BLINCYTO® (blinatumomab)

Important Risk Minimisation Information for Doctors

This educational brochure contains important information regarding the administration of BLINCYTO and the risks of medication errors, neurologic events and cytokine release syndrome

This educational material is essential to ensure the safe and effective use of the product and appropriate management of the important selected risks and therefore it is advised to be read carefully before prescribing and administering the medicine

Please ensure each patient or caregiver is provided a copy of the patient educational material and Consumer Medicine Information for reference

This document is not a comprehensive list of Safety events; please refer to the Product Information for further information.

Please refer to the full Approved Product Information before prescribing, available from Amgen Australia Pty Ltd or http://www.amgen.com.au/Blincyto.PI

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.

Important information regarding BLINCYTO therapy

The following actions should be taken to prevent or minimise the risk of medication errors, neurologic events and cytokine release syndrome.

Medication errors

- Ensure that patients receive the recommended daily dose by patient weight. Patients weighing greater than or equal to 45 kg receive a fixed-dose and for patients weighing less than 45 kg, the dose is calculated using the patient's body surface area (BSA):

BLINCYTO Recommended Dosage for Relapsed or Refractory B-cell Precursor ALL:

Patient Weight	Treatment Cycle 1			Subsequent Treatment Cycles	
	Days 1-7	Days 8-28	Days 29-42	Days 1-28	Days 29-42
Greater than or Equal to 45 kg (fixed-dose)	9 micrograms/day	28 micrograms/day	14-day treatment-free interval	28 micrograms/day	14-day treatment-free interval
Less than 45 kg *(BSA-based dose)*	5 micrograms/m^2/day *(not to exceed 9 micrograms/day)*	15 micrograms/m^2/day *(not to exceed 28 micrograms/day)*		15 micrograms/m^2/day *(not to exceed 28 micrograms/day)*	

BLINCYTO Recommended Dosage for MRD-positive B-cell Precursor ALL:

Patient Weight	**Treatment Cycle(s)**	
	Days 1-28	**Days 29-42**
Greater than or equal to 45 kg *(fixed-dose)*	28 micrograms/day	14-day treatment-free interval

- See Dosage and Administration section of the PI
- To minimise the occurrence of medication errors, please counsel patients on the following:
  - Instruct patients not to unlock the pump
  - If the pump does not appear to perform properly at any time (e.g. alarm goes off), instruct patients and caregivers not to try to fix the pump and tell them to contact you or the nurse immediately
  - Instruct patients not to change any pump settings on purpose (with the exception of stopping the pump in case of emergency)

Neurologic events	• See dosage adjustments section of Product Information for management of severe (Grade 3) and life-threatening (Grade 4) neurologic events
	• Monitor patients for signs and symptoms of neurologic events (e.g. confusion, disorientation, dizziness, tremor, seizure) prior to and throughout the treatment cycle
	• The majority of events resolved following interruption of BLINCYTO, but some resulted in treatment discontinuation
	• Consider utilising a writing test periodically to evaluate for the early detection of neurologic events
	• Be aware that elderly patients may experience a higher rate of neurologic events, including cognitive disorder, encephalopathy, and confusion
	• **Withhold dose if Grade 3 (severe) neurologic event occurs and discontinue BLINCYTO permanently if Grade 4 (life-threatening) neurologic event occurs**
	• The median time to onset of any neurologic toxicity was 9 days, however symptoms may appear earlier or later
	• It is essential to counsel patients regarding the potential neurologic effects and to advise patients:
	  ○ **Not to drive, operate heavy machines or engage in hazardous activities while receiving BLINCYTO**
	  ○ To contact you if they experience neurologic symptoms
	• There is limited experience with BLINCYTO in patients with active ALL in the central nervous system (CNS) or a history of neurologic events (patients with a history or presence of clinically relevant CNS pathology were excluded from clinical trials)

Cytokine Release Syndrome (CRS)	• Cytokine Release Syndrome (CRS) which may be life-threatening or fatal has been reported in patients receiving BLINCYTO • Monitor for signs and symptoms of CRS, some of which may be pyrexia, asthenia, headache, hypotension, total bilirubin increased, and nausea; In some cases, disseminated intravascular coagulation, capillary leak syndrome, and haemophagocytic lymphohistiocytosis/macrophage activation syndrome have been reported in the setting of CRS • Highest elevation of cytokines was observed 2 days following the start of BLINCYTO • Management of these events may require temporary interruption or permanent discontinuation of BLINCYTO. Discontinue BLINCYTO permanently if a Grade 4 non-neurologic event occurs • Refer to Dosage and Administration section of Product Information for further information on management of non-neurologic events

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 Precautions and Dosage and Administration).*

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/m^2 (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. 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