 🗆 Define concentration				
	mL / mg v				
	Form: Pre-filled container V Empty container:			Û	
	Vehicle: NaCl 0.9% 🗸 in 🖌 250.00 mL from NaCl 0.9% 250mL bag Viaflo - No Overfill - non-PVC Baxter			4	
	Administration: by intravenous infusion 🕖 Duration: 1 Days 0 h 0 min. 🗆 Deviati	ng stability: 4 d	0 h	0 min	
	Date O Relative Date: 17/06/2024 Day in cycle: 1 Time: 08:00				
	Place of delivery: TRN - Training Oncology/Haematology Day 😳 Cost center: TRN - Training Consultant 🐵 Order no:				
	Create preparation notes Edit comments Insert rules	Edit services / additic	onal articles <u>E</u>	led planning	g
			✓ Save	样 Cancel	

The stabiliser to be added has been built as an additional article and appears on the parts list as below

Create / edit parts list	reate / edit parts list					
Planned preparation time: <u>17/06/2024 14:03</u> Preparation	method: Volumetric 🗸					
Products						
Blincyto Powder for solution for infusion: 10.38µg Remainder:28.12µg	1х 38.5µg (4444444444444444444444444444) Diluent: 3mL Water for Injections from 1x 10mL Mini Pla	sco Connectnon-PVC B. Braun (ABEBDHSY)	38.5µg 🎽 📝			
Total syringes 1x Luer Lok Syringe 5mL polypropylene, 1x Luer Lok Syringe 1	mL polypropylene					
Containers and additional articles (per medication	on)		2	,		
Med.# 260920, ADAM AUDREY, for Mon, 17/06/2024 08:0 Blincyto Powder for solution for infusion 10.38µg in 250n	0 (TRN - Training Oncology/Haematology Day Ward) nL NaCl 0.9%, by intravenous infusion	1x NaCl 0.9% 250mL bag Viaflo - No Overfill - non-PVC Baxter (546), 1x Blincyto stabiliser - add 5.5 mL stabiliser to 250 mL infusion bag (*), 1x Complexity Band 4 (1 USE THIS BAND) (*)	of 📋 🍞	1		

The instructions are viewable as below

Image 5: Example List of preparations

required reconstitution processes	
lincyto Powder for solution for infusion	Required quantity: 10.38µ
Reconstitute:	
 Blincyto 38.5µg (Lot: 444444444444444444444444444444444444	10mL Mini Plasco Connect non-PVC B. Braun, Lot: ABEBDHSY)
ADAM AUDREY, d.o.b. 16/09/1986 (Med.# 260920), Mon, 17/06/2024 08:00	TRN - Training Oncology/Hae matology Day War
Blincyto Powder for solution for infusion 0.83mL (10.38µg) in 250.00mL Na	CI 0.9%, by intravenous infusion
Beginning of preparation: Add the stabiliser first, then the blincyto and then remove all the air from t	he bag
Withdrawal:	
 0.83mL (12.5µg/mL) from Blincyto 38.5µg (Lot: 444444444444444444444444444444444444	
Injection:	
 Inject entire drawn up stock solution (0.83mL) into NaCI 0.9% 250mL bag Viaflo - No Overfi 	II - non-PVC Baxter (Lot: 546)
Stick the label on: NaCl 0.9% 250mL bag Viaflo - No Overfill - non-PVC Baxter	

Note the preparation instruction has been added 'Add the stabiliser first, then the blincyto and then remove all the air from the bag

Image 6: Example In-isolator preparation label

IN-ISOLATOR PREPARATION LABEL					
AUDREY ADAM #	23				
Planned Prep: 17/06/2024 14:03					
Admin Due: Mon, 17/06/2024 (08:00 Med#260920				
Blincyto 12.5 µg/mL 10.38µg V	olume to add to bag: 0.83mL				
Add volume to NaCl 0.9% 250 mL	bag Viaflo - No Overfill - non-PVC				
by intravenous infusion	Time Prepared:				
Storage: 2-8 degrees Celsius	Preparer:				
	Check:				

Note the use of a stabiliser does not appear on the label above. The preparation instructions can be used for manufacturer or a note can be added during pharmacist verification

Image 7: Example of NCIS infusion labels

Example of NCIS Infusion INN label	Example of NCIS infusion label
Keep out of reach of children	Keep out of reach of children
Blinatumomab 10.38µg Final Conc 0.04138 µg/mL in 250mL NaCl 0.9% bag Viaflo - No Overfill - non-PVC Total Vol: 250.83mL by intravenous infusion over 24 h Med#260920 AUDREY ADAM	Blincyto 12.5 µg/mL 10.38µg (Blinatumomab) Final Conc 0.04138 µg/mL in 250mL NaCl 0.9% bag Viaflo - No Overfill - non-PVC Total Vol: 250.83mL by intravenous infusion over 24 h Med# 260920 AUDREY ADAM
Hospital Number: DOB: 16/09/1986	Hospital Number: DOB: 16/09/1986
Admindue: Non, 17/06/2024 08:00 (Day 250) TrainingOncology/Haematology Day Ward Blincyto. U se 0.2 micron lowprotein binding in-line filter Store at: 2-8 degrees Celsius Expiry: 21/06/2024 14:03	Admindue: Mon, 17/06/2024 08:00 (Day 250) Training Oncology/Haematology Day Ward Blincyto. Use 0.2 micron low protein binding in-line filter Store at: 2-8 degrees Celsius Expiry: 21/06/2024 14:03

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4. Administration of blinatumomab

In order to correctly prepare blinatumomab it is necessary to prescribe and prepare an excess dose (see table 2 below). During administration the volume of blinatumomab to be infused is **always 240mls** and the **bag should never be emptied**. See NCCP regimens and the Summary of Product Characteristics for detailed information on the administration of blinatumomab.

Table 2: Blinatumomab adult doses to be administered²

Volume of blinatumomab to be infused is always 240mls and the bag should never be emptied			
Infusion Duration	Infusion Rate	Total dose to be prescribed and prepared (including excess) for 9 mcg per day dosage	Total dose to be prescribed and prepared (including excess) for 28 mcg per day dosage
24 hours	10mL/hr	10.38 mcg* rounded to 2 decimal places	32.5 mcg
48 hours	5mL/hr	21.25 mcg	65 mcg
72 hours	3.3mL/hr	31.25 mcg	100 mcg
96 hours	2.5mL/hr	41.25 mcg	133.75 mcg

² SmPC for Blincyto accessed 17.06.2024 at <u>https://www.ema.europa.eu/en/medicines/human/EPAR/blincyto#product-info</u>