b) If cat is significantly acidemic: 2.5 mEq (total dose) potassium or 15–30 mg/kg as potassium citrate PO q12h (Wolf 2006b)
c) When cats with CRF are hypokalemic: 2–4 mEq (total dose) of potassium per day as potassium citrate or potassium gluconate. (DiBartola and Chew 2006a)

### Monitoring

Depending on patient's condition, product chosen and reason for use:

- Serum potassium, sodium, bicarbonate, chloride
- Acid/base status
- Urine pH, Urinalysis
- Serum creatinine, CBC, particularly in chronic renal failure

### Chemistry/Synonyms

Generally used as alkalinizing agents, citric acid and citrate salts are available in several commercially available dosage forms. Citric acid occurs as an odorless or practically odorless, colorless, translucent crystal with a strong acidic taste. It is very soluble in water. Potassium citrate occurs as odorless, transparent crystals or a white, granular powder having a cooling, saline taste. It is freely soluble in water. 108 mg of potassium citrate contains approximately 1 mEq of potassium. Sodium citrate occurs as colorless crystals or a white, granular powder. The hydrous form is freely soluble in water.

Potassium citrate may also be known as citrate of potash, or citric acid tripotassium salt monohydrate. Sodium citrate and citric acid solutions may also be known as Shohl's solution.

### Storage/Stability

Store solutions and potassium citrate tablets in tight containers at room temperature unless otherwise recommended by manufacturer.

### Dosage Forms/Regulatory Status

**VETERINARY-LABELED PRODUCTS:**

Potassium Citrate and Fatty Acids Granules: each 5 grams (one scoop) contains 300 mg potassium citrate (approximately 2.8 mEq of potassium) and 423 mg total fatty acids; also contains several amino acids—quantities not labeled; *Nutrived® Potassium Citrate Granules* for *Cats* and *Dogs* (Vedco); (OTC)

**HUMAN-LABELED PRODUCTS:**

Potassium Citrate Tablets: 5 mEq (540 mg), 10 mEq (1080 mg); *Urocit-K®;* (Mission); (Rx)

*Potassium Citrate/Sodium Citrate Combinations:*

Tablets: 50 mg potassium citrate and 950 mg sodium citrate. *Citrolith®* (Beach Pharm); (Rx)

Syrup: 550 mg potassium citrate, 500 mg sodium citrate, 334 mg citric acid/5 mL (1mEq K, 1 mEq Na per mL equivalent to 2 mEq bicarbonate); in 120 and 480 mL, *Polycitra®* (Willen); (Rx)

Solution: 550 mg K citrate, 500 mg sodium citrate, 334 mg citric acid/5 mL (1 mEq K, 1 mEq Na per mL; equiv to 2 mEq bicarbonate) in 120 and 480 mL. *Polycitra-LC®* (Willen); (Rx).

1100 mg potassium citrate, 334 mg citric acid/5 mL, (2 mEq K/mL; equiv. to 2 mEq bicarbonate) in 120 and 480. *Polycitra-K®* (Willen); (Rx)

Crystals for Reconstitution: 3300 mg K citrate, 1002 mg citric acid per UD packet (equiv. To 30 mEq bicarbonate) in single dose packets. *Polycitra-K®* (Willen); (Rx)

*Citric Acid/Sodium Citrate Combinations:*

Solutions: Sodium Citrate Dihydrate 490 mg sodium citrate and Citric Acid 640 mg per 5 mL (1 mEq sodium equiv to 1 mEq bicarbonate/mL) in 500 mL and UD 15 and 30 mL, *Oracit®*; (Carolina Medical); (Rx)

Sodium Citrate Dihydrate 500 mg sodium citrate and Citric 334 mg per 5 mL (1 mEq sodium equiv to 1 mEq bicarbonate/mL) in 120 and 473 mL and UD 15 and 30 mL; *Bicitra®;* (Alza Corp); (Rx)

*Potassium Citrate, Sodium Citrate/Citric Acid Solutions:*

550 mg potassium citrate monohydrate, 500 mg sodium citrate dihydrate, 334 mg citric acid monohydrate per 5 mL (1 mEq potassium and 1 mEq sodium per mL and is equivalent to 2 mEq bicarbonate in 60 oz bottles; *Cytra-LC®* (Cypress); (Rx)

1100 mg potassium citrate monohydrate and 334 mg citric acid monohydrate per 5 mL (2 mEq potassium per mL and is equivalent to 2 mEq bicarbonate) in 473 mL; *Cytra-K®* (Cypress); (Rx)

20 mEq potassium, 30 mEq citrate (20 g dextrose, 5 g fructose, 35 mEq chloride, 45 mEq sodium)/L in 1 liter; *Naturalyte® Oral Electrolyte Solution* (Unico); (OTC)

## CLARITHROMYCIN

**(klar-*ith*-ro-my-sin) Biaxin®**

**MACROLIDE ANTIBIOTIC**

### Prescriber Highlights

- **Macrolide antibiotic that may useful for treating atypical mycobacterial infections or treatment of *Helicobacter* spp. infections in dogs, cats, & ferrets; *Rhodococcus equi* infections in foals**
- **Appears to be well tolerated by domestic animals, but clinical experience is limited**
- **Many potential drug interactions**
- **Expense may be an issue**

### Uses/Indications

In small animal medicine, clarithromycin is primarily of interest in treating atypical mycobacterial infections or treatment of *Helicobacter* spp. infections in cats and ferrets. In equine medicine, clarithromycin may be useful in treating *Rhodococcus equi* infections in foals.

### Pharmacology/Actions

Clarithromycin, like other macrolide antibiotics, penetrate susceptible bacterial cell walls and bind to the 50S ribosomal subunit inhibiting protein synthesis. The drug is usually bacteriostatic, but may be bactericidal at high concentrations in very susceptible organisms.

Clarithromycin's spectrum of activity is similar to that of erythromycin, but it also has activity against a variety of bacteria that are not easily treated with other antibiotics (*e.g.*, atypical mycobacteria). Activity against gram-positive aerobic cocci is similar to that of erythromycin, but lower concentrations are required to be effective against susceptible organisms. The drug is typically not effective against oxacillin-resistant Staph or coagulase-negative Staph. Clarithromycin also has activity against *Rhodococcus equi*. Activity against gram-negative aerobic bacteria includes *Haemophilus influenzae, Pasturella multocida, Legionella pneumophilia, Bordetella pertussis* and *Campylobacter* spp. Clarithromycin has inhibitory activity against a variety of atypical mycobacteria, including *M. avium complex* and *M. leprae*. Clarithromycin has good activity against *Mycoplasma pneumoniae* and *Ureaplasma ureatlyticum*. Other or-

ganisms where clarithromycin may have therapeutic usefulness include: *Nocardia* spp. *Toxoplasma gondii, Helicobacter pylori, Borrelia burgdorferi,* and *Cryptosporidium parvum.*

### Pharmacokinetics

In horses (foals), the drug is apparently well absorbed after intragastric administration with peak serum concentrations occurring about 1.5 hours after dosing. Elimination half-life is about 4.8 hours.

In dogs, clarithromycin bioavailability ranges from 60–83% with the higher values obtained when given to fasted animals.

### Contraindications/Precautions/Warnings

In humans, clarithromycin is contraindicated in patients hypersensitive to it or other macrolide antibiotics (*e.g.*, erythromycin, azithromycin).

### Adverse Effects

The adverse effect profile for clarithromycin in domestic animals is not well described. With limited clinical experience, it appears to be well tolerated in dogs, cats, ferrets, and foals. Like all orally administered antibiotics, GI disturbances are possible. Pinnal or generalized erythema may be associated with this drug when used in cats.

Adverse effects in humans include gastrointestinal adverse effects (primarily nausea, vomiting, abdominal pain, abnormal taste, diarrhea) that, when compared with erythromycin, are milder and occur less frequently. Approximately 4% of treated humans develop transient, mildly elevated BUN levels. Rarely, prolonged QT interval (torsades de pointes), hepatotoxicity, thrombocytopenia, or hypersensitivity reactions have been reported. Pseudomembranous colitis secondary to *Clostridium difficile* has been reported after clarithromycin use.

### Reproductive/Nursing Safety

In humans, the FDA categorizes clarithromycin as a category ***C*** drug for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans*). Teratogenic studies in rats and rabbits failed to document any teratogenic effects in some studies, but, at high dosages (yielding plasma levels 2–17 times achieved in humans with maximum recommended dosages) in pregnant rats, rabbits and monkeys, some effects (cleft palate, cardiovascular abnormalities, fetal growth retardation) were noted.

Clarithromycin is excreted into milk of lactating animals and levels may be higher in milk than in the dam's plasma, but this is unlikely to be of clinical significance.

### Overdosage/Acute Toxicity

Generally, overdoses of clarithromycin are usually not serious with only gastrointestinal effects seen. Patients ingesting large overdoses may be given activated charcoal/cathartic to remove any unabsorbed drug. Forced diuresis, peritoneal dialysis, or hemodialysis do not appear to be effective in removing the drug from the body.

### Drug Interactions

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

- **CISAPRIDE:** Clarithromycin can inhibit the metabolism of cisapride and the manufacturer states that use of these drugs together (in humans) is contraindicated
- **FLUCONAZOLE:** Possible increased clarithromycin levels
- **DIGOXIN:** Clarithromycin may increase the serum levels of digoxin
- **OMEPRAZOLE:** Clarithromycin and omeprazole can increase the plasma levels of one another
- **WARFARIN:** Clarithromycin may potentiate the effects of oral anticoagulant drugs
- **ZIDOVUDINE:** Clarithromycin may decrease serum concentrations of zidovudine

Clarithromycin, like erythromycin, can inhibit the metabolism of other drugs that use the CYP3A subfamily of the cytochrome P450 enzyme system. Depending on the therapeutic index of the drug(s) involved, therapeutic drug monitoring and/or dosage reduction may be required if the drugs must be used together. These drugs include:

- **ALFENTANIL**
- **BROMOCRIPTINE**
- **BUSPIRONE**
- **CARBAMAZEPINE**
- **DISOPYRAMIDE** (also risk of increased QT interval)
- **METHYLPREDNISOLONE**
- **MIDAZOLAM, ALPRAZOLAM, TRIAZOLAM**
- **QUINIDINE** (also risk of increased QT interval)
- **RIFABUTIN**
- **TACROLIMUS** (**systemic**)
- **THEOPHYLLINE**

### Laboratory Considerations

- No clarithromycin-related laboratory interactions noted.

### Doses

- **DOGS:**

  For treatment of severe or refractory cases of canine leproid granuloma syndrome:

  a) Using a combination of clarithromycin 15–25 mg/kg total daily dose PO given divided q8–12h; and rifampin 10–15 mg/kg PO once daily. Usually treatment should be continued for 4–8 weeks until lesions are at least substantially reduced in size and ideally have resolved completely. (Malik, Martin et al. 2001)

  For susceptible infections:

  a) 2.5–10 mg/kg PO twice daily (Boothe 1999)

  b) 5–10 mg/kg PO q12h (Greene and Watson 1998)

- **CATS:**

  For treatment of feline leprosy:

  a) Using a regimen of either two or three of the following drugs: clarithromycin: 62.5 mg per cat q12h; clofazimine: 25–50 mg once per day or 50 mg every other day; rifampin: 10–15 mg/kg once a day. (Malik, Hughes et al. 2002)

  For treatment of *Nocardia* (*N. nova*) infections:

  a) Combination therapy with: amoxicillin 20 mg/kg PO twice daily with clarithromycin 62.5–125 mg (total dose per cat) PO twice daily and/or doxycycline 5 mg/kg or higher PO twice daily. (Malik 2006a)

  For treatment of *H. pylori* infections:

  a) Combination therapy with: clarithromycin 7.5 mg/kg PO twice daily; metronidazole 10–15 mg/kg PO twice daily; amoxicillin 20 mg/kg PO twice daily for 14 days. (Simpson 2003b)

  For treatment of *M. tuberculosis-bovis* variant infections:

  a) Using all three drugs: Clarithromycin 5–10 mg/kg PO q12h; rifampin 10–20 mg/kg PO once daily, enrofloxacin 5–10 mg/kg PO q12–24h. Treatment must continue for at least 2 months. Maintenance for additional 4 months using (at same dosages enrofloxacin and clarithromycin or rifampin and enrofloxacin). (Greene and Gunn-Moore 1998)

  For susceptible infections:

  a) 7.5 mg/kg PO q12h (Greene and Watson 1998)

■ **FERRETS:**

For treatment of *Helicobacter mustelae* infections:

a) Clarithromycin 12.5 mg/kg PO q8h with ranitidine bismuth citrate (**Note:** not currently available in the USA) 24 mg/kg PO q8h. Mild to moderate antral gastritis may persist even if *H. mustelae* eradicated. (Marini, Fox et al. 1999)

b) 12.5–50 mg/kg q8–24h with omeprazole at 0.7 mg/kg PO once daily (q24h) (Fisher 2005)

■ **HORSES:**

For treatment of *Rhodococcus equi* infection in foals:

a) 7.5 mg/kg PO q12h (Jacks, Giguere et al. 2002), (Chaffin 2006b)

b) 7.5 mg/kg PO q12h in combination with rifampin at 5 mg/kg PO q12h or 10 mg/kg PO q24h. (Giguere 2003b)

### Monitoring

■ Antibacterial efficacy
■ Adverse effects

### Client Information

■ If using the oral suspension, do *not* refrigerate; keep at room temperature and discard 14 days after reconstituting
■ This drug may be given without regard to meals
■ Clarithromycin can interact with many other drugs; do not give any drugs to the animal without the veterinarian's knowledge

### Chemistry/Synonyms

Clarithromycin is a semi-synthetic macrolide antibiotic related to erythromycin. It differs from erythromycin by the methylation of position 6 in the lactone ring. Clarithromycin occurs as a white to off-white crystalline powder. It is practically insoluble in water, slightly soluble in ethanol, and soluble in acetone. It is slightly soluble in a phosphate buffer at pH's of 2–5.

Clarithromycin may also be known as: 6-*O*-Methylerythromycin, TE-031, A-56268, *Adel®, Biaxin®, Biclar®, Bremon®, Clamicin®, Clamycin®, Claribid®, Clarimac®, Clarimax®, Claritab®, Cyllind®, Gervaken®, Heliclar®, Helicodid®, Karin®, Klacid®, Klaciped®, Klaricid®, Klaridex®, Kofron®, Lagur®, Mabicrol®, Macladin®, Maclar®, Mavid®, Monaxin®, Monocid®, Naxy®, Veclam®,* and *Zeclar®.*

### Storage/Stability

The conventional 250 mg tablets should be protected from light and stored in well-closed containers at 15–30°C (59–86°F). The conventional or extended-release 500 mg tablets should be stored in well-closed containers at controlled room temperature (20–25°C; 68–77°F). The granules for reconstitution into an oral suspension should be stored in well-closed containers at 15–30°C. After reconstitution, it should be stored at room temperature (do not refrigerate) and any unused drug discarded after 14 days.

### Dosage Forms/Regulatory Status

**VETERINARY-LABELED PRODUCTS:** None

**HUMAN-LABELED PRODUCTS:**

Clarithromycin Film-coated Tablets: 250 mg & 500 mg; Extended-release Tablets: 500 mg & 1000 mg; Clarithromycin (Teva; Ranbaxy); *Biaxin®* & *Biaxin® XL* (Abbott), generic; (Rx)

Clarithromycin Granules for Oral Suspension: 25 mg/mL, 50 mg/mL in 50 mL and 100 mL; *Biaxin®* (Abbott), generic; (Rx)

A pre-packaged combination containing lansoprazole, amoxicillin and clarithromycin for *H. pylori* is marketed as *Prevpak®* (TAP); (Rx)

**Clavulanate/Amoxicillin — See Amoxicillin/Clavulanate**
**Clavulanate/Ticarcillin — See Ticarcillin /Clavulanate**

# CLEMASTINE FUMARATE

(*klem*-as-teen) Tavist®

ANTIHISTAMINE

## Prescriber Highlights

- Oral antihistamine with greater anticholinergic, but less sedative activity
- Poor pharmacokinetic profile for oral administration in dogs or horses
- Contraindications: Hypersensitivity
- Caution: Prostatic hypertrophy, bladder neck obstruction, severe cardiac failure, angle-closure glaucoma, or pyeloduodenal obstruction
- Most likely adverse effects: DOGS: Sedation, paradoxical hyperactivity & anticholinergic effects (dryness of mucous membranes, etc.); CATS: Diarrhea

### Uses/Indications

Clemastine may be used for symptomatic relief of histamine$_1$-related allergic conditions.

### Pharmacology/Actions

Like other $H_1$-receptor antihistamines, clemastine acts by competing with histamine for sites on $H_1$-receptor sites on effector cells. They do not block histamine release, but can antagonize its effects. Clemastine has greater anticholinergic activity, but less sedation than average.

### Pharmacokinetics

In dogs, oral bioavailability is very low (3%). Clemastine has a high volume of distribution (13.4 L/kg; 98% protein bound) and clearance (2.1 L/hr/kg). After IV administration, elimination half-life is about 4 hours and completely inhibited wheal formation for 7 hours. Oral administration at 0.5 mg/kg only yielded minor inhibition of wheal formation. The authors of the study (Hansson, Bergvall et al. 2004) concluded that most oral dosage regimens in the literature are likely to give too low a systemic exposure of the drug to allow effective therapy.

In horses, clemastine has poor oral bioavailability (3–4%), a volume of distribution at steady-state of 3.8 L/kg, a clearance (TBC) of 0.79 L/hr/Kg and a terminal half-life of about 5.4 hours. The authors concluded that the drug is not appropriate for oral administration in the horse and must be dosed at least 3–4 times a day intravenously to maintain therapeutic plasma concentrations. (Torneke, Ingvast-Larsson et al. 2003)

In humans, clemastine has a variable bioavailability (20–70%); its distribution is not well characterized, but does distribute into milk. Metabolic fate has not been clearly determined, but it appears to be extensively metabolized and those metabolites are eliminated in the urine. In humans, its duration of action is about 12 hours.

### Contraindications/Precautions/Warnings

Clemastine is contraindicated in patients hypersensitive to it. It should be used with caution in patients with prostatic hypertrophy, bladder neck obstruction, severe cardiac failure, angle-closure glaucoma, or pyeloduodenal obstruction.