Visual compatibility of blinatumomab with selected drugs during simulated Y-site administration

Blinatumomab is a bispecific T-cell engager antibody construct that binds specifically to CD19 expressed on the surface of cells of B-lineage origin and CD3 expressed on the surface of T cells. Blinatumomab was approved by the European Medicines Agency for the treatment of adults with Philadelphia chromosome-negative acute relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). The Food and Drug Administration has also approved the drug for treatment of ALL in both adult and pediatric patients.

Blinatumomab is administered over 4 weeks as a continuous infusion. Blinatumomab, supplied as a 38.5-µg single-dose vial, must be reconstituted before administration and then added to a 250-mL infusion bag of 0.9% sodium chloride injection. A stabilizer solution is provided inside the blinatumomab package and must be added to the infusion bag before the blinatumomab solution is introduced. The physical in-use stability of the diluted solution is 96 hours at 15–25 °C.

As previously described, physicochemical drug–drug interactions may appear during Y-site administration by nurses, posing a risk to patients that will increase with continuous or multiple infusions. However, there is no reported information regarding the compatibility of blinatumomab with other i.v. drugs commonly administered to patients. We evaluated the visual compatibility of blinatumomab with 39 commonly coadministered i.v. drugs to gain insight on this issue.

Two blinatumomab concentrations were tested based on the recommended doses and practical administration guidelines. Blinatumomab was diluted to achieve final concentrations of 0.125 and 0.375 µg/mL. Thirty-nine drugs obtained from commercial sources were identified as commonly prescribed simultaneously with blinatumomab in our patients.

A method involving 1:1 mixing of tested drugs was used to simulate the mixing of blinatumomab with the tested drugs during administration. Equal volumes (1 mL) of blinatumomab solution and each tested drug solution were mixed in glass tubes. The effect of mixing order was ascertained by studying both the tested drug added to blinatumomab solution and the blinatumomab solution added to the tested drug. Tubes were stirred manually to ensure complete mixing. Visual observations were performed in front of both a matte black panel held in a vertical position and a nonglare white panel held in a vertical position under normal fluorescent light. All sample mixtures were visually inspected for color change, haze, fibers, particles, gas generation, and precipitate formation. Observations were conducted by 3 different researchers to confirm results. Visual examination was performed immediately and 60, 150, 240, and 720 minutes after mixing.

Only 3 of the tested drugs (caffeine citrate, hydrocortisone, liposomal amphotericin B) demonstrated visual compatibility with the 2 concentrations of blinatumomab at all time points, regardless of the order of mixing.

Particles, flakes, thin needles, or haze transiently appeared with 14 drugs (caspofungin, ceftazidime, ceftriaxone, clonazepam, cotrimoxazole, daptomycin, imipenem–cilastatin, midazolam, naloxone, nefopam, ondansetron, pantoprazole, Pedivan, vancomycin). A persistent reaction resulting in particulate formation appeared with 22 drugs (acetaminophen, albumin, alizapride, ciprofloxacin, cloxacillin, dexamethasone, dexchlorpheniramine, furosemide, Glucidion G 5%, heparin, hydroxyzine, meropenem, methylprednisolone, metronidazole, morphine, nalbuphine, omeprazole, phloroglucinol, potassium chloride, rasburicase, teicoplanin, tranexamic acid) at least 1 time, for 1 concentration, or for 1 order of mixing.
LETTERS

A total of 36 drugs were identified as visually incompatible with blinatumomab. As such, blinatumomab should not be administered simultaneously with these drugs through a common i.v. port. Blinatumomab was visually compatible with only 3 of the 39 drugs tested; further studies should be conducted to ensure the chemical stability of these mixtures.


Théau Du Repaire (pharmacy intern)
Pharmacy Department
La Timone University Teaching Hospital
Marseille, France

Petula Vigne (pharmacy intern)
Pharmacy Department
La Timone University Teaching Hospital
Marseille, France

Amaury Guedon, Pharm.D., Ph.D.
Pharmacy Department
La Timone University Teaching Hospital
Marseille, France

Raphaëlle Fanciullino, Pharm.D., Ph.D.
Pharmacy Department
Conception University Teaching Hospital
Marseille, France

Laurence Gauthier-Villano, Pharm.D.
Pharmacy Department
La Timone University Teaching Hospital
Marseille, France

Pierre Bertault Peres, Pharm.D., Ph.D.
Pharmacy Department
La Timone University Teaching Hospital
Marseille, France

Bertrand Pourroy, Pharm.D., Ph.D.
Pharmacy Department
Conception University Teaching Hospital
Marseille, France

The authors have declared no potential conflicts of interest.

Keywords: blinatumomab, drug incompatibility, drug stability, intravenous, oncology, pediatrics

Copyright © 2017, American Society of Health-System Pharmacists, Inc. All rights reserved. 1079-2082/17/0802-1217.
DOI 10.2146/ajhp170111

Auditing sterile compounding competency with video observation

The competency assessment of personnel involved in sterile compounding is of the utmost importance in reducing the potential for contaminated products. Didactic training, written tests, media-fill tests, and observational audits are recommended or required, depending on each state’s regulations. The serious harm that may result from contaminated, wrong-dose, mislabeled, or otherwise poor quality compounded sterile products is well documented, especially after the fungal meningitis outbreak in 2012.

To ensure that the pharmacy at Texas Health Presbyterian Hospital Flower Mound produces the safest and most effective sterile compounds, our management team developed a new observational audit process to validate sterile compounding competencies after initial competency is established. The process uses saved video camera footage to retrospectively review staff compliance with all steps in the sterile compounding process.

Video footage is captured by cameras that are mounted to the ceiling and enclosed in a plastic cover to minimize particle generation and enable staff to clean them easily. Two cameras, 1 in the anteroom and 1 in the buffer area, are positioned to maximize the view of each phase of compounding, from entering the anteroom and preparing supplies to appropriate doffing techniques if the gown is saved to be reused during the same shift.

The choice to utilize video footage was based on previous experience with in-person competency assessments, which are nearly impossible to adequately perform without the staff member knowing what is being done. Our managers believed that personnel purposefully slowed down and more thoroughly completed each step when they knew they were being observed. To verify that typical behaviors are audited, pharmacy managers randomly select a time when staff members prepare sterile compounds and review the footage.

Pharmacy managers developed an evaluation tool, which outlines 40 specific requirements during the compounding process. A success rate of ≧95% was established...