

Issue 14 November 2015

Suggested Action Items

- Refer bulletin to pharmacy and medication safety committee to assess the type of amphotericin B product(s) on formulary and to review safeguards against substitution errors.
- Refer bulletin to leadership committees and educators to disseminate information about the various formulations of amphotericin B and potential harm from errors with these products.
- Circulate bulletin to physicians and other front-line staff.
- Use bulletin as an educational resource in your hospital safety huddles or rounds.

Distributed to:

- Chief executive officers
- Chiefs of staff
- Board chairs
- Quality/patient safety leads
- Directors of pharmacy
- Directors of nursing



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Errors Continue with Amphotericin B

Amphotericin B is an antimicrobial drug used in the treatment of severe fungal infections. It is available in 3 formulations for intravenous use in Canada: “conventional” amphotericin B (Fungizone), amphotericin B lipid complex (Abelcet), and liposomal amphotericin B (AmBisome). Lipid-based forms of the drug appear to have less severe toxic effects,¹ but the conventional form of the drug is still available, and many Ontario hospitals reportedly stock multiple formulations. ISMP Canada and ISMP (US) have published several bulletins and alerts on concerns about the risks of inadvertently substituting one formulation for another.²⁻⁴

The recommended dose of conventional amphotericin B (Fungizone) is 1.5 mg/kg/day,⁵ much less than the recommended dose for both liposomal amphotericin B (AmBisome), 3-6 mg/kg/day,⁶ and amphotericin B lipid complex (Abelcet), 5mg/kg/day.⁷ Inadvertent substitution of conventional amphotericin B for the liposomal or lipid complex dose will result in an overdose of the active drug, potentially leading to severe toxic effects, such as cardiac and cardiorespiratory arrest.⁵ Conversely, substituting the liposomal or lipid complex formulation for conventional amphotericin B could lead to treatment failure through under-dosing of the active ingredient.

Given the serious risks associated with substitution errors involving amphotericin B and the continuing occurrence of these errors, hospitals are urged to assess current practices and implement system-based safeguards for this medication.

Advice for Hospitals

Make medication safety a strategic priority:

- Consider including amphotericin B on the hospital’s list of high-alert medications to support additional safety redundancies.

Make system-based changes to enhance safety:

- Consider carrying only one amphotericin B formulation on formulary, if clinically appropriate.
- If more than one formulation is required, consider the following:
 - Create order sets that include the patient’s weight, the dose per weight, and the dose calculation for all amphotericin B orders.
 - For all medication order communication (e.g., order sets, computerized order entry), ensure that “amphotericin B” is preceded by the medication descriptor (e.g., conventional, lipid complex, or liposomal) and is followed by the trade name (i.e., liposomal amphotericin B [AmBisome]).
- Segregate storage areas in the fridge for different formulations, and use cautionary labels.
- Institute dose warnings for amphotericin B products, with “hard stops” where possible, in order-entry software (pharmacy and prescriber) and infusion pumps.

Sustain high-quality practice:

- Ensure clinical review and order-entry verification by a pharmacist for all amphotericin B orders. For after-hours orders, this may require a pharmacist consult prior to the first dose.

- Consider restricting the preparation and dispensing of amphotericin B to pharmacy (i.e., vials of amphotericin B unavailable in floor stock, automated dispensing cabinets) to preserve a redundant check system.

Case Summary

A handwritten order for amphotericin B (liposomal) 5 mg/kg daily × 5 days was scanned to a hospital pharmacy during the day shift. In the pharmacy, the conventional form of amphotericin B was incorrectly selected during order entry and dispensed for administration at 2300h, the default time in the computerized pharmacy order-entry system. The handwritten transcription of the order onto the medication administration record (MAR) was noted as amphotericin B; the word “liposomal” was not included. The order specified that the medication was to be infused over a period of 4 hours, and an infusion of 300 mg was started at 2300h. The patient experienced shivering and chills, which prompted involvement of a critical care response team, and the medication was stopped. The infusion was subsequently resumed after administration of ranitidine, diphenhydramine and hydrocortisone. The incorrect dispensing and administration of conventional amphotericin B was discovered by a pharmacist the next morning. The patient’s clinical status deteriorated, requiring admission to the intensive care unit, followed by transfer to an external facility for plasmapheresis.

Learning from Analysis

The facility where this incident occurred identified a number of contributing factors including availability of more than one formulation; difficulty in interpreting the original order; presentation of the conventional formulation first in the computerized pharmacy order system; difficulty accessing the drug information in a new online parenteral drug manual; and a pre-existing default administration time of 2300h, when clinical advice from a pharmacist was less readily available.

Since this incident, the facility has started to carry just one formulation of this drug, liposomal amphotericin B (AmBisome), and has enhanced the availability of parenteral drug information for nursing staff. The default time for administration of amphotericin B has been changed to the day shift. An order set was developed, which includes the patient’s weight, the dose per weight, and the dose calculation, as well as space for lab investigations, IV fluids, and pre-medication orders. ISMP Canada also recommends the use of infusion pumps with software that can assist in reducing drug errors by alerting the user if the dose ordered is outside a specified dosing range.

Conclusion

Patient harm continues to arise from substitution errors involving the various formulations of amphotericin B. Strategies such as carrying only one formulation, developing order sets, utilizing supportive technology and ensuring clinical review by a pharmacist prior to the first dose may help to reduce the possibility of this type of error being repeated.

References for this bulletin are available at:

www.ismp-canada.org/download/ocil/ISMPCONCIL2015-14_AmphotericinB_References.pdf

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We gratefully acknowledge the review of this bulletin by the facility where the incident described took place.

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