BLINCYTO®
(blinatumomab)

Important Risk Minimisation Information for Physicians

This brochure content was approved according to the guidelines of the Ministry of Health in October 2021

Israeli version 3.0 final October 2021 derived from EU Version 7.0 Approved: June 2021

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Guide for Physicians

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The information in this guide is not intended as a replacement for the Israeli Prescribing Information (PI).
Please read the BLINCYTO Israeli PI, in conjunction with this guide.

This guide has been developed for physicians involved in the care of patients treated with BLINCYTO to provide you with further information about **how to minimise or prevent the following risks associated with the use of BLINCYTO:**

- **Neurologic events**
- **Medication errors**

Healthcare professionals are asked to report any suspected adverse reactions. Adverse events can be reported to the Ministry of Health via **https://sideeffects.health.gov.il/**
Or report to local distributor Medison: pv@Medison.co.il

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TABLE OF CONTENTS

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1 OVERVIEW

In order to minimise the risk of neurological events and medication errors, please:

- Provide nurses involved in the administration of BLINCYTO or care of your BLINCYTO treated patients with the Guide for Nurses, which contains important information regarding the administration of BLINCYTO and the risks of medication errors and neurological events
- Provide pharmacists involved with dispensing and preparing BLINCYTO for administration to your patients with the Guide for Pharmacists which contains important information regarding the preparation of BLINCYTO and the risk of medication errors
- Ensure the patient **receives and understands** the content of the following regarding the risks of neurological events and medication errors:
  - Guide for Patients and Caregivers
  - Patient Card
  - Patient Information Leaflet
- Report any suspected adverse reactions or medication errors that your patients have encountered or experienced (refer to page 1 for instructions)

1.1 Important Information About BLINCYTO Treatment

- BLINCYTO is given by continuous intravenous infusion as monotherapy for the treatment of:
  - Adults with CD19-positive relapsed or refractory B precursor acute lymphoblastic leukaemia (ALL). Patients with Philadelphia chromosome positive B-precursor ALL should have failed treatment with at least 2 tyrosine kinase inhibitors (TKIs) and have no alternative treatment options
  - Adults with Philadelphia chromosome negative CD19 positive B precursor ALL in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%
  - Pediatric patients aged 1 year or older with Philadelphia chromosome negative CD19 positive B precursor ALL which is refractory or in relapse after receiving at least two prior therapies or in relapse after receiving prior allogeneic hematopoietic stem cell transplantation

  - Pediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor ALL as part of the consolidation therapy

- Hospitalisation and supervision by a healthcare professional is recommended for BLINCYTO treatment. The duration of the patient's hospitalisation will be dependent on their malignancy and the treatment cycle, please refer to Section 4.2 of the BLINCYTO PI for further details.
- The recommended daily dose of BLINCYTO is by patient weight:
  - Patients greater than or equal to 45 kg receive a fixed-dose
  - For patients less than 45 kg, the dose is calculated using the patient's body surface area
- Please refer to Section 4.2 of the BLINCYTO PI for the recommended daily dose by patient's weight or body surface area, the recommended number of treatment cycles, and premedication/additional medication recommendations.
- Discuss the infusion duration with your patients as there is a choice of bag change frequency. However, the target therapeutic dose of BLINCYTO delivered does not change.
- In the case of toxicities, consideration can be made to interrupt or discontinue the infusion of BLINCYTO. Please refer to Dose adjustment under Section 4.2 of the BLINCYTO PI for further details.

1.2 Important Information on Neurologic Events

- Neurologic events, including events with a fatal outcome, have been observed during treatment with BLINCYTO. Events have included encephalopathy, seizures, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders.
- Elderly patients can receive BLINCYTO, but may be more susceptible to serious neurologic events.
- Patients with a medical history of neurologic signs and symptoms may experience a higher rate of neurologic events (such as tremor, dizziness, confusional state, encephalopathy, and ataxia) when receiving BLINCYTO.
- The majority of neurologic events are clinically reversible and resolve following BLINCYTO interruption.
- For clinical management of neurologic events, please refer to Neurologic events under Section 4.4 of the BLINCYTO PI.

Action required from you beyond standard working practice to minimise or prevent neurologic events:

- Counsel the patient (see Section 2 of this guide for details)
- Prior to, and throughout the treatment cycle, assess patients for signs and symptoms of neurological events:
  - Eg, headache, tremor, aphasia, paraesthesia, seizure, cognitive disorder, memory impairment, dizziness, somnolence, hypoaesthesia, or ataxia (see Section 4.4 of the BLINCYTO PI for further information)
  - Regular writing tests should be considered to detect and monitor signs of neurological events
- In patients with a history or presence of clinically relevant central nervous system (CNS) pathology, hospitalisation is recommended at a minimum for the first 14 days of the first cycle. In the second cycle, hospitalisation is recommended at a minimum for 2 days.
- If convulsion, or grade 3 or 4 neurological toxicity occurs, interruption or discontinuation of BLINCYTO is recommended. Please see Section 4.2 of the BLINCYTO PI for further details.

1.3 Important Information on Medication Errors

- Medication errors are unintended errors in the prescribing, dispensing, or administration of a medicinal product while in the control of the healthcare professional or patient/caregiver.
- Medication errors have been observed with BLINCYTO treatment.
- Medication errors may result in underdose or overdose of BLINCYTO. Underdose may lead to less than expected efficacy and overdose may increase the risk of adverse reactions.

Action required from you beyond standard working practice to minimise or prevent medication errors:

- Counsel the patient (see Section 2 of this guide for details)
- Measure the patient's weight or calculate the body surface area so that the correct BLINCYTO dosage can be calculated

2 COUNSELLING THE PATIENT BLINCYTO interruption.

It is essential to counsel your patients on the following whilst receiving BLINCYTO.

2.1 Neurologic Events

- Advise patients to call their healthcare provider to ask for emergency medical help immediately if they experience any of the following neurologic events:
  - Shaking (or tremor), abnormal sensations, seizures, memory loss, confusion, disorientation, loss of balance, or difficult speaking
- Advise patients to travel home safely and to not drive or operate moving vehicles/heavy machinery, or engage in hazardous activities whilst receiving BLINCYTO.

2.2 Medication Errors

- Advise patients on the following:
  - **Do not** unlock the pump
  - **Do not** try to fix the pump if the pump does not appear to perform properly (eg, alarm goes off)
  - **Do not** change any pump settings on purpose, with the exception of stopping the pump in case of emergency
  - To contact their healthcare provider immediately if experiencing:
    - A problem with the pump or the pump alarm sounds
    - Unexpected stopping of the infusion pump
    - An empty infusion bag before the scheduled bag change

2.3 Provide Patient with Educational Materials

- Ensure the patient receives and understands the content of the following:
  - Guide for Patients and Caregivers
  - Patient Card
  - Patient Information Leaflet