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DEAR HEALTHCARE PROFESSIONAL LETTER

Risks of medication errors with the different formulations of parenteral amphotericin B: Abelcet®, AmBisome® and Fungizone®

Dear healthcare professional,

In agreement with Saudi Food and Drug Authority (SFDA), Gilead, Acino and Bristol-Myers Squibb would like to draw your attention to a possible risk for errors of prescription, dispensing, preparation or administration with Abelcet®, AmBisome® and Fungizone®. Those errors are mainly related to the administration of Fungizone® instead of AmBisome® at a dosage and administration rate recommended for AmBisome® leading to unintentional amphotericin B overdose, which could lead to serious cardiac or renal injury.

Summary

- Amphotericin B for infusion is an antifungal available in three different formulations: one phospholipidic formulation (Abelcet®), one liposomal formulation (AmBisome®) and the conventional formulation (Fungizone®).

- **Parenteral amphotericin B formulations are NOT INTERCHANGEABLE:** substitution of one amphotericin B medicinal product by another is dangerous and should not occur.

- **Importance of prescribing these medications with their tradenames:** In order to avoid the risk of confusion between Abelcet®, AmBisome® and Fungizone®:
  - It is important that these medications are prescribed with their tradenames in addition to their INN (International Non proprietary Name) in order to avoid any risk of confusion between the different formulations of parenteral amphotericin B
  - Verify the tradename and the prescribed dose before preparation and administration.

- Reminder for specific modalities of preparation and administration:
  - **CAUTION: Amphotericin B is not compatible with 0.9% sodium chloride solution or solution containing any bacteriostatic agent (can lead to precipitation of the solute). Do not mix with other medications or electrolytes.** Those medicinal products should not be administered by an intravenous line having contained 0.9% sodium chloride unless this line has been flushed with a glucose solution for injections. If this is not possible, they should be administered via an alternative, clean infusion line.
  - **Fungizone® and AmBisome®: reconstitution with water for injection ONLY**
  - Abelcet® suspension: no reconstitution step
  - **Abelcet®, Fungizone® and AmBisome®: dilution with glucose solution for injections ONLY**

List of medicinal products containing amphotericin B for infusion – SPC (Summary of Product Characteristics)

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Comparative Table

Medicinal product	**Abelcet ®** Suspension to be diluted for infusion **Lipid complex of amphotericin B**	**Ambisome®** Lyophilisate for Dispersion for Infusion **Liposomal amphotericin B**	**Fungizone®** Powder for solution for injection **Deoxycholate amphotericin B**
Instructions for reconstitution and dilution	No reconstitution. Dilution with 5% dextrose injection to obtain a final concentration 1mg/ml.For pediatric patients and patients with cardiovascular disease the drug may be diluted with 5% Dextrose to 0.1 mg/ml for peripheral infusion and 0.2-0.5 mg/ml for central infusion in infants who can not tolerate large fluid volume.	Reconstitution of the 50 mg powder with 12 ml of water for injections (4 mg/ml) Use of a 5 µm filter during dilution Dilution with a glucose solution for injection (5%, 10% or 15%), to obtain a final concentration between 0.20 mg/ml and 2 mg/ml.	• Reconstitution of the 50 mg vial with 10 ml of water for injections (5 mg/mL) • Perform the dilution with 500mL of 5% glucose solution for a final concentration of 0.1 mg/ml. The concentration of the administered solution should not exceed 0.1 mg/ml.
Posology and method of administration	A test dose of 1mg should be given over a period of 10mins,then infusion must be stopped and the patient should be carefully observed for 30mins for any signs of hypersensitivty. If the patient shows no signs of hypersensitivity the infusion may be continued. As for use with all amphotericin B products, facilities for cardiopulmonary resuscitation should be readily at hand when administering Abelcet for the first time, due to the possible occurrence of anaphylactoid reactions. The recommended dose is **5 mg/kg/day** for 14 to 21 days. Abelcet® should be administered as an intravenous infusion at a flow rate of 2.5 mg/kg/hour An in-line filter maybe used for intravenous infusion of Abelcet. The mean pore diameter of the filter should be no less than 15 microns. For severe systemic infections treatment is generally recommended for at least 14 days.	AmBisome should be administered by intravenous infusion over a **30 – 60 minutes** period. The recommended dose is **1 mg/kg/day to 3 mg/kg/day**, as indicated	The recommended dose is **0.3 mg/kg administered over a period of 2 to 6 hours.** This drug should be administered by slow intravenous infusion given over a period of approximately 2 to 6 hours, The concentration of the intravenous infusion should not exceed 0.1 mg/ml (1 mg/10 ml). • **Under no circumstances should a total daily dose of 1.5 mg/kg be exceeded.**

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	Abelcet has been administered for as long as 28 months, and cumulative doses have been 73.6g without significant toxicity. Use in patients with renal or liver disease Systemic fungal infections in patients with renal or liver disease have been treated a successfully with Abelcet at doses comparable to the recommended dose on a bodyweight basis. In the event of renal function deteriorating on Abelcet, a risk/benefit assessment should be made before deciding whether to continue treatment. In the absence of a valid dose adaptation schedule, it is recommended that the dose of Abelcet is temporarily reduced to 2.5 mg/kg or the infusions given at longer intervals. With the current state of knowledge, however, there is no schedule that guarantees both the efficacy and the safety of the treatment.		

It is important to carefully read and follow the instructions located on the vial label and carton before performing any reconstitution/dilution of any parenteral amphotericin B formulation.

Kindly note that neither Abelcet® nor Fungizone® are registered in Saudi Arabia, but both are supplied under import permit to some institutions / hospitals.

Reporting of suspected adverse reactions
As a reminder, there is a need to report any suspected adverse reactions to the National Pharmacovigilance and Drug Safety Center (NPC):
Call: 19999
Or by email: npc.drug@sfda.gov.sa
Fax: +966 11 2057662 /
Online: https://ade.sfda.gov.sa/

We thank you to take into account such information.

Yours Sincerely,

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