Storage/Stability/Compatibility

Clavulanate products should be stored at temperatures less than 24°C (75°F) in tight containers. Potassium clavulanate is reportedly very susceptible to moisture and should be protected from excessive humidity.

After reconstitution, oral suspensions are stable for 10 days when refrigerated. Unused portions should be discarded after that time. If kept at room temperature, suspensions are reportedly stable for 48 hours. The veterinary oral suspension should be reconstituted by adding 14 mL of water and shaking vigorously; refrigerate and discard any unused portion after 10 days.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Oral Tablets (4:1 ratio):

62.5 mg: Amoxicillin 50 mg/12.5 mg clavulanic acid (as the potassium salt)

125 mg: Amoxicillin 100 mg/25 mg clavulanic acid (as the potassium salt)

250 mg: Amoxicillin 200 mg/50 mg clavulanic acid (as the potassium salt)

375 mg: Amoxicillin 300 mg/75 mg clavulanic acid (as the potassium salt); *Clavamox Tablets*® (Pfizer); (Rx). Approved for use in dogs and cats.

Powder for Oral Suspension:

Amoxicillin 50 mg/12.5 mg clavulanic acid (as the potassium salt) per mL in 15 mL dropper bottles; C*lavamox® Drops* (Pfizer); (Rx). Approved for use in dogs and cats.

HUMAN-LABELED PRODUCTS:

Note: Human-labeled amoxicillin/clavulanate products have varying ratios of amoxicillin:clavulanate ranging from 2:1 to 7:1.

Amoxicillin (as trihydrate)/Clavulanic Acid (as potassium salt) Tablets: Amoxicillin 250 mg/125 mg clavulanic acid; Amoxicillin 500 mg/125 mg clavulanic acid; Amoxicillin 875 mg/125 mg clavulanic acid; *Augmentin*® (GlaxoSmithKline); generic (Rx)

Chewable Tablets: Amoxicillin 125 mg/31.25 mg clavulanic acid; Amoxicillin 200 mg/28.5 mg clavulanic acid; 250 mg/62.5 mg clavulanic acid & 400 mg/57 mg clavulanic acid; *Augmentin*® (GlaxoSmithKline); generic; (Rx)

Powder for Oral Suspension—Amoxicillin/Clavulanic Acid (as potassium salt) after reconstitution: Amoxicillin 125 mg/31.25 mg clavulanic acid per 5 mL in 75 mL, 100 mL & 150 mL; Amoxicillin 200 mg/28.5 mg clavulanic acid per 5 mL in 50 mL, 75 mL &100 mL; Amoxicillin 250 mg/62.5 mg clavulanic acid per 5 mL in 75 mL, 100 mL & 150 mL; Amoxicillin 400 mg/57 mg clavulanic acid per 5 mL in 50 mL, 75 mL & 100 mL; 600 mg/42.9 mg clavulanic acid per 5 mL in 75 mL, 100 mL, 125 mL & 200 mL; *Augmentin*® & *Augmentin ES-600*® (GlaxoSmithKline); *Amoclan*® (West-ward); generic; (Rx)

AMPHOTERICIN B DESOXYCHOLATE AMPHOTERICIN B LIPID-BASED

(am-foe-***ter***-i-sin ***bee***) Abelcet®, Fungizone®

ANTIFUNGAL

Prescriber Highlights

- Systemic antifungal used for serious mycotic infections
- Must be administered IV
- Nephrotoxicity is biggest concern, particularly with the deoxycholate form; newer lipid based products are less nephrotoxic & penetrate into tissues better, but are more expensive
- Renal function monitoring essential
- Drug interactions

Uses/Indications

Because the potential exists for severe toxicity associated with this drug, it should only be used for progressive, potentially fatal fungal infections. Veterinary use of amphotericin has been primarily in dogs, but other species have been treated successfully. For further information on fungal diseases treated, see the Pharmacology and Dosage sections.

The liposomal form of amphotericin B can be used to treat Leishmaniasis.

Pharmacology/Actions

Amphotericin B is usually fungistatic, but can be fungicidal against some organisms depending on drug concentration. It acts by binding to sterols (primarily ergosterol) in the cell membrane and alters the permeability of the membrane allowing intracellular potassium and other cellular constituents to "leak out." Because bacteria and rickettsia do not contain sterols, amphotericin B has no activity against those organisms. Mammalian cell membranes do contain sterols (primarily cholesterol) and the drug's toxicity may be a result of a similar mechanism of action, although amphotericin binds less strongly to cholesterol than ergosterol.

Amphotericin B has *in vitro* activity against a variety of fungal organisms, including Blastomyces, Aspergillus, Paracoccidioides, Coccidioides, Histoplasma, Cryptococcus, Mucor, and Sporothrix. Zygomycetes is reportedly variable in its response to amphotericin. Aspergillosis in dogs and cats does not tend to respond satisfactorily to amphotericin therapy. Additionally, amphotericin B has *in vivo* activity against some protozoa species, including *Leishmania* spp. and *Naegleria* spp.

It has been reported that amphotericin B has immunoadjuvant properties but further work is necessary to confirm the clinical significance of this effect.

Pharmacokinetics

Pharmacokinetic data on veterinary species is apparently unavailable. In humans (and presumably animals), amphotericin B is poorly absorbed from the GI tract and must be given parenterally to achieve sufficient concentrations to treat systemic fungal infections. After intravenous injection, the drug reportedly penetrates well into most tissues but does not penetrate well into the pancreas, muscle, bone, aqueous humor, or pleural, pericardial, synovial, and

peritoneal fluids. The drug does enter the pleural cavity and joints when inflamed. CSF levels are approximately 3% of those found in the serum. Approximately 90–95% of amphotericin in the vascular compartment is bound to serum proteins. The newer "lipid" forms of amphotericin B have higher penetration into the lungs, liver and spleen than the conventional form.

The metabolic pathways of amphotericin are not known, but it exhibits biphasic elimination. An initial serum half-life of 24–48 hours, and a longer terminal half-life of about 15 days have been described. Seven weeks after therapy has stopped, amphotericin can still be detected in the urine. Approximately 2–5% of the drug is recovered in the urine in unchanged (biologically active) form.

Contraindications/Precautions/Warnings

Amphotericin is contraindicated in patients who are hypersensitive to it, unless the infection is life-threatening and no other alternative therapies are available.

Because of the serious nature of the diseases treated with systemic amphotericin, it is not contraindicated in patients with renal disease, but it should be used cautiously with adequate monitoring.

Adverse Effects

Amphotericin B is notorious for its nephrotoxic effects; most canine patients will show some degree of renal toxicity after receiving the drug. The proposed mechanism of nephrotoxicity is via renal vasoconstriction with a subsequent reduction in glomerular filtration rate. The drug may directly act as a toxin to renal epithelial cells. Renal damage may be more common, irreversible and severe in patients who receive higher individual doses or have preexisting renal disease. Usually, renal function will return to normal after treatment is halted, but may require several months to do so.

Newer forms of lipid-complexed and liposome-encapsulated amphotericin B significantly reduce the nephrotoxic qualities of the drug. Because higher dosages may be used, these forms may also have enhanced effectiveness. A study in dogs showed that amphotericin B lipid complex was 8–10 times less nephrotoxic than the conventional form.

The patient's renal function should be aggressively monitored during therapy. A pre-treatment serum creatinine, BUN (serum urea nitrogen/SUN), serum electrolytes (including magnesium if possible), total plasma protein (TPP), packed cell volume (PCV), body weight, and urinalysis should be done prior to starting therapy. BUN, creatinine, PCV, TPP, and body weight are rechecked before each dose is administered. Electrolytes and urinalysis should be monitored at least weekly during the course of treatment. Several different recommendations regarding the stoppage of therapy when a certain BUN is reached have been made. Most clinicians recommend stopping, at least temporarily, amphotericin treatment if the BUN reaches 30–40 mg/dL, serum creatinine >3 mg/dL or if other clinical signs of systemic toxicity develop such as serious depression or vomiting.

At least two regimens have been used in the attempt to reduce nephrotoxicity in dogs treated with amphotericin desoxycholate. Mannitol (12.5 grams or 0.5–1 g/kg) given concurrently with amphotericin B (slow IV infusion) to dogs may reduce nephrotoxicity, but may also reduce the efficacy of the therapy, particularly in blastomycosis. Mannitol treatment also increases the total cost of therapy. Sodium loading prior to treating has garnered considerable support in recent years. A tubuloglomerular feedback mechanism that induces vasoconstriction and decreased GFR has been postulated for amphotericin B toxicity; increased sodium load at the glomerulus may help prevent that feedback. One clinician (Foil 1986), uses 5 mL/kg of normal saline given in two portions, before and after amphotericin B dosing and states that is has been ". . . helpful in averting renal insufficiency. . . ."

Cats are apparently more sensitive to the nephrotoxic aspects of amphotericin B, and many clinicians recommend using reduced dosages in this species (see Dosage section).

Adverse effects reported in horses include: tachycardia, tachypnea, lethargy, fever, restlessness, anorexia, anemia, phlebitis, polyuria and collapse.

Other adverse effects that have been reported with amphotericin B include: anorexia, vomiting, hypokalemia, distal renal tubular acidosis, hypomagnesemia, phlebitis, cardiac arrhythmias, non-regenerative anemia and fever (may be reduced with pretreatment with NSAIDs or a low dosage of steroids). Calcinosis cutis has been reported in dogs treated with amphotericin B. Amphotericin B can increase creatine kinase levels.

Reproductive/Nursing Safety

The safety of amphotericin B during pregnancy has not been established, but there are apparently no reports of teratogenicity associated with the drug. The risks of therapy should be weighed against the potential benefits. In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as in class: ***A*** (*Probably safe. Although specific studies may not have proved the safety of all drugs in dogs and cats, there are no reports of adverse effects in laboratory animals or women.*)

Overdosage/Acute Toxicity

No case reports were located regarding acute intravenous overdose of amphotericin B. Because of the toxicity of the drug, dosage calculations and solution preparation procedures should be double-checked. If an accidental overdose is administered, renal toxicity may be minimized by administering fluids and mannitol as outlined above in the Adverse Effects section.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving amphotericin B and may be of significance in veterinary patients:

- **CORTICOSTEROIDS:** May exacerbate the potassium-losing effects of amphotericin
- **DIGOXIN:** Amphotericin B-induced hypokalemia may exacerbate digoxin toxicity
- **FLUCYTOSINE:** Synergy (*in vitro*) between amphotericin and flucytosine may occur against strains of Cryptococcus and Candida, but increased flucytosine toxicity may also occur
- **NEPHROTOXIC DRUGS** (**aminoglycosides, polymyxin B, colistin, cisplatin, cyclosporine, methoxyflurane or vancomycin**): Since the renal effects of other nephrotoxic drugs may be additive with amphotericin B, avoid, if possible the concurrent or sequential use of these AGENTS
- **POTASSIUM-DEPLETING DRUGS** (*e.g.,* **thiazide or loop diuretics**)
- **SALINE SOLUTIONS OR WITH SOLUTIONS CONTAINING A PRESERVATIVE:** Reconstituting amphotericin B with these solutions may cause precipitation
- **SKELETAL MUSCLE RELAXANTS** (**tubocurarine**): Amphotericin B-induced hypokalemia may enhance curariform effects

Doses

All dosages are for amphotericin B desoxycholate (regular amphotericin B) unless specifically noted for the lipid-based products.

Note: Some clinicians have recommended administering a 1 mg test dose (less in small dogs or cats) IV over anywhere from 20 minutes to 4 hours and monitoring pulse, respiration rates, temperature, and if possible, blood pressure. If a febrile reaction occurs some clinicians recommend adding a glucocorticoid to the IV infusion solution or using an antipyretic prior to treating, but these practices are controversial.

A published study (Rubin et al. 1989) demonstrated less renal impairment and systemic adverse effects in dogs who received amphotericin B IV slowly over 5 hours in 1 L of D_5W than in dogs who received the drug IV in 25 mL of D_5W over 3 minutes.

DOGS:

For treatment of susceptible systemic fungal infections:

a) Two regimens can be used; after diluting vial (as outlined below in preparation of solution section), either:
   1) Rapid-Infusion Technique: Dilute quantity of stock solution to equal 0.25 mg/kg in 30 mL of 5% dextrose. Using butterfly catheter, flush with 10 mL of D_5W. Infuse amphotericin B solution IV over 5 minutes. Flush catheter with 10 mL of D_5W and remove catheter. Repeat above steps using 0.5 mg/kg 3 times a week until 9–12 mg/kg accumulated dosage is given.
   2) Slow IV Infusion Technique: Dilute quantity of stock solution to equal 0.25 mg/kg in 250–500 mL of D5W. Place indwelling catheter in peripheral vein and give total volume over 4–6 hours. Flush catheter with 10 mL of D_5W and remove catheter. Repeat above steps using 0.5 mg/kg 3 times a week until 9–12 mg/kg accumulated dosage is given. (Noxon 1989)

b) In dehydrated, sodium-depleted animals, must rehydrate before administration. Dosage is 0.5 mg/kg diluted in D5W. In dogs with normal renal function, may dilute in 60–120 mL of D5W and give by slow IV over 15 minutes. In dogs with compromised renal function, dilute in 500 mL or 1 liter of D_5W and give over slowly IV over 3–6 hours. Re-administer every other day if BUN remains below 50 mg/dl. If BUN exceeds 50 mg/dl, discontinue until BUN decreases to at least 35 mg/dl. Cumulative dose of 8–10 mg/kg is required to cure blastomycosis or histoplasmosis. Coccidioidomycosis, aspergillosis and other fungal diseases require a greater cumulative dosage. (Legendre 1995)

c) For treating systemic mycoses using the lipid-based products: *AmBisome®*, *Amphocil®* or *Abelcet®*: Give test dose of 0.5 mg/kg; then 1–2.5 mg/kg IV q48h (or Monday, Wednesday, Friday) for 4 weeks or until the total cumulative dose is reached. Use 1 mg/kg dose for susceptible yeast and dimorphic fungi until a cumulative dose of 12 mg/kg is reached; for more resistant filamentous fungal infections (*e.g.*, pythiosis) use the higher dose 2–2.5 mg/kg until a cumulative dose of 24–30 mg/kg is reached. (Greene and Watson 1998)

d) For treating systemic mycoses using the amphotericin B lipid complex (ABLC; *Abelcet®*) product: 2–3 mg/kg IV three days per week for a total of 9–12 treatments (cumulative dose of 24–27 mg). Dilute to a concentration of 1 mg/mL in dextrose 5% (D5W) and infuse over 1–2 hours (Grooters 1999)

e) For systemic mycoses using amphotericin B lipid complex (*Abelcet®*): Dilute in 5% dextrose to a final concentration of 1 mg/mL and administer at a dosage of 2–3 mg/kg three times per week for 9–12 treatments or a cumulative dosage of 24–27 mg/kg (Schulman and Marks 2005)

For blastomycosis (see general dosage guidelines above):

a) Amphotericin B 0.5 mg/kg 3 times weekly until a total dose of 6 mg/kg is given, with ketoconazole at 10–20 mg/kg (30 mg/kg for CNS, bone or eye involvement) divided for 3–6 months (Foil 1986)

b) Amphotericin B 0.15–0.5 mg/kg IV 3 times a week with ketoconazole 20 mg/day PO once daily or divided twice daily; 40 mg/kg divided twice daily for ocular or CNS involvement (for at least 2–3 months or until remission then start maintenance). When a total dose of amphotericin B reaches 4–6 mg/kg start maintenance dosage of amphotericin B at 0.15–0.25 mg/kg IV once a month or use ketoconazole at 10 mg/kg PO either once daily, divided twice daily or ketoconazole at 2.5–5 mg/kg PO once daily. If CNS/ocular involvement use ketoconazole at 20–40 mg/kg PO divided twice daily (Greene, O'Neal, and Barsanti 1984)

c) For severe cases, using amphotericin B lipid complex (*Abelcet®*): 1–2 mg/kg IV three times a week (or every other day) to a cumulative dose of 12–24 mg/kg (Taboada 2000)

For cryptococcosis (see general dosage guidelines above):

a) Amphotericin B 0.5–0.8 mg/kg SC 2–3 times per week. Dose is diluted in 0.45% NaCl with 2.5% dextrose (400 mL for cats, 500 mL for dogs less than 20 kg and 1000 mL for dogs greater than 20 kg). Concentrations greater than 20 mg/L result in local irritation and sterile abscess formation. May combine with flucytosine or the azole antifungals. (Taboada 2000)

For histoplasmosis (see general dosage guidelines above):

a) Amphotericin B 0.15–0.5 mg/kg IV 3 times a week with ketoconazole 10–20 mg/day PO once daily or divided twice daily (for at least 2–3 months or until remission then start maintenance). When a total dose of amphotericin B reaches 2–4 mg/kg, start maintenance dosage of amphotericin B at 0.15–0.25 mg/kg IV once a month or use ketoconazole at 10 mg/kg PO either once daily, divided twice daily or at 2.5–5 mg/kg PO once daily (Greene, O'Neal, and Barsanti 1984)

b) As an alternative to ketoconazole treatment: 0.5 mg/kg IV given over 6–8 hours. If dose is tolerated, increase to 1 mg/kg given on alternate days until total dose of 7.5–8.5 mg/kg cumulative dose is achieved (Macy 1987)

For Leishmaniasis:

a) Using the liposomal form of Amphotericin B: 3–3.3 mg/kg IV 3 times weekly for 3–5 treatments (Lappin 2000)

b) Using *AmBisome®* (lipid-based product): Give initial test dose of 0.5 mg/kg, then 3–3.3 mg/kg IV every 72–96 hours until a cumulative dose of 15 mg/kg is reached. May be possible to give the same cumulative dose with a lower level every 48 hours. (Greene, Hartmannn et al. 2006)

For gastrointestinal pythiosis:

a) Resect lesions that are surgically removable to obtain 5–6 cm margins. Follow-up medical therapy using the amphotericin B lipid complex (ABLC; *Abelcet®*) product: 1–2 mg/kg IV three times weekly for 4 weeks (cumulative dose 12–24 mg). May alternatively use itraconazole at 10 mg/kg PO once daily for 4–6 months. (Taboada 1999)

CATS:

For treatment of susceptible systemic fungal infections:

a) Rapid-Infusion Technique: After diluting vial (as outlined below in preparation of solution section), dilute quantity of stock solution to equal 0.25 mg/kg in 30 mL of 5% dextrose. Using butterfly catheter, flush with 10 mL of D_5W. Infuse amphotericin B solution IV over 5 minutes. Flush catheter with 10 mL of D_5W and remove catheter. Repeat above steps

using 0.25 mg/kg 3 times a week until 9–12 mg/kg accumulated dosage is given. (Noxon 1989)

For cryptococcosis (see general dosage guidelines above):

a) As an alternative therapy to ketoconazole: Amphotericin B: 0.25 mg/kg in 30 mL D_5W IV over 15 minutes q48h with flucytosine at 200 mg/kg/day divided q6h PO. Continue therapy for 3–4 weeks after clinical signs have resolved or until BUN >50 mg/dl. (Legendre 1989)

b) Amphotericin B 0.15–0.4 mg/kg IV 3 times a week with flucytosine 125–250 mg/day PO divided two to four times a day. When a total dose of amphotericin B reaches 4–6 mg/kg, start maintenance dosage of amphotericin B at 0.15–0.25 mg/kg IV once a month with flucytosine at dosage above or with ketoconazole at 10 mg/kg PO once daily or divided twice daily (Greene, O'Neal, and Barsanti 1984)

c) Amphotericin B 0.5–0.8 mg/kg SC 2–3 times per week. Dose is diluted in 0.45% NaCl with 2.5% dextrose (400 mL for cats, 500 mL for dogs less than 20 kg and 1000 mL for dogs greater than 20 kg). Concentrations greater than 20 mg/L result in local irritation and sterile abscess formation. May combine with flucytosine or the azole antifungals. (Taboada 2000)

d) For treating systemic mycoses using the amphotericin B lipid complex (ABLC; *Abelcet*®) product: 1 mg/kg IV three days per week for a total of 12 treatments (cumulative dose of 12 mg). Dilute to a concentration of 1 mg/mL in dextrose 5% (D5W) and infuse over 1–2 hours (Grooters 1999)

For histoplasmosis (see general dosage guidelines above):

a) Amphotericin B: 0.25 mg/kg in 30 mL D_5W IV over 15 minutes q48h with ketoconazole at 10 mg/kg q12h PO. Continue therapy for 4–8 weeks or until BUN >50 mg/dl. If BUN increases greater than 50 mg/dl, continue ketoconazole alone. Ketoconazole is used long-term (at least 6 months of duration. (Legendre 1989)

b) Amphotericin B 0.15–0.5 mg/kg IV 3 times a week with ketoconazole 10 mg/day PO once daily or divided twice daily (for at least 2–3 months or until remission, then start maintenance). When a total dose of amphotericin B reaches 2–4 mg/kg, start maintenance dosage of amphotericin B at 0.15–0.25 mg/kg IV once a month or use ketoconazole at 10 mg/kg PO either once daily, divided twice daily or at 2.5–5 mg/kg PO once daily (Greene, O'Neal, and Barsanti 1984)

For blastomycosis (see general dosage guidelines above):

a) Amphotericin B: 0.25 mg/kg in 30 mL D_5W IV over 15 minutes q48h with ketoconazole: 10 mg/kg q12h PO (for at least 60 days). Continue amphotericin B therapy until a cumulative dose of 4 mg/kg is given or until BUN >50 mg/dl. If renal toxicity does not develop, may increase dose to 0.5 mg/kg of amphotericin B. (Legendre 1989)

b) Amphotericin B 0.15–0.5 mg/kg IV 3 times a week with ketoconazole 10 mg/day PO once daily or divided twice daily (for at least 2–3 months or until remission then start maintenance). When a total dose of amphotericin B reaches 4–6 mg/kg start maintenance dosage of amphotericin B at 0.15–0.25 mg/kg IV once a month or use ketoconazole at 10 mg/kg PO either once daily, divided twice daily or ketoconazole at 2.5–5 mg/kg PO once daily. If CNS/ocular involvement, use ketoconazole at 20–40 mg/kg PO divided twice daily. (Greene, O'Neal, and Barsanti 1984)

■ **RABBITS/RODENTS/SMALL MAMMALS:**

a) Rabbits: 1 mg/kg/day IV (Ivey and Morrisey 2000)

■ **HORSES:**

For treatment of susceptible systemic fungal infections:

a) For fungal pneumonia: Day 1: 0.3 mg/kg IV; Day 2: 0.4 mg/kg IV; Day 3: 0.6 mg/kg IV; days 4–7: no treatment; then every other day until a total cumulative dose of 6.75 mg/kg has been administered (Foreman 1999)

b) For phycomycoses and pulmonary mycoses: After reconstitution (see below) transfer appropriate amount of drug to 1L of D5W and administer using a 16 g needle IV at a rate of 1 L/hr. Dosage schedule follows: Day 1: 0.3 mg/kg IV; Day 2: 0.45 mg/kg IV; Day 3: 0.6 mg/kg IV; then every other day for 3 days per week (MWF or TTHSa) until clinical signs of either improvement or toxicity occur. If toxicity occurs, a dose may be skipped, dosage reduced or dosage interval lengthened. Administration may extend from 10–80 days. (Brumbaugh 1987)

For intrauterine infusion: 200–250 mg. Little science is available for recommending doses, volume infused, frequency, diluents, etc. Most intrauterine treatments are commonly performed every day or every other day for 3–7 days. (Perkins 1999)

■ **LLAMAS:**

For treatment of susceptible systemic fungal infections:

a) A single case report. Llama received 1 mg test dose, then initially at 0.3 mg/kg IV over 4 hours, followed by 3 L of LRS with 1.5 mL of B-Complex and 20 mEq of KCl added. Subsequent doses were increased by 10 mg and given every 48 hours until reaching 1 mg/kg q48h IV for 6 weeks. Animal tolerated therapy well, but treatment was ultimately unsuccessful (Coccidioidomycosis). (Fowler 1989)

■ **BIRDS:**

For treatment of susceptible systemic fungal infections:

a) For raptors and psittacines with aspergillosis: 1.5 mg/kg IV three times daily for 3 days with flucytosine or follow with flucytosine. May also use intratracheally at 1 mg/kg diluted in sterile water once to 3 times daily for 3 days in conjunction with flucytosine or nebulized (1 mg/mL of saline) for 15 minutes twice daily. Potentially nephrotoxic and may cause bone marrow suppression. (Clubb 1986)

b) 1.5 mg/kg IV q12h for 3–5 days; topically in the trachea at 1 mg/kg q12h; 0.3–1 mg/mL nebulized for 15 minutes 2–4 times daily (Flammer 2003a)

■ **REPTILES:**

For susceptible fungal respiratory infections:

a) For most species: 1 mg/kg diluted in saline and given intratracheally once daily for 14–28 treatments (Gauvin 1993)

Monitoring

Also see Adverse Effects section

- BUN and serum creatinine every other day while dosage is being increased, and at least weekly thereafter during therapy
- Serum electrolytes (sodium, potassium and magnesium) weekly
- Liver function tests weekly
- CBC weekly
- Urinalysis weekly
- TPP at least weekly
- Animal's weight

Client Information

- Clients should be informed of the potential seriousness of toxic effects that can occur with amphotericin B therapy
- The costs associated with therapy

Chemistry/Synonyms

A polyene macrolide antifungal agent produced by Streptomyces nodosus, amphotericin B occurs as a yellow to orange, odorless or practically odorless powder. It is insoluble in water and anhydrous alcohol. Amphotericin B is amphoteric and can form salts in acidic or basic media. These salts are more water soluble but possess less antifungal activity than the parent compound. Each mg of amphotericin B must contain not less than 750 micrograms of anhydrous drug. Amphotericin A may be found as a contaminant in concentrations not exceeding 5%. The commercially available powder for injection contains sodium desoxycholate as a solubilizing agent.

Newer lipid-based amphotericin B products are available that have less toxicity than the conventional desoxycholate form. These include amphotericin B cholesteryl sulfate complex (amphotericin B colloidal dispersion, ABCD, *Amphotec®*), amphotericin B lipid complex (ABLC, *Abelcet®*), and amphotericin B liposomal (ABL, L-AMB, *Ambisome®*).

Amphotericin B may also be known as: amphotericin; amphotericin B cholesteryl sulfate complex, amphotericin B lipid complex, amphotericin B liposome, amphotericin B phospholipid complex, amphotericin B-Sodium cholesteryl sulfate complex, anfotericina B, or liposomal amphotericin B; many trade names are available.

Storage/Stability/Compatibility

Vials of amphotericin B powder for injection should be stored in the refrigerator (2–8°C), protected from light and moisture. Reconstitution of the powder must be done with sterile water for injection (no preservatives—see directions for preparation in the Dosage Form section below).

After reconstitution, if protected from light, the solution is stable for 24 hours at room temperature and for 1 week if kept refrigerated. After diluting with D5W (must have pH >4.3) for IV use, the manufacturer recommends continuing to protect the solution from light during administration. Additional studies however, have shown that potency remains largely unaffected if the solution is exposed to light for 8–24 hours.

Amphotericin B deoxycholate is reportedly **compatible** with the following solutions and drugs: D5W, D5W in sodium chloride 0.2%, heparin sodium, heparin sodium with hydrocortisone sodium phosphate, hydrocortisone sodium phosphate/succinate and sodium bicarbonate.

Amphotericin B deoxycholate is reportedly **incompatible** with the following solutions and drugs: normal saline, lactated Ringer's, D5-normal saline, D5-lactated Ringer's, amino acids 4.25%–dextrose 25%, amikacin, calcium chloride/gluconate, carbenicillin disodium, chlorpromazine HCl, cimetidine HCl, diphenhydramine HCl, dopamine HCl, edetate calcium disodium (Ca EDTA), gentamicin sulfate, kanamycin sulfate, lidocaine HCl, metaraminol bitartrate, methyldopate HCl, nitrofurantoin sodium, oxytetracycline HCl, penicillin G potassium/sodium, polymyxin B sulfate, potassium chloride, prochlorperazine mesylate, streptomycin sulfate, tetracycline HCl, and verapamil HCl. Compatibility is dependent upon factors such as pH, concentration, temperature and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Amphotericin B Desoxycholate Powder for Injection: 50 mg in vials; *Amphocin®* (Gensia Sicor); *Fungizone® Intravenous* (Apothecon); generic (Pharma-Tek); (Rx)

Directions for reconstitution/administration: Using strict aseptic technique and a 20 gauge or larger needle, rapidly inject 10 mL of sterile water for injection (without a bacteriostatic agent) directly into the lyophilized cake; immediately shake well until solution is clear. A 5 mg/mL colloidal solution results. Further dilute (1:50) for administration to a concentration of 0.1 mg/mL with 5% dextrose in water (pH >4.2). An in-line filter may be used during administration, but must have a pore diameter >1 micron.

Amphotericin B Lipid-Based Suspension for Injection: 100 mg/20 mL (as lipid complex) in 10 mL & 20 mL vials with 5 micron filter needles: *Abelcet®* (Enzon); (Rx)

Amphotericin B Lipid-Based Powder for Injection: 50 mg/vial (as cholesteryl) in 20 mL vials; 100 mg (as cholesteryl) in 50 mL vials; *Amphotec®* (Sequus Pharmaceuticals); 50 mg (as liposomal) in single-dose vials with 5-micron filter; *AmBisome®* (Fujisawa; (Rx)

Amphotericin B is also available in topical formulations: *Fungizone®* (Apothecon); (Rx)

AMPICILLIN
AMPICILLIN SODIUM
AMPICILLIN TRIHYDRATE

(am-pi-***sill***-in; sul-***bak***-tam) Polyflex®

AMINOPENICILLIN

Prescriber Highlights

- Bactericidal aminopenicillin with same spectrum as amoxicillin (ineffective against bacteria that produce beta-lactamase)
- Most likely adverse effects are GI-related, but hypersensitivity & other adverse effects rarely occur; may cause more GI effects than amoxicillin when used orally
- More susceptible than is amoxicillin to food reducing oral absorption
- Available in both parenteral & oral forms

Uses/Indications

In dogs and cats, ampicillin is not as well absorbed after oral administration as amoxicillin and its oral use has largely been supplanted by amoxicillin. It is used commonly in parenteral dosage forms when an aminopenicillin is indicated in all species.

The aminopenicillins, also called the "broad-spectrum" or ampicillin penicillins, have increased activity against many strains of gram-negative aerobes not covered by either the natural penicillins or penicillinase-resistant penicillins, including some strains of *E. coli,* Klebsiella, and Haemophilus.

Pharmacology/Actions

Like other penicillins, ampicillin is a time-dependent, bactericidal (usually) agent that acts via inhibiting cell wall synthesis. Ampicillin and the other aminopenicillins have increased activity against many strains of gram-negative aerobes not covered by either the natural penicillins or penicillinase-resistant penicillins, including some strains of *E. coli,* Klebsiella and Haemophilus. Like the natural penicillins, they are susceptible to inactivation by beta-lactamase-producing bacteria (*e.g.*, Staph aureus). Although not as active as the natural penicillins, they do have activity against many anaerobic bacteria, including Clostridial organisms. Organisms that are