ADVERSE EVENT MANAGEMENT

BLINCYTO® ADVERSE EVENT MANAGEMENT

NEUROLOGICAL EVENTS

In patients with relapsed or refractory B-ALL:

In the phase III clinical study with BLINCYTO® (N = 267), 61.0% of patients experienced one or more neurologic adverse reactions (including psychiatric disorders), primarily involving the central nervous system.[1]

Serious and grade ≥3 neurologic adverse reactions were observed in 6.7% and 9.4% of patients respectively, of which the most common were encephalopathy, aphasia, confusional state, and somnolence.[1]

The majority of neurologic events (80.7%) were clinically reversible.[1]

The median time to the first event was within the first two weeks of treatment.[1]

One case of fatal encephalopathy has been reported in an earlier phase II single-arm study.[1]

In patients with MRD+ B-ALL:

Neurologic events were reported for 71.5% of adult patients with MRD+ B-ALL of which 22.6% were considered serious.[1]

Grade ≥3 and grade ≥4 events, respectively, were reported for 16.1% and 2.2% of adult patients with MRD+ B-ALL.[1]

Patients receiving BLINCYTO® should be clinically monitored for signs and symptoms of neurologic events.[1]

Management of these signs and symptoms may require either temporary interruption or discontinuation of BLINCYTO®.[1]

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

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INFECTIONS

Patients with ALL are immunocompromised and consequently at increased risk for serious infections. In patients receiving BLINCYTO®, serious infections, including sepsis, pneumonia, bacteraemia, opportunistic infections, and catheter site infections have been observed, some of which were life-threatening or fatal.[1]

Patients with Eastern Cooperative Oncology Group (ECOG) performance status (PS) ≥2 experienced a higher incidence of serious infections than those with ECOG PS <2.[1]

Monitor patients for signs and symptoms of infection and treat appropriately.

Management of infections may require either temporary interruption or discontinuation of BLINCYTO®.

CYTOKINE RELEASE SYNDROME (CRS)

Serious adverse events that may be associated with CRS included pyrexia, asthenia, headache, hypotension, total bilirubin increased, and nausea; these events infrequently led to BLINCYTO® discontinuation. In some cases, disseminated intravascular coagulation, capillary leak syndrome and haemophagocytic lymphohistiocytosis/macrophage activation syndrome have been reported in the setting of CRS.[1]

To mitigate the risk of CRS, it is important to initiate BLINCYTO® (Cycle 1, Days 1–7) at the recommended starting dose.

Patients should be closely monitored for signs or symptoms of these events.

Management of these events may require either temporary interruption or discontinuation of BLINCYTO®.

TUMOUR LYSIS SYNDROME (TLS)

TLS, which may be life-threatening or fatal, has been observed in patients receiving BLINCYTO®.[1]

Appropriate prophylactic measures including hydration should be used for the prevention of TLS during BLINCYTO® treatment.

Patients receiving BLINCYTO® should be closely monitored for signs and symptoms of TLS.

Management of these events may require either temporary interruption or discontinuation of BLINCYTO®.

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NEUTROPENIA/FEBRILE NEUTROPENIA

Neutropenia and febrile neutropenia, including life-threatening cases, have been observed in patients receiving BLINCYTO®.[1]

Monitor laboratory parameters (including, but not limited to WBC count and ANC) during BLINCYTO® infusion and treat appropriately.

ELEVATED LIVER ENZYMES

Treatment with BLINCYTO® was associated with transient elevations in liver enzymes.[1]

The majority of the events were observed within the first week of BLINCYTO® initiation and did not require interruption or discontinuation of BLINCYTO®.[1]

In the pivotal clinical study with BLINCYTO®, (n=267), 21.7% of patients reported elevated liver enzymes.[1]

Serious and grade ≥3 adverse reactions (such as ALT increased, AST increased, and blood bilirubin increased) were observed in 1.1% and 12.7% of patients respectively.[1]

The median time to onset to the first event was 3 days from the start of BLINCYTO® treatment initiation and did not require interruption or discontinuation of BLINCYTO®.[1]

Elevated liver enzyme events were reported for 12.4% of adult patients with MRD+ B-ALL.[1]

Grade ≥3 and grade ≥4 events, respectively, were reported for 8.0% and 4.4% of adult patients with MRD+ B-ALL.[1]

The duration of hepatic adverse reactions has generally been brief and with rapid resolution, often when continuing uninterrupted treatment with BLINCYTO®.[1]

Monitor ALT, AST, GGT and total blood bilirubin prior to the start of and during BLINCYTO® treatment[1]

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PANCREATITIS

Pancreatitis, life-threatening or fatal, has been reported in patients receiving BLINCYTO® in clinical trials and the post-marketing setting. High-dose steroid therapy may have contributed, in some cases, to the pancreatitis.[1]

Evaluate patients who develop signs and symptoms of pancreatitis.[1]

Management of pancreatitis may require either temporary interruption or discontinuation of BLINCYTO®.[1]

INFUSION REACTIONS

Patients should be observed closely for infusion reactions, especially during the first infusion of the first cycle and treated appropriately.[1]

Management of infusion reactions may require either temporary interruption or discontinuation of BLINCYTO®.[1]

MEDICATION ERRORS

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]

LEUKOENCEPHALOPATHY

Cranial magnetic resonance imaging (MRI) changes showing leukoencephalopathy have been observed in patients receiving BLINCYTO®, especially in patients with prior treatment with cranial irradiation and anti-leukaemic chemotherapy (including systemic high dose methotrexate or intrathecal cytarabine). The clinical significance of these imaging changes is unknown.[1]

RECOMMENDATIONS ABOUT IMMUNISATION

Vaccination with live virus vaccines is not recommended for at least 2 weeks prior to the start of BLINCYTO® treatment, during treatment, and until recovery of B-lymphocytes to normal range following last cycle of BLINCYTO®.[1]

RECOMMENDATIONS ABOUT CONTRACEPTION

Women of childbearing potential should use contraception during and for at least 48 hours after treatment with BLINCYTO®.[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
Interruptor 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®