

ISMP Canada Safety Bulletin

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WARNING: Prevent Mix-ups between Conventional amphotericin B (Fungizone®) and Lipid-based amphotericin B products (AmBisome® or Abelcet®)

ISMP Canada has been advised of two cases in Canada where patients received conventional amphotericin B desoxycholate (Fungizone®) intravenously (IV), when the intended product was a lipid-based amphotericin B product (AmBisome® or Abelcet®). Since the recommended dose for conventional amphotericin B is much lower than the doses recommended for lipid-based products, the consequences of such substitution errors result in the administration of toxic doses of amphotericin B that are potentially lethal. Similar accidents and one near miss incident, have been described in the U.S.¹⁻⁴

Conventional amphotericin B (Fungizone®) doses **should never exceed 1.5 mg/kg/day**, and usually do not exceed 1 mg/kg/day. An average daily dose of amphotericin B (Fungizone®) in a 70 kg adult patient is **70 mg or less**. The amphotericin B lipid-based products (AmBisome® or Abelcet®) are dosed at up to 5 mg/kg/day. A typical daily dose of the lipid-based product for this same patient would be **350 mg**. Because of the toxicity of amphotericin B, a dose of 350 mg given in error as conventional amphotericin B could lead to serious renal and/or cardiorespiratory complications and possibly death. The U.S. error reports included two deaths as a result of substitution errors where conventional amphotericin B was administered at dosages intended for the lipid complex or liposomal product.^{1,2}

The reports submitted to ISMP Canada included information about prevention strategies that were implemented at the locations where the errors occurred. We believe that the risk for these errors in hospitals or outpatient settings is high. Theoretically, any hospital or Pharmacy that carries the conventional amphotericin B product is at risk for a substitution error if a lipid-based product is ordered. We ask that you consider implementing the following suggested system safeguards regardless of which amphotericin B products you may currently have on hand. You will note from the recommendations that there are important **roles for PHYSICIANS and NURSES and PHARMACISTS to prevent medication errors with amphotericin B products.**

1. When writing orders, or communicating order information use both the **complete generic name** and the **brand name**: “regular amphotericin B (Fungizone)” **or** “liposomal

amphotericin B (AmBisome)” **or** “lipid complex amphotericin B (Abelcet)”.

2. Communicate the patient weight and dose calculation in the order.
3. When “re-orders” are written indicate the full order, including the **dose** and **brand name**. “Continue amphotericin B” should be considered an incomplete order.
4. When transcribing information to the Medication Administration Record (MAR), include both the complete generic name and the brand name.
5. Ensure that both the generic name and brand name appear in Pharmacy order entry systems. Ensure all labels used in dispensing include both the generic and brand name.
6. Add warning statements (or warning screens) describing the risk for error, and add maximum dose “flags”, to computerized medication order entry systems.
7. Promote the use of computer systems for all order entry. Review situations when medications are prepared without the support of either a pharmacy order entry system, or a physician order entry system. Computer systems, when optimized, can provide critical medication system safeguards, including prevention of an excessive amphotericin B dose.
8. In order to preserve a redundant check system, amphotericin B products are best restricted to dispensing by a pharmacist after required preparation and labelling is accomplished.
9. Always “question” the need to add more than two vials of any drug to one IV solution. Using more than two containers for a single dose should raise “automatic warning flags” and be a “trigger” to all staff to perform extra checks to the order and preparation procedures.
10. In the Pharmacy, conventional and lipid based products should not be stored together. Consider the use of cautionary labels or another mechanism (e.g. warning sign) to remind staff about the differences between products.
11. Storage of amphotericin B products in patient care areas and automated dispensing equipment is discouraged.
12. Add a warning statement to any I.V. guideline documents or drug charts produced by the hospital, specifically describing the potential for error-induced injury with amphotericin B products.

13. Ensure that drug information is easily and readily accessible in all patient-care areas.
14. Verify brand name and dose and patient weight when obtaining a medication history.
15. Verify the dose if you are unfamiliar about the drug and/or dose prior to prescribing / dispensing and/or administering the drug.
16. If staff, patients or family members notice a change in the solution's appearance - stop and verify that the correct drug is being used. Lipid-based products may be seen as a "milky" amber colour rather than as a clear amber-coloured solution for the conventional product. In one of the cases described by ISMP USA³, the patient's wife identified the dispensing error. She noticed that the colour of the IV solution (Fungizone[®]) was darker than the previously administered, and correct, lipid-based solution.
17. Teach patients (or their family) about the drug and dose they are receiving. This is particularly important if the patient

will continue therapy on an out-patient basis. We now have ample evidence that the educated patient will add safety to our system.

Although the reports received by ISMP USA and ISMP Canada affected adult patients, there are case reports in the literature which describe accidental overdose errors with amphotericin B in neonates.^{6,7} It is suggested that any review of potential medication use system improvements include Neonatal Intensive Care Units.

Consider sharing this information with all physician, nursing, and pharmacy staff.

Permission is granted to copy this newsletter in its entirety in order to communicate the information to retail pharmacies or home care agencies associated with your organization.

References:

1. Wiegman S. Cohen M. editors. ISMP Medication Safety Alert. Institute for Safe Medication Practices. Volume 2, Issue 23, November 19, 1997.
2. Wiegman S. Cohen M. editors. Hazard Alert! Confusion over liposomal products can lead to serious patient harm. ISMP Medication Safety Alert. Institute for Safe Medication Practices. January 28, 1998.
3. Cohen M. Another Ampho-terrible Mix-Up. ISMP Medication Safety Alert. Institute for Safe Medication Practices. Volume 3, Issue 14, July 15 1998.
4. Smetzer J. Cohen M. editors. ISMP Medication Safety Alert. Institute for Safe Medication Practices. Volume 4, Issue 18, September 8, 1999.
5. Cohen M. Special Alert! Medication Errors with Lipid-based Drug Products. ISMP Medication Safety Alert. Institute for Safe Medication Practices. August 18, 1998.
6. Perlman JM. Acarregui M. Gard JW. Fatal Overdose of Amphotericin B in Two Pre-term Infants. *Developmental Pharmacology & Therapeutics*. 17(3-4):187-90, 1991.
7. Koren G. Lau A. Kenyon CF. Kroppert D. Klien J. Clinical Course and Pharmacokinetics Following a Massive Overdose of Amphotericin B in a neonate. *Journal of Toxicology – Clinical Toxicology*. 28(3): 371-8, 1990.

Florinef[®] Tablet Colour Change

We have received correspondence from a pharmacist notifying us that the Florinef[®] 0.1mg tablets have changed in colour from pink to white. This has caused confusion to patients. The manufacturer has responded to the pharmacist, indicating that an auxiliary label describing the colour change will be added to future product lots.

ISMP Canada is a national voluntary medication incident and 'near miss' reporting program founded for the purpose of sharing the learning experiences from medication errors. Implementation of preventative strategies and system safeguards to decrease the risk for error-induced injury and thereby promote medication safety in healthcare is our collaborative goal.

To report a medication error to ISMP Canada: (i) visit our website www.ismp-canada.org or (ii) email us at info@ismp-canada.org or (iii) phone us at 905-886-4291. ISMP Canada guarantees confidentiality and security of information received. ISMP Canada respects the wishes of the reporter as to the level of detail to be included in our publications.