AZITHROMYCIN

(ay-zith-roe-*my*-sin) Zithromax®

MACROLIDE ANTIBIOTIC

Prescriber Highlights

- Oral & parenteral human macrolide antibiotic; potentially useful for a wide range of infections in veterinary patients
- Very long tissue half-lives in dogs & cats
- Contraindications: Hypersensitivity to macrolides
- Caution: Hepatic disease
- Adverse Effects: Potentially GI distress, but less so than with erythromycin
- Relatively expensive, but prices are dropping secondary to the availability of generic products

Uses/Indications

Azithromycin with its relative broad spectrum and favorable pharmacokinetic profile may be useful for a variety of infections in veterinary species. Little data is published at this time, however. Azithromycin has been shown to be ineffective in the treatment of *Mycoplasma haemofelis* in cats.

Azithromycin may be potentially useful for treating Rhodococcus infections in foals.

Pharmacology/Actions

Like other macrolide antibiotics, azithromycin inhibits protein synthesis by penetrating the cell wall and binding to the 50S ribosomal subunits in susceptible bacteria. It is considered a bacteriostatic antibiotic.

Azithromycin has a relatively broad spectrum. It has *in vitro* activity (does not necessarily indicate clinical efficacy) against gram-positive organisms such as *Streptococcus pneumoniae*, *Staph aureus*; gram-negative organisms such as *Haemophilus influenzae*; *Bordetella* spp.; and *Mycoplasma pneumoniae*, *Borrelia burgdorferi* and *Toxoplasma* spp.

Pharmacokinetics

The pharmacokinetics of azithromycin have been described in cats and dogs. In dogs, the drug has excellent bioavailability after oral administration (97%). Tissue concentrations apparently do not mirror those in the serum after multiple doses and tissue half-lives in the dogs may be up to 90 hours. Greater than 50% of an oral dose is excreted unchanged in the bile. In cats, oral bioavailability is 58%. Tissue half-lives are less than in dogs, and range from 13 hours in adipose tissue to 72 hours in cardiac muscle. As with dogs, cats excrete the majority of a given dose in the bile.

In foals, azithromycin is variably absorbed after oral administration with a mean systemic bioavailability ranging from 40–60%. It has a very high volume of distribution (11.6–18.6 L/kg). Elimination half-life is approximately 20–26 hours. The drug concentrates in bronchoalveolar cells and pulmonary epithelial fluid. Elimination half-life in PMN's is about 2 days. In adult horses, oral bioavailability is low (1–7%).

When compared to erythromycin, azithromycin has better absorption characteristics, longer tissue half-lives, and higher concentrations in tissues and white blood cells.

Goats have an elimination half-life of 32.5 hours (IV), 45 hours (IM), an apparent volume of distribution (steady-state) of 34.5 L/kg and a clearance of 0.85 L/kg/hr.

Rabbits have an elimination half-life of 24.1 hours (IV), and 25.1 hours (IM). IM injection has a high bioavailability, but causes some degree of muscle damage at the injection site.

Sheep have an elimination half-life average of 48 hours (IV), 61 hours (IM), an apparent volume of distribution (steady-state) of 34.5 L/kg and a clearance of 0.52 L/kg/hr.

Contraindications/Precautions/Warnings

Azithromycin is contraindicated in animals hypersensitive to any of the macrolides. It should be used with caution in patients with impaired hepatic function.

Adverse Effects

Azithromycin can cause vomiting in dogs if high doses are given. When compared to erythromycin, azithromycin has less GI adverse effects. Other adverse effects, particularly those associated with the liver, may become apparent in dogs and cats as more experience is attained. Local IV site reactions have occurred in patients receiving IV azithromycin.

Reproductive/Nursing Safety

Safety during pregnancy has not been fully established; use only when clearly necessary. 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.*)

Overdosage/Acute Toxicity

Acute oral overdoses are unlikely to cause significant morbidity other than vomiting, diarrhea and GI cramping.

Drug Interactions

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

- **ANTACIDS (oral; magnesium- and aluminum-containing)**: May reduce the rate of absorption of azithromycin; suggest separating dosages by 2 hours
- **CISAPRIDE**: No data on azithromycin, but other macrolides contraindicated with cisapride; use with caution
- **CYCLOSPORINE**: Azithromycin may potentially increase cyclosporine blood levels; monitor carefully
- **DIGOXIN**: No data on azithromycin, but other macrolides can increase digoxin levels; monitor carefully
- **PIMOZIDE**: Azithromycin use is contraindicated in patients taking pimozide (unlikely to be used in vet med—used for Tourette's disorder in humans). Acute deaths have occurred.

Doses

- **DOGS:**

  For susceptible infections:

  a) 5–10 mg/kg PO once daily for 3–5 days (Trepanier 1999), (Sykes 2003)

  b) 5 mg/kg PO once daily for 2 days, then every 3–5 days for a total of 5 doses (Aucoin 2002b)

  c) For "Derm" infections: 5–10 mg/kg PO once daily for 5–7 days. For animals that are difficult to pill, a dose given every 5 days (after the initial 5–7 day course of therapy) may be effective if continued treatment is necessary. (Merchant 2000)

d) For canine pyoderma: 10 mg/kg PO once daily for 5–10 days (Ramadinha, Ribeiro et al. 2002)

e) For *Babesia gibsoni* (Asian genotype) infections: Atovaquone 13.3 mg/kg PO q8h with a fatty meal and Azithromycin 10 mg/kg PO once daily. Give both drugs for 10 days. Reserve immunosuppressive therapy for cases that are not rapidly responding (3–5 days) to anti-protozoal therapy. (Birkenheuer, Levy et al. 2004), (Birkenheuer 2006)

■ **CATS:**

For susceptible infections:

a) 5–10 mg/kg PO once daily for 3–5 days (Trepanier 1999), (Sykes 2003)

b) 5 mg/kg PO once daily for 2 days, then every 3–5 days for a total number of doses of 5 (Aucoin 2002b)

c) For "Derm" infections: 7–15 mg/kg PO q12h daily for 5–7 days. For animals that are difficult to pill, a dose given every 5 days (after the initial 5–7 day course of therapy) may be effective if continued treatment is necessary. (Merchant 2000)

d) For susceptible upper respiratory infections: 5–10 mg/kg PO once daily for 5 days, then q72h (every 3rd day) long-term. If there is an initial positive response to the antibiotic, therapy should be continued for 6–8 weeks without changing the antibiotic. (Scherk 2006)

■ **HORSES:**

For treatment of *R. equi* infections in foals:

a) 10 mg/kg PO once daily. Because of persistence of high levels in bronchoalveolar cells and pulmonary epithelial lining fluid, after 5 days of once daily treatment, every other day (q48h) dosing may be appropriate. (Jacks, Giguere et al. 2001)

■ **RODENTS/SMALL MAMMALS:**

a) Rabbits: For Staphylococcus osteomyelitis: 50 mg/kg PO once daily with 40 mg/kg of rifampin q12h PO (Ivey and Morrisey 2000)

b) Rabbits: For jaw abscesses: 15–30 mg/kg PO once daily (q24h). Systemic antibiotic treatment is continued for 2–4 weeks post-operatively. Advise owners to discontinue treatment if anorexia or diarrhea occurs. (Johnson 2006f)

c) Guinea pigs: For Pneumonia: 15–30 mg/kg PO once daily (q24h). Advise owners to discontinue treatment if soft stools develop. (Johnson 2006d)

Monitoring

■ Clinical efficacy
■ Adverse effects

Client Information

■ Give medication as prescribed. Do not refrigerate oral suspension and shake well before each use. If using the suspension, preferably give to an animal with an empty stomach. Discard any unused oral suspension after 14 days.
■ Contact veterinarian if animal develops severe diarrhea or vomiting, or if condition deteriorates after beginning therapy.

Chemistry/Synonyms

A semisynthetic azalide macrolide antibiotic, azithromycin dihydrate occurs as a white crystalline powder. In one mL of water at neutral pH and at 37° C, 39 mg are soluble. Although commercial preparations are available as the dihydrate, potency is noted as the anhydrous form.

Azithromycin may also be known as: azithromycinum, acitromicina, CP-62993, or XZ-450; many trade names are available.

Storage/Stability/Compatibility

The commercially available tablets should be stored at temperatures less than 30°C. Products for reconstitution for oral suspension should be stored between 5–30°C before reconstitution with water. After reconstitution the multiple dose product may be stored between 5–30°C for up to ten days and then discarded. The single dose packets should be given immediately after reconstitution.

The injectable product should be stored below 30°C. After reconstitution with sterile water for injection, solutions containing 100 mg/mL are stable for 24 hours if stored below 30°C. Azithromycin injection is physically and chemically **compatible** with several intravenous solutions, including: half-normal and normal saline, D5W, LRS, D5 with 0.3% or 0.45% sodium chloride, and D5 in LRS. When azithromycin injection is diluted into 250–500 mL of one of the above solutions, it remains physically and chemically stable for 24 hours at room temperature and up to 7 days if kept refrigerated at 5°C.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

Preparations compounded for dogs and cats may be available from compounding pharmacies.

HUMAN-LABELED PRODUCTS:

Azithromycin Tablets: 250 mg, 500 mg & 600 mg (as dihydrate); *Zithromax*® (Pfizer); generic; (Rx)

Azithromycin Powder for Oral Suspension: 100 mg/5 mL (as dihydrate) when reconstituted in 300 mg bottles; 200 mg/5 mL in 600 mg, 900 mg, & 1200 mg bottles; and 1 g/packet (as dihydrate) in 2 single-dose packets; *Zithromax*® (Pfizer); generic; 167 mg per 5 mL (as dihydrate) when reconstituted in 2 g bottles; *Zmax*®(Pfizer); (Rx)

Azithromycin Powder for Injection (lyophilized): 500 mg in 10 mL vials; *Zithromax*® (Pfizer); generic; (Rx)

AZTREONAM

(az-***tree***-oh-nam) Azactam®

INJECTABLE MONOBACTAM ANTIBACTERIAL

Prescriber Highlights

- Monobactam injectable antibiotic with good activity against a variety of gram-negative aerobic bacteria
- May be considered for use for treating serious infections, when aminoglycosides or fluoroquinolones are ineffective or relatively contraindicated
- Very limited information available regarding dosing & adverse effect profile

Uses/Indications

Aztreonam is a monobactam antibiotic that may be considered for use in small animals for treating serious infections caused by a wide variety of aerobic and facultative gram-negative bacteria, including strains of *Citrobacter*, *Enterobacter*, *E. coli*, *Klebsiella*, *Proteus, Pseudomonas* and *Serratia*. The drug exhibits good penetration into most tissues and low toxic potential and may be of benefit in treating infections when an aminoglycoside or a fluoroquinolone are either ineffective or are relatively contraindicated. Any consideration for using aztreonam must be tempered with the knowledge that little