Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Mannitol for injection 20%: 20 g/100 mL in 100 mL single-dose vials. *Am-Vet® Mannitol Injection 20%* (IVX); generic (Phoenix Pharm, Neogen); (Rx). Labeled for use in canine species.

Mannitol for Injection 18%: 180 mg/mL in 100 mL vials; *Mannitject®* (Butler); generic (Vedco); (Rx). Labeled for use in dogs

HUMAN-LABELED PRODUCTS:

Mannitol for Injection

Mannitol Injection: 5% (50 mg/mL; 275 mOsm/l) in 1000 mL;

10% (100 mg/mL; 550 mOsm/l) in 500 mL and 1000 mL;

15% (150 mg/mL; 825 mOsm/l) in 150 mL & 500 mL;

20% (200 mg/mL; 1100 mOsm/l) in 250 mL and 500 mL;

25% (250 mg/mL; 1375 mOsm/l) in 50 mL vials and syringes (12.5 grams/vial); generic; (Rx)

Mannitol Solution: Genitourinary Irrigants: 5 g/100 mL in distilled water (275 mOsm/L) in 2000 mL; *Resectisol®* (Kendall McGaw); (Rx)

MARBOFLOXACIN

(mar-boe-***flox***-a-sin) Zeniquin®

FLUOROQUINOLONE ANTIBIOTIC

Prescriber Highlights

- Veterinary oral fluoroquinolone antibiotic effective against a variety of pathogens
- Not effective against anaerobes
- Contraindications: Hypersensitivity to fluoroquinolones; Relatively contraindicated for young, growing animals due to cartilage abnormalities
- Caution: Hepatic or renal insufficiency, seizure patients, or dehydration
- Adverse Effects: GI distress; does not appear to cause ocular toxicity in cats
- Drug interactions

Uses/Indications

Marbofloxacin is labeled for the treatment of susceptible bacterial infections in dogs and cats.

Pharmacology/Actions

Marbofloxacin is a bactericidal agent. The bactericidal activity of marbofloxacin is concentration dependent, with susceptible bacteria cell death occurring within 20–30 minutes of exposure. Like other fluoroquinolones, marbofloxacin has demonstrated a significant post-antibiotic effect for both gram - and + bacteria and is active in both stationary and growth phases of bacterial replication.

Its mechanism of action is not thoroughly understood, but it is believed to act by inhibiting bacterial DNA-gyrase (a type-II topoisomerase), preventing DNA supercoiling and DNA synthesis.

Marbofloxacin has a similar spectrum of activity as the other veterinary commercially available agents. These agents have good activity against many gram-negative bacilli and cocci, including most species and strains of *Pseudomonas aeruginosa*, *Klebsiella* spp., *E. coli*, Enterobacter, Campylobacter, Shigella, Salmonella, Aeromonas, Haemophilus, Proteus, Yersinia, Serratia, and Vibrio species. Other organisms that are generally susceptible include *Brucella* spp., *Chlamydia trachomatis*, Staphylococci (including penicillinase-producing and methicillin-resistant strains), Mycoplasma, and *Mycobacterium* spp. (not the etiologic agent for Johne's Disease).

The fluoroquinolones have variable activity against most streptococci and are not usually recommended to use for these infections. These drugs have weak activity against most anaerobes and are ineffective in treating anaerobic infections.

Resistance does occur by mutation, particularly with *Pseudomonas aeruginosa, Klebsiella pneumonia,* Acinetobacter, and Enterococci, but plasmid-mediated resistance is thought to occur only rarely.

Pharmacokinetics

In dogs, marbofloxacin is characterized as being rapidly absorbed after oral administration with a bioavailability of 94%. Peak plasma levels occur in about 1.5 hours. Protein binding is low and the apparent volume of distribution is 1.2–1.9 L/kg. Elimination half-life averages 9–12 hours. The drug is eliminated unchanged in the urine (40%) and bile/feces. Only about 15% of a dose is metabolized in the liver.

In cats, absorption after oral dosing is nearly complete and peak serum levels occur about 1–2 hours post-dose. Terminal elimination half-life is about 13 hours.

Renal impairment does not significantly alter dosing requirements.

Contraindications/Precautions/Warnings

Like other quinolones, marbofloxacin is labeled as contraindicated in small and medium breed dogs up to 8 months of age, large breeds to 12 months old, and giant breeds to 18 months old. It is also labeled as contraindicated in cats under 12 months of age. Quinolones are also contraindicated in patients hypersensitive to them.

Marbofloxacin can (rarely) cause CNS stimulation and should be used with caution in patients with seizure disorders.

The FDA has prohibited the use of this drug in food-producing animals.

Adverse Effects

With the exception of potential cartilage abnormalities in young animals (see Contraindications above), the adverse effect profile of marbofloxacin is usually limited to GI distress (vomiting, anorexia, soft stools, diarrhea) and decreased activity.

Other fluoroquinolones have, in rare incidences, caused elevated hepatic enzymes, ataxia, seizures, depression, lethargy, and nervousness in dogs. Hypersensitivity reactions or crystalluria could potentially occur.

It is not known if marbofloxacin can also cause the ocular toxicity that has been reported with high dose enrofloxacin in cats. While unlikely, FDA's Adverse Drug Reaction database has received 14 reports (as of July 3, 2007) of blindness associated with marbofloxacin. Causal effect cannot be proven, but use higher dosages carefully.

Reproductive/Nursing Safety

Safety of marbofloxacin during pregnancy has not been established.

Overdosage/Acute Toxicity

It is unlikely an acute overdose of marbofloxacin would result in signs more serious than either anorexia or vomiting, but the adverse effects noted above could occur. Dogs receiving 55 mg/kg per day for 12 days developed anorexia, vomiting, dehydration, tremors, red skin, facial swelling, lethargy, and weight loss.

Drug Interactions

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

- **ANTACIDS/DAIRY PRODUCTS:** Containing cations (Mg^{++}, Al^{+++}, Ca^{++}) may bind to marbofloxacin and prevent its absorption; separate doses of these products by at least 2 hours
- **ANTIBIOTICS, OTHER** (**aminoglycosides, 3rd-generation cephalosporins, penicillins—extended-spectrum**): Synergism may occur, but is not predictable, against some bacteria (particularly *Pseudomonas aeruginosa*) with these compounds. Although marbofloxacin has minimal activity against anaerobes, *in vitro* synergy has been reported when used with **clindamycin** against strains of Peptostreptococcus, Lactobacillus and *Bacteroides fragilis*.
- **CYCLOSPORINE:** Fluoroquinolones may exacerbate the nephrotoxicity and reduce the metabolism of cyclosporine (used systemically)
- **FLUNIXIN:** Has been shown in dogs to increase the AUC and elimination half-life of enrofloxacin and enrofloxacin increases the AUC and elimination half-life of flunixin; it is unknown if marbofloxacin also causes this effect or if other NSAIDs interact with marbofloxacin in dogs
- **GLYBURIDE:** Severe hypoglycemia possible
- **IRON, ZINC** (**oral**): Decreased marbofloxacin absorption; separate doses by at least two hours
- **METHOTREXATE:** Increased MTX levels possible with resultant toxicity
- **NITROFURANTOIN:** May antagonize the antimicrobial activity of the fluoroquinolones and their concomitant use is not recommended
- **PHENYTOIN:** Marbofloxacin may alter phenytoin levels
- **PROBENECID:** Blocks tubular secretion of ciprofloxacin and may also increase the blood level and half-life of marbofloxacin
- **SUCRALFATE:** May inhibit absorption of marbofloxacin; separate doses of these drugs by at least 2 hours
- **THEOPHYLLINE:** Marbofloxacin may increase theophylline blood levels
- **WARFARIN:** Potential for increased warfarin effects

Laboratory Considerations

- In some human patients, the fluoroquinolones have caused increases in liver enzymes, BUN, and creatinine and decreases in hematocrit. The clinical relevance of these mild changes is not known at this time.

Doses

- **DOGS & CATS:**
  a) For susceptible infections (urinary tract, skin and soft tissue): 2.75–5.5 mg/kg PO once daily. Give for 2–3 days beyond cessation of clinical signs (skin/soft tissue infections); and for at least 10 days (urinary tract). If no improvement noted after 5 days, reevaluate diagnosis. Maximum duration of treatment is 30 days. (Package insert; *Zeniquin*®—Pfizer)

Monitoring

- Clinical efficacy
- Adverse effects

Client Information

- Give as the veterinarian prescribes; do not stop treating just because the animal appears well.

Chemistry/Synonyms

A synthetic fluoroquinolone antibiotic, marbofloxacin is soluble in water, but solubility decreases as pH increases.

Marbofloxacin may also be known as Ro 9-1168, *Marbocyl*®, or *Zeniquin*®.

Storage/Stability

Marbofloxacin tablets should be stored below 30°C.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Marbofloxacin Oral Tablets: 25 mg, 50 mg, 100 mg, 200 mg; *Zeniquin*® (Pfizer); (Rx). Approved for use in dogs and cats. Must not be used in food animals.

HUMAN-LABELED PRODUCTS: None

MAROPITANT CITRATE

(mar-***oh***-pit-ent) Cerenia®

NEUROKININ (NK_1) RECEPTOR ANTAGONIST ANTIEMETIC

Prescriber Highlights

- Veterinary approved antiemetic for use in dogs 16 weeks of age & older; also used extra-label in cats
- Acts at the emetic center; therefore effective for emesis mediated via either peripheral or central mechanisms
- Subcutaneous injection is approved for the prevention & treatment of acute vomiting;
- Oral form is approved for the prevention of acute vomiting & the prevention of vomiting due to motion sickness; different oral dosages for each indication
- Oral dose is higher than subcutaneous dose due to decreased bioavailability of the oral tablet

Monograph by Dinah Jordan, PharmD, DICVP

Uses/Indications

Maropitant citrate injectable solution is indicated for the prevention and treatment of acute vomiting in dogs; maropitant citrate tablets are indicated for the prevention of acute vomiting and the prevention of vomiting due to motion sickness in dogs. Both are also used extra-label in cats.

Pharmacology/Actions

Maropitant is a neurokinin-1 (NK_1) receptor antagonist, which acts in the central nervous system by inhibiting Substance P, the key neurotransmitter involved in vomiting. Maropitant suppresses both peripheral & centrally mediated emesis.

Pharmacokinetics

In dogs, maropitant is rapidly absorbed after oral (PO) & subcutaneous (SC) administration. Peak plasma concentrations (Tmax) occur in less than 1 hour following 1 mg/kg subcutaneous administration and less than 2 hours after oral administration of 2 or 8 mg/kg. After oral administration bioavailability is 24% (2 mg/kg) and 37% (8 mg/kg), suggesting first pass metabolism which becomes saturated at the higher dose. Feeding status does not affect bioavailability.