Important Safety Information on BLINCYTO® (blinatumomab) and Benzyl Alcohol Toxicity for Pediatric Patients

2018/06/12

Audience
Healthcare professionals including hematologists, oncologists, hospital and oncology pharmacists, and cancer clinic staff

Key Messages

- **Serious and fatal adverse reactions including "gasping syndrome" can occur in pediatric patients, particularly in neonates and infants treated with BLINCYTO containing benzyl alcohol as a preservative.**
- **BLINCYTO has recently been authorized with an additional option of preparing a 7-day infusion bag containing benzyl alcohol for patients weighing greater than or equal to 22 kg. It is not recommended for use in patients weighing less than 22 kg.**
- **When preparing bags of BLINCYTO solution for infusion in neonates, infants and patients weighing less than 22 kg, healthcare professionals are advised to only utilize preservative-free saline.**
- **The Canadian Product Monograph has been updated to reflect this new safety information.**

What is the issue?
BLINCYTO has recently been authorized with an additional option of preparing a 7-day infusion bag, using bacteriostatic 0.9% sodium chloride containing 0.9% benzyl alcohol as a preservative. Benzyl alcohol has the potential to cause serious and fatal adverse reactions when administered intravenously to neonates and infants. Therefore, 0.9% sodium chloride containing 0.9% benzyl alcohol is not recommended for use in the preparation of BLINCYTO intended to be administered to neonates, infants, or patients weighing less than 22 kg.

Products affected
BLINCYTO (blinatumomab) for injection

Background information
BLINCYTO is indicated for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). BLINCYTO has also been issued marketing authorization with conditions, for the treatment of pediatric patients with Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL, pending the results of studies to verify its clinical benefit.

BLINCYTO has recently been authorized for the option of preparing a 7-day infusion bag using bacteriostatic 0.9% sodium chloride solution containing 0.9% benzyl alcohol as a preservative. The preservative benzyl alcohol has been associated with serious and fatal adverse reactions, including "gasping syndrome" in pediatric patients, particularly in premature neonates and infants. The "gasping syndrome" (characterized by gasping respirations, central nervous system depression, metabolic acidosis, and high levels of benzyl alcohol and its metabolites found in the blood and urine) has been associated with benzyl alcohol dosages of 99 mg/kg/day or more in neonates and low-birth-weight infants. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. Premature and low-birth weight infants may be more likely to develop these adverse reactions because they may be less able to metabolize benzyl alcohol. The minimum amount of benzyl alcohol at which toxicity may occur is not known.

Information for consumers
BLINCYTO is a prescription medicine used to treat adults and children with acute lymphoblastic leukemia that has come back after a previous treatment (relapsed) or if there was no response to the first treatment (refractory). Acute lymphoblastic leukemia is a cancer of the blood in which a particular kind of white blood cell is growing out of control.

Serious side effects including death have happened in newborns or infants who have received benzyl alcohol intravenously. The 7-day bags of BLINCYTO solution for infusion, which contain benzyl alcohol as a preservative, are not recommended for use in the preparation of BLINCYTO intended to be administered to neonates, infants, or patients weighing less than 22 kg.

Patients and caregivers should discuss any questions or concerns about this information with their healthcare professional.

Patients and caregivers should also inform their healthcare professional if they experience any other side effects.

Information for healthcare professionals
Healthcare professionals are reminded to:

- For use in neonates, infants, and patients weighing less than 22 kg, only prepare BLINCYTO solution for infusion (over 24, 48, 72, or 96 hours) with preservative-free saline. The recently authorized option of preparing 7-day bags of BLINCYTO solution for infusion containing benzyl alcohol is not recommended for use in neonates, infants, or patients weighing less than 22 kg.

- Consider the combined daily metabolic load of benzyl alcohol from all sources of drugs containing benzyl alcohol when prescribing BLINCYTO with benzyl alcohol preservative to patients. The minimum amount of benzyl alcohol at which toxicity may occur is not known.

Action taken by Health Canada
Health Canada, in collaboration with Amgen Canada Inc., has updated the Canadian Product Monograph (CPM) for BLINCYTO. Health Canada is communicating this important safety information to healthcare professionals and via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site (www.healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php). This communication update will be further distributed through the MedEffect™ e-Notice email notification system.

Report health or safety concerns
Managing marketed health product-related side effects depends on health care professionals and consumers reporting them. Any case of benzyl alcohol toxicity or other serious or unexpected side effects in patients receiving BLINCYTO should be reported to Amgen Canada Inc. or Health Canada.

Amgen Canada Inc.
6775 Financial Drive, Suite 100
Mississauga, Ontario L5N 0A4
Safety Tel: 1-866-512-6436 or Fax: 1-888-264-3655
Safety e-mail: safetycanada@amgen.com

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate
E-mail: mailto:mhpd_dpsc.public@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

Sincerely,

Dr. Ponda Motsepe-Ditshego
Executive Medical Director
AMGEN Canada Inc.