Turn to the liposomal amphotericin B agent that can be kinder to the kidneys*[1]

*Based on results from a randomized, double-blind, multicenter study of 244 febrile neutropenic patients who previously received broad-spectrum antibacterial therapy, receiving either AmBisome® (amphotericin B) liposome for injection 3 mg/kg/day (n=85) or 5 mg/kg/day (n=81), or Abelcet® 5 mg/kg/day (n=78). The primary endpoint was safety and the study was not designed to draw statistically meaningful conclusions related to efficacy. Abelcet is not labeled for this indication.

INDICATIONS AND USAGE

AmBisome is indicated for the following:

- Empirical therapy for presumed fungal infection in febrile, neutropenic patients
- Treatment of Cryptococcal Meningitis in HIV-infected patients
- Treatment of patients with *Aspergillus* species, *Candida* species, and/or *Cryptococcus* species infections refractory to amphotericin B deoxycholate, or in patients where renal impairment or unacceptable toxicity precludes the use of amphotericin B deoxycholate
- Treatment of visceral leishmaniasis. In immunocompromised patients with visceral leishmaniasis treated with AmBisome, relapse rates were high following initial clearance of parasites

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

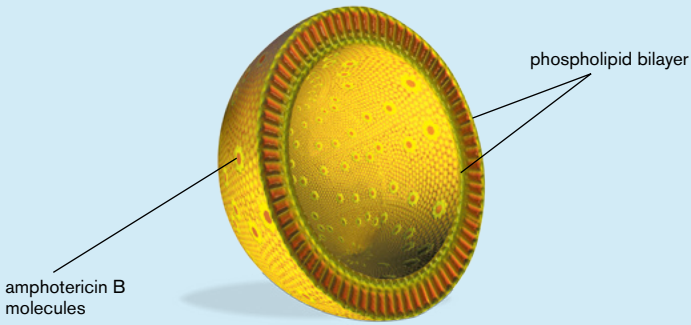
AmBisome is contraindicated in those patients who have demonstrated or have a known hypersensitivity to amphotericin B deoxycholate or any other constituents of the product, unless benefit of therapy outweighs the risk.

Please see Important Safety Information throughout brochure.
Click here for full Prescribing Information for AmBisome.

AmBisome®
(amphotericin B) liposome for injection

A true single-bilayer liposomal drug-delivery system[1]

Cross-section view of liposome[1]



Mechanism of action

Amphotericin B, the active ingredient of Am**B**isome® (amphotericin B) liposome for injection, acts by binding to the sterol component, ergosterol, of the cell membrane of susceptible fungi. It forms transmembrane channels leading to alterations in cell permeability through which monovalent ions (Na+, K+, H+, and Cl-) leak out of the cell, resulting in cell death. While amphotericin B has a higher affinity for the ergosterol component of the fungal cell membrane, it can also bind to the cholesterol component of the mammalian cell leading to cytotoxicity. Am**B**isome, the liposomal preparation of amphotericin B, has been shown to penetrate the cell wall of both extracellular and intracellular forms of susceptible fungi.

Liposomes are closed, spherical vesicles created by mixing proportions of amphophilic substances (such as phospholipids and cholesterol) so that they arrange themselves into multiple concentric bilayer membranes when hydrated in aqueous solutions.

Components of Am**B**isome

Amphotericin B	50 mg
Sucrose	900 mg
Hydrogenated soy phosphatidylcholine	213 mg
Distearoyl phosphatidylglycerol, sodium salt	84 mg
Cholesterol	52 mg
Disodium succinate hexahydrate	27 mg
α-Tocopherol	0.64 mg

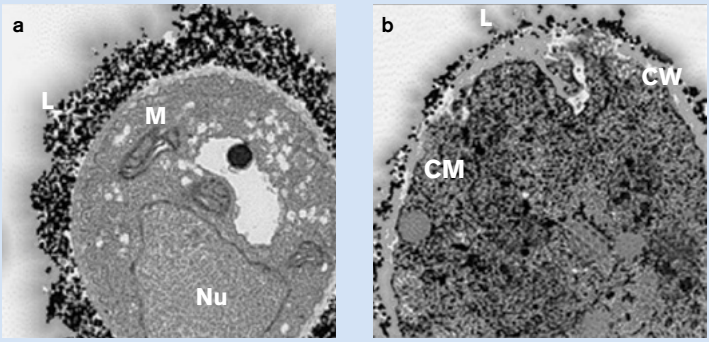
Am**B**isome may contain hydrochloric acid and/or sodium hydroxide as pH adjusters.

Please see Important Safety Information throughout brochure.
Click here for full Prescribing Information for AmBisome.

In vitro data show liposomal targeting of fungal cell wall[2]

Results from *in vitro* studies

- Initial *in vitro* studies of Am**B**isome and liposomes without drug show that both types of liposomes bind to or target the fungi, but only Am**B**isome is disrupted following binding. The data suggest that after disruption, amphotericin B damages the yeast cell membrane, allowing the dye to enter the cytoplasm of the cells



Adapted by permission from Macmillan Publishers Ltd: Adler-Moore J. Am**B**isome targeting to fungal infections. Bone Marrow Transplant 1994;14(Suppl 5):S3-7, copyright 1994.

A. fumigatus incubated with gold-labeled liposomes:
(a) without Am**B**isome, showing lipid from the liposomes in association with the surface of the fungal cell wall. Nu=nucleus; L=gold-labeled lipid of liposomes; M=mitochondria. (b) with Am**B**isome, showing lipid from the liposomes in association with the surface of the fungal cell wall, penetrating through the cell wall, and lipid accumulating in the cytoplasm. CW=cell wall; CM=cell membrane.

***In vitro* data do not necessarily correlate to clinical outcomes.**

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS

Anaphylaxis has been reported with amphotericin B–containing drugs, including Am**B**isome. If a severe reaction occurs, the Am**B**isome infusion should be immediately discontinued and the patient should not receive further infusions of Am**B**isome.

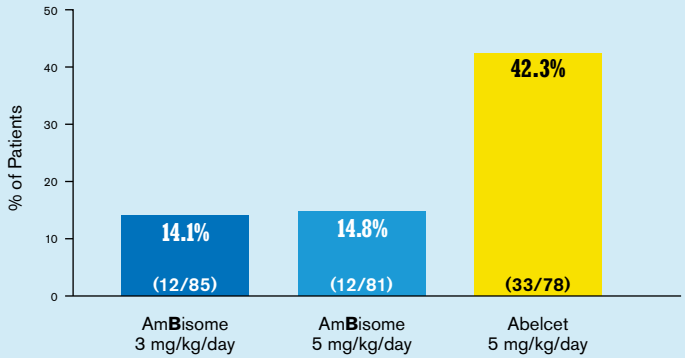
General: During the initial dosing period, patients should be under close observation. Am**B**isome has been shown to be significantly less toxic than amphotericin B deoxycholate; however, adverse events may still occur.

AmBisome®
(amphotericin B) liposome for injection

Incidence of nephrotoxicity[1]

In a clinical study, AmBisome® (amphotericin B) liposome for injection demonstrated lower incidence of nephrotoxicity than Abelcet[1]

Significantly lower incidence of nephrotoxicity*†



*Results from a randomized, double-blind, multicenter study of 244 febrile neutropenic patients who previously received broad-spectrum antibacterial therapy, receiving either AmBisome 3 mg/kg/day (n=85) or 5 mg/kg/day (n=81), or Abelcet 5 mg/kg/day (n=78). **The primary endpoint was safety and the study was not designed to draw statistically meaningful conclusions related to efficacy.**

†Nephrotoxicity was defined as a serum creatinine value 2 times baseline.

Abelcet is not indicated for empiric treatment of febrile neutropenic patients.

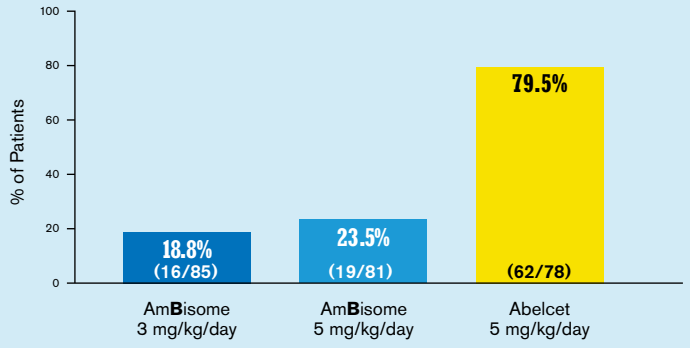
Other adverse events

In the clinical study noted above, common adverse events occurring at an incidence of 10% or more and more frequently in patients taking AmBisome compared to those taking Abelcet include: abdominal pain, sepsis, transfusion reaction, chest pain, diarrhea, bilirubinemia, edema, hypocalcemia, hypokalemia, hypomagnesemia, anxiety, confusion, headache, rash.

Please see Important Safety Information throughout brochure.
Click here for full Prescribing Information for AmBisome.

Incidence of infusion-related chills/rigors[1]

Significantly lower incidence of infusion-related chills/rigors on Day 1*[1]



*Results from a randomized, double-blind, multicenter study of 244 febrile neutropenic patients who previously received broad-spectrum antibacterial therapy, receiving either AmBisome 3 mg/kg/day (n=85) or 5 mg/kg/day (n=81), or Abelcet 5 mg/kg/day (n=78). **The primary endpoint was safety and the study was not designed to draw statistically meaningful conclusions related to efficacy.**

Abelcet is not indicated for empiric treatment of febrile neutropenic patients.

Fewer discontinuations vs Abelcet

- Treatment discontinuations due to an adverse event were higher among patients in the Abelcet group than in the AmBisome groups

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS

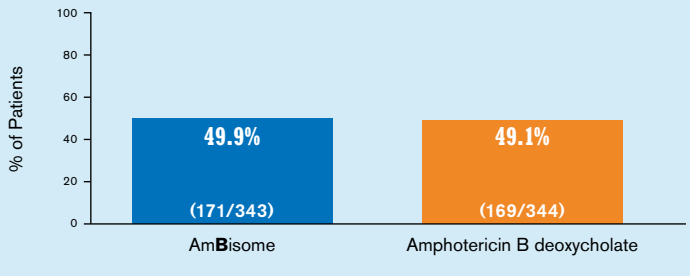
Laboratory Tests: Patient management should include laboratory evaluation of renal, hepatic, and hematopoietic function, and serum electrolytes (magnesium and potassium).

Drug-Laboratory Interactions: Serum Phosphate false elevation. False elevations of serum phosphate may occur when samples from patients receiving AmBisome are analyzed using the PHOSm assay.

AmBisome®
(amphotericin B) liposome for injection

AmBisome® (amphotericin B) liposome for injection delivered empiric antifungal power[1]

AmBisome vs amphotericin B deoxycholate: efficacy*†[1]



*Results from a randomized, double-blind, multicenter study evaluating the efficacy of AmBisome and amphotericin B deoxycholate in 687 patients with persistent fever and neutropenia. Patients received either a mean dose of AmBisome 3 mg/kg/day (n=343) or amphotericin B deoxycholate 0.6 mg/kg/day (n=344).

†Therapeutic success required: (a) resolution of fever during the neutropenic period, (b) absence of an emergent fungal infection, (c) patient survival for at least 7 days post-therapy, (d) no discontinuation of therapy due to toxicity or lack of efficacy, and (e) resolution of any study-entry fungal infection.

Please see Important Safety Information throughout brochure.
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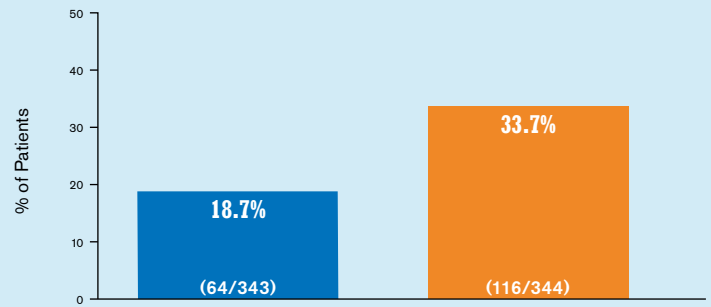
AmBisome demonstrated lower incidence of nephrotoxicity[1]

AmBisome vs amphotericin B deoxycholate: nephrotoxicity*[11]



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†Nephrotoxicity was defined as a serum creatinine value 2 times baseline.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS

Drug Interactions: No formal drug-interaction studies have been conducted with AmBisome. However, the following drugs are known to interact with amphotericin B and may interact with AmBisome: antineoplastic agents, corticosteroids and corticotropin (ACTH), digitalis glycosides, flucytosine, azoles (e.g. ketoconazole, miconazole, clotrimazole, fluconazole), leukocyte transfusions, other nephrotoxic medications, and skeletal muscle relaxants. (Please see Package Insert, Drug Interactions)

ADVERSE REACTIONS

The commonly reported adverse reactions across all studies with an incidence of >20% with AmBisome include: rash, hyperglycemia, hypokalemia, hypomagnesemia, diarrhea, nausea, vomiting, anemia, increased alkaline phosphatase, increased blood urea nitrogen, chills, insomnia, increased creatinine, and dyspnea.

AmBisome®
(amphotericin B) liposome for injection

A broad range of indications

Recommended initial dose for each indication for adult and pediatric patients

AmBisome® (amphotericin B) liposome for injection is not interchangeable or substitutable on a mg per mg basis with other amphotericin B products. Different amphotericin B products are not equivalent in terms of pharmacodynamics, pharmacokinetics and dosing.[1]

Indication See below for full indications	AmBisome dose*[1] (mg/kg/day)	Abelcet dose[3] (mg/kg/day)
Empiric therapy	3	N/A
Invasive fungal infections†‡ *Aspergillus* *Candida* *Cryptococcus*	3–5	5
Cryptococcal meningitis in HIV-infected patients	6	N/A
Visceral leishmaniasis Immunocompetent patients	3 (days 1–5) and 3 on days 14, 21	N/A
Immunocompromised patients	4 (days 1–5) and 4 on days 10, 17, 24, 31, 38	N/A

*The toxicity of Am**B**isome due to overdose has not been defined. Repeated daily doses up to 10 mg/kg in pediatric patients and 15 mg/kg in adult patients have been administered in clinical trials with no reported dose-related toxicity.

†Abelcet is indicated for the treatment of invasive fungal infections in patients who are refractory to or intolerant of conventional amphotericin B therapy.

‡Dosing and rate of infusion for Am**B**isome should be individualized to the needs of the specific patient to ensure maximum efficacy while minimizing systemic toxicities or adverse events.

HIV=human immunodeficiency virus

N/A=not applicable

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- Treatment of visceral leishmaniasis. In immunocompromised patients with visceral leishmaniasis treated with Am**B**isome, relapse rates were high following initial clearance of parasites

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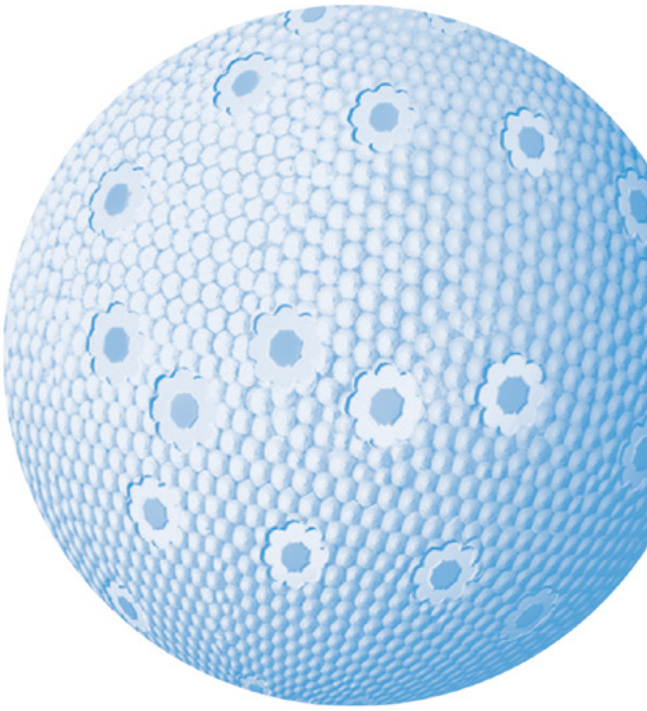

IMPORTANT SAFETY INFORMATION (CONTINUED)

ADVERSE REACTIONS

Infusion related reactions include chills/rigors, fever, nausea, vomiting, hypertension, tachycardia, dyspnea, and hypoxia. There were a few reports of flushing, back pain with or without chest tightness, and chest pain associated with Am**B**isome administration; on occasion this has been severe. Where these symptoms were noted, reaction developed within a few minutes after the start of infusion and disappeared rapidly when the infusion was stopped. These symptoms do not occur with every dose and usually do not recur on subsequent administrations when the infusion rate is slowed.

AmBisome®
(amphotericin B) liposome for injection

Experienced at being kinder to kidneys*[1]

- Significantly lower incidence of nephrotoxicity vs Abelcet
  - 14.1% of patients treated with Am**B**isome® (amphotericin B) liposome for injection 3 mg/kg/day experienced nephrotoxicity compared with 42.3% of patients treated with Abelcet 5 mg/kg/day
- Significantly fewer infusion-related events of chills/rigors and fewer discontinuations than Abelcet
- A broad range of indications

*Based on results from a randomized, double-blind, multicenter study of 244 febrile neutropenic patients who previously received broad-spectrum antibacterial therapy, receiving either Am**B**isome 3 mg/kg/day (n=85) or 5 mg/kg/day (n=81), or Abelcet 5 mg/kg/day (n=78). The primary endpoint was safety and the study was not designed to draw statistically meaningful conclusions related to efficacy. Abelcet is indicated for the treatment of invasive fungal infections in patients who are refractory to or intolerant of conventional amphotericin B therapy.

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References: 1. Am**B**isome [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Adler-Moore J. AmBisome targeting to fungal infections. Bone Marrow Transplant 1994;14(Suppl 5):S3-7. **3.** Abelcet [package insert]. Gaithersburg, MD: Leadiant Biosciences, Inc.

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AmBisome® (amphotericin B) liposome for injection