FLUOROQUINOLONES (Veterinary—Systemic)

This monograph includes information on the following:
Ciprofloxacin, Danofloxacin, Difloxacin, Enrofloxacin, Marbofloxacin, and Orbifloxacin.

Some commonly used *brand names* for veterinary-labeled products are:

A180 [Danofloxacin]
Baytril Injectable Solution [Enrofloxacin]
Baytril Injectable Solution 2.27% [Enrofloxacin]
Baytril 100 Injectable Solution [Enrofloxacin]
Baytril Tablets [Enrofloxacin]
Baytril Taste Tabs [Enrofloxacin]
Dicural Tablets [Difloxacin]
Orbax Tablets [Orbifloxacin]
Zeniquin Tablets [Marbofloxacin]

Some commonly used *brand names* for human-labeled products are: *Cipro* [Ciprofloxacin] and *Cipro I.V.* [Ciprofloxacin].

Note: For a listing of dosage forms and brand names by country and availability, see the *Dosage Forms* section(s).

Category: Antibacterial (systemic).

Indications

Note: The text between [EL-US] and [EL] describes uses that are not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

General considerations

The fluoroquinolone antimicrobials are rapidly bactericidal against a variety of clinically important organisms, are well tolerated by animals, and can be administered by a variety of routes.{R-95} The members of this group that are currently labeled for use in animals have the same quinolone structure, each with modifications that account for pharmacokinetic variations in the medications but do not significantly change the antibacterial spectrum of activity.{R-1; 95-98; 100; 102; 112}

Fluoroquinolones exhibit good activity against most gram-negative bacteria, including *Escherichia coli*, *Enterobacter* species, *Klebsiella* species, *Pasteurella* species, *Proteus* species, and *Salmonella* species. *Pseudomonas aeruginosa* is variably susceptible, usually having a higher minimum inhibitory concentration (MIC) than other susceptible organisms.{R-1; 95-98; 100; 102; 112} Ciprofloxacin and marbofloxacin may be more active than other fluoroquinolones against *P. aeruginosa* strains.{R-199}

Some gram-positive bacteria are susceptible to fluoroquinolones. *Staphylococcus aureus* and *Staphylococcus intermedius* usually are susceptible.{R-1; 96-98; 112} However, the MIC values for staphylococci typically are higher than for gram-negative bacteria and staphylococcal resistance to fluoroquinolones has been a problem in human patients.{R-95}

Chlamydia, mycobacteria, mycoplasma, and ureaplasma can also be moderately to very susceptible to fluoroquinolones.{R-9}

Local factors that affect activity are cations at the site of infection and low pH; however, fluoroquinolones are active in abscesses in spite of often unfavorable environmental conditions.{R-95}

Bacterial resistance to fluoroquinolones most commonly occurs by alteration of the target, DNA-gyrase (topoisomerase II), via mutation (gyr-A). Less commonly, but perhaps more importantly for gram-positive bacteria, mutation occurs at the topoisomerase-IV target (parC).{R-9; 21; 86} Other mechanisms of resistance occur when bacteria decrease the ability of the drug to enter the cell or increase active transport out of the cell.{R-9; 21} Resistance is usually chromosomally developed and, therefore, remains after antimicrobial therapy ends.{R-90; 95} Cross-resistance of enrofloxacin with other fluoroquinolones can occur.{R-9; 10; 50} Changes in levels of resistance to fluoroquinolones over time by *Campylobacter* and *Salmonella* species are being monitored because of their possible impact on human health.{R-55; 56; 91}

Accepted

Infections, bacterial (treatment), including
Cystitis, urinary, bacterial (treatment);
Respiratory infections, bacterial (treatment); or
Skin and soft tissue infections (treatment)—

Cats: [EL-US,CAN] Enrofloxacin injection[EL], enrofloxacin tablets,{R-1; 104} marbofloxacin tablets,{R-97; 101} and orbifloxacin tablets{R-98; 100} are indicated in the treatment of susceptible bacterial infections in cats. Clinical efficacy has been established specifically in the treatment of skin and soft tissue infections.{R-1; 97; 98; 100; 102}

Dogs: Difloxacin tablets,{R-96; 99} enrofloxacin injection and tablets,{R-1; 104} marbofloxacin tablets,{R-97; 101} and orbifloxacin tablets{R-98; 100} are indicated in the treatment of susceptible bacterial infections in dogs. Clinical efficacy has been established specifically in the treatment of skin and soft tissue infections and urinary tract infections, as noted on product labeling.{R-96-101} Clinical efficacy has also been established for enrofloxacin injection and tablets in the treatment of respiratory tract infections in dogs.{R-1} [EL-US,CAN] There is evidence to suggest that enrofloxacin is as effective as chloramphenicol or tetracycline in the treatment of *Rocky Mountain spotted fever* in dogs.[EL]{R-84}

Pneumonia (treatment)—*Cattle:* Danofloxacin injection and enrofloxacin injection are indicated in the treatment of bovine respiratory disease caused by susceptible organisms, including *Mannheimia* (*Pasteurella*) *haemolytica* and *Pasteurella multocida*.{R-2; 57; 150-152} [EL-CAN] Enrofloxacin injection is also labeled for use in the treatment of bovine respiratory disease caused by *Histophilus somni*.[EL]{R-2}

Potentially effective

Infections, bacterial (treatment)—
[EL-US,CAN] *Bustards, camels, ducks, emus, llamas, oryx, red pacu, African grey parrots,* and *pythons*:[EL] In the U.S., extra-label use is banned in ducks and in other animals to be used for

Evidence Quality

A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Insufficient evidence to support a recommendation for use
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use

Evidence Type

1	Species-specific evidence from at least one large randomized and controlled trial (RCT) or multiple small RCTs
2	Species-specific evidence from a small RCT, disease models, large case studies, pharmacokinetic studies using surrogate endpoints, or evidence from well-designed trials in a different species that is considered appropriate for comparison
3	Dramatic results from either well-designed, species-specific trials without controls or small case studies
4	Pharmacokinetic studies without surrogate endpoints
5	*In vitro* studies
6	Opinions of respected authorities on the basis of clinical experience or reports of expert committees

food production—Although the safety and efficacy of enrofloxacin have not been established, dose recommendations for use in the treatment of susceptible bacterial infections have been made, based on pharmacokinetic data, for bustards,{R-41} camels,{R-45} ducks,{R-42} emus,{R-43} llamas,{R-46} oryx,{R-47} red pacu,{R-44} African grey parrots,{R-39; 40} and pythons.{R-48} Further clinical studies are necessary. See also the *Regulatory Considerations* section.

EL US,CAN *Horses*:EL For use only in animals not to be used for food production—Although the safety and efficacy of enrofloxacin, marbofloxacin, and orbifloxacin in the treatment of susceptible bacterial infections in horses have not been established, pharmacokinetic evidence is available to suggest that they may be effective (Evidence rating: B-2).{R-25-27; 79-80; 136; 171-173; 188} Due to reports of articular cartilage damage in foals from administration of enrofloxacin, these antibiotics should not be administered to horses less than 3 years of age, except as a last resort for severe infections not treatable with other medications.{R-25; 26; 85} Although there have been reports of unpublished studies showing articular damage from enrofloxacin administration to adult horses, subsequent studies have shown no effect on cartilage in adults when used continuously for up to 21 days.{R-86}

EL US,CAN *Pigs,* potbellied and miniature:EL In the U.S., extra-label use is banned in pigs, including potbellied and miniature pigs—Although the safety and efficacy of enrofloxacin in the treatment of susceptible bacterial infections in pigs have not been established, there is some pharmacokinetic evidence to suggest that this therapy may be effective.{R-29} See also the *Regulatory Considerations* section.

EL US,CAN *Sheep,* pet and research:EL In the U.S., extra-label use is banned in sheep—Although the safety and efficacy of enrofloxacin in the treatment of susceptible bacterial infections in sheep have not been established, there is some pharmacokinetic evidence to suggest that this therapy may be effective.{R-28} See also the *Regulatory Considerations* section.

EL US,CAN *Bartonella* infections (treatment)EL; or

EL US,CAN *Hemobartonella felis* infections (treatment)EL—*Cats:* Although the safety and efficacy have not been established, enrofloxacin has been used in an attempt to eradicate *Bartonella* bacteremia in cats.{R-72; 73} Controlled therapeutic trials investigating the efficacy of enrofloxacin in clearing *Bartonella* from cats show a positive response in some animals, but tests used to document that an infection has been cleared remain unreliable, making the results difficult to interpret.{R-72} It should not be assumed that a *Bartonella* infection is cleared by a course of enrofloxacin. Long-term monitoring is necessary.{R-72; 73}
Although the safety has not been clearly established, a controlled, randomized study demonstrated the efficacy of enrofloxacin in the treatment of *Hemobartonella felis* infection, by showing it more quickly resolved clinical signs, raised hematocrit, and decreased organism counts than in control animals. In this study, some cats treated with a high dose of enrofloxacin or with doxycycline were apparently cleared of the organism.{R-83; 148}

EL US,CAN Brucellosis (treatment)EL—*Dogs:* Historically, the treatment of dogs infected with *Brucella canis* has been controversial. Due to the zoonotic potential and the difficulty in clearing the infection, some have advocated euthanasia of infected animals. Studies using a combination of tetracycline and dihydrostreptomycin did demonstrate that infected animals, following neutering, could be cured of the infection.{R-139} However, dihydrostreptomycin is no longer available in the US. The Centers for Disease Control recommend a combination of doxycycline and rifampin for the treatment of brucellosis in human patients.{R-140} In a clinical trial, rifampin plus ciprofloxacin, a metabolite of enrofloxacin, was shown to be as effective as the standard rifampin and doxycycline regimen in the treatment of human brucellosis.{R-137} It is not known whether the fluoroquinolones have any efficacy in the treatment of canine brucellosis.

EL US,CAN Chlamydial infections (treatment)EL—*Cats:* There are no studies to document the effectiveness of the veterinary fluoroquinolones, difloxacin, enrofloxacin, marbofloxacin, and orbifloxacin, in the treatment of chlamydial infections in cats. Clinical trials of related human-labeled fluoroquinolones in the treatment of genital, respiratory, or ocular chlamydial infections in human patients have shown efficacy; however, concern exists that the organisms are not eradicated and recrudecense is common.

EL US,CAN Endophthalmitis, bacterial (treatment)EL—*Cats* and *dogs:* There are no specific studies to document the effectiveness of the veterinary fluoroquinolones, difloxacin, enrofloxacin, marbofloxacin and orbifloxacin, in the treatment of bacterial endophthalmitis due to susceptible organisms. However, these bactericidal drugs have been shown to produce aqueous and vitreous humor concentrations within the therapeutic range for many pathogens.{R-1; 102; 179} Also, related human-labeled fluoroquinolones, including ciprofloxacin (a metabolite of enrofloxacin), have been reported as efficacious in several small studies and case reports in human patients.{R-120-125}

EL US,CAN Meningitis, bacterial (treatment)EL—*Cats* and *dogs:* There are no studies to document the effectiveness of the veterinary fluoroquinolones, difloxacin, enrofloxacin, marbofloxacin, and orbifloxacin, in the treatment of bacterial meningitis due to susceptible organisms. However, these bactericidal drugs have been shown to reach concentrations in the central nervous system that are within the therapeutic range for many pathogens.{R-1; 102} Also, related human-labeled fluoroquinolones, including ciprofloxacin (a metabolite of enrofloxacin), have been reported as efficacious in several small studies and case reports in human patients.{R-126-132} Although the potential for fluoroquinolones to induce seizures has been suggested as a reason to avoid these drugs in the treatment of meningitis, the above mentioned human studies, as well as disease models in animals, have failed to indicate an increased incidence of seizures in fluoroquinolone-treated subjects. Careful monitoring for seizures is nevertheless advised if fluoroquinolones are used in such infections.

EL US,CAN Mycobacterial infections (treatment)EL—*Cats:* Although the safety and efficacy have not been established, enrofloxacin and ciprofloxacin have been used in the treatment of mycobacterial infections in cats, based on case reports of successful treatment of cutaneous lesions of opportunistic mycobacteria.{R-75; 76; 142} There is some evidence to suggest that fluoroquinolones are effective in the treatment of tubercular mycobacteriosis, an often serious but also often asymptomatic or insidious disease in cats. Cats are also prone to infection with *Mycobacterium lepraemurium*, which is a nontubercular form of mycobacteria. Safety and efficacy of fluoroquinolones have not yet been proven in the treatment of *M. lepraemurium*, but successful treatment of the cutaneous form of mycobacterial infection with enrofloxacin indicates possible efficacy in the treatment of nontubercular forms.{R-142}

EL US,CAN Mycoplasmal infections (treatment)EL—Although the efficacy has not been established, fluoroquinolones have been used to treat infections caused by *Mycoplasma* species in animals. Activity of these antibiotics against *Mycoplasma* can be variable but enrofloxacin and danofloxacin have been shown to be consistently more active *in vitro* (minimum inhibitory concentrations [MIC] of 0.05 to 1.0 mcg/mL) against veterinary isolates than flumequine.{R-143}

EL US,CAN Pasteurellosis (treatment)EL—*Rabbits,* pet and research: In the U.S., extra-label use is banned in rabbits—Although the safety and efficacy have not been established, there are some research data suggesting that parenteral enrofloxacin can resolve clinical signs of pasteurellosis in many naturally infected rabbits, even though the organism is not consistently eradicated.{R-67-69} See also the *Regulatory Considerations* section.

Unaccepted

EL US,CAN Ehrlichiosis (treatment)EL—*Cats* and *dogs:* The American College of Veterinary Internal Medicine Infectious Disease Study Group has stated that the treatment of choice for ehrlichiosis is

doxycycline and that enrofloxacin has not been found to be an effective treatment.{R-149} A small, short-term (15-day) study without follow-up showed that enrofloxacin can be as effective as doxycycline in the treatment of naturally aquired ehrlichiosis in dogs;{R-77} however, another study of experimentally induced disease in which dogs were monitored after 21-day enrofloxacin therapy showed poor efficacy in clearing the infection.{R-138}

Regulatory Considerations

U.S.—

Federal law prohibits the extralabel use of fluoroquinolones in food-producing animals (21 CFR 530.41). The prohibition is based on a finding by the Food and Drug Administration (FDA) that the extralabel use of these antibiotics in food-producing animals presents a risk to the public health because it could increase the level of drug-resistant zoonotic pathogens at the time of slaughter.{R-106} Some researchers are concerned that such use can lead to the transfer of pathogens resistant to fluoroquinolones from animals to human beings.

Food animals are designated by the FDA on a species basis. For example, all pigs, including potbellied and miniature pigs, are considered food-producing animals. In addition, animals that are not members of a species routinely used for food production in the United States would also be considered food-producing animals if they or their products are processed for human consumption.{R-202}

Danofloxacin, difloxacin, enrofloxacin, marbofloxacin, and orbifloxacin are restricted to use by or on the order of a licensed veterinarian.{R-1; 2; 94; 96-98} Withdrawal times have been established for danofloxacin and enrofloxacin.{R-2; 151}

Ciprofloxacin is not labeled for veterinary use.

Canada—

Danofloxacin, difloxacin, enrofloxacin, marbofloxacin, and orbifloxacin are restricted to use by or on the order of a licensed veterinarian. Withdrawal times have been established for danofloxacin and enrofloxacin.{R-150; 152}

Ciprofloxacin is not labeled for veterinary use.

Chemistry

Chemical group: Quinolone carboxylic acid derivatives.{R-1}

Chemical name:

Ciprofloxacin—3-Quinolinecarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-.{R-7}

Danofloxacin mesylate—3-Quinolinecarboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-7-(5-methyl-2,5-diabicyclo[2.2.1]hept-2-yl)-4-oxo-, (1*S*)-, monomethanesulfonate.{R-7}

Difloxacin hydrochloride—3-Quinolinecarboxylic acid, 6-fluoro-1-(4-fluorophenyl)-1,4-dihydro-7-(4-methyl-1-piperazinyl)-4-oxo, monohydrochloride.{R-7}

Enrofloxacin—3-Quinolinecarboxylic acid, 1-cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1,4-dihydro-4-oxo-.{R-7}

Marbofloxacin—9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7*H*-pyrido[3,2,1-*ij*][4,1,2]benzoxadiazine-6-carboxylic acid.{R-7}

Orbifloxacin—1-Cyclopropyl-7-(*cis*-3,5-dimethyl-1-piperazinyl)-5,6,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid.{R-7}

Molecular formula:

Ciprofloxacin—$C_{17}H_{28}FN_3O_3$.{R-7}

Danofloxacin mesylate—$C_{19}H_{20}FN_3O_3 \cdot CH_4O_3S$.{R-7}

Difloxacin hydrochloride—$C_{21}H_{19}F_2N_3O_3 \cdot HCl$.{R-7}

Enrofloxacin—$C_{19}H_{22}FN_3O_3$.{R-7}

Marbofloxacin—$C_{17}H_{19}FN_4O_4$.{R-7; 97}

Orbifloxacin—$C_{19}H_{20}F_3N_3O_3$.{R-7; 98}

Molecular weight:

Ciprofloxacin—331.34.{R-7}

Danofloxacin mesylate—453.48.{R-7}

Difloxacin hydrochloride—435.85.{R-7}

Enrofloxacin—359.39.{R-7}

Marbofloxacin—362.36.{R-7; 97}

Orbifloxacin—395.38.{R-7; 98}

Description:

Ciprofloxacin Hydrochloride USP—Faintly yellowish to light yellow crystals.{R-105}

Difloxacin hydrochloride—White to light yellow powder.

Enrofloxacin—Pale yellow crystals with a melting point of 219 to 221 °C.

Orbifloxacin—White to pale yellow crystalline powder.{R-82}

pKa:

Ciprofloxacin—Carboxylic acid group, 6.1; tertiary amine, 7.8.{R-95}

Difloxacin—Carboxylic acid group, 4.33; methyl substituted nitrogen group, 9.05.{R-96}

Enrofloxacin—Carboxylic acid group, 6.0; tertiary amine, 8.8.{R-95}

Orbifloxacin—5.95 and 9.01.{R-98}

Solubility:

Ciprofloxacin hydrochloride—Sparingly soluble in water; slightly soluble in acetic acid and in methanol; very slightly soluble in dehydrated alcohol; practically insoluble in acetone, in acetonitrile, in ethyl acetate, in hexane, and in methylene chloride.{R-105}

Difloxacin—Poorly water soluble at neutral pH, more soluble under acidic conditions, and highly water soluble under basic conditions.{R-96}

Enrofloxacin—Slightly soluble in water at pH 7.

Marbofloxacin—Soluble in water; less soluble under alkaline conditions.{R-97}

Orbifloxacin—Slightly soluble in water; more soluble in both acidic and alkaline conditions.{R-98}

Pharmacology/Pharmacokinetics

Note: See also *Table I* and *Table II* at the end of this monograph.

Mechanism of action/Effect: Bactericidal.{R-2; 95-100} The fluoroquinolones inhibit bacterial DNA gyrase or topoisomerase IV (a type II topoisomerase), thereby preventing DNA supercoiling and replication.{R-1; 2; 86} Cell respiration and division end, and other processes are interrupted, including membrane integrity.{R-1} Mammalian cell topoisomerase II is not affected by fluoroquinolones until drug concentrations are at least 100 times higher than concentrations recommended to inhibit the bacteria.{R-95}

Fluoroquinolones enter cells via porins and accumulate rapidly in susceptible bacteria.{R-9} Some bacteria are able to pump the antibiotic agent back out of the cell by an energy-dependent efflux transport system.{R-9}

The efficacy of the fluoroquinolones is concentration dependent as measured by either the maximum concentration above MIC (C_{max} : MIC) or the area under the curve above MIC (AUC_{24} : MIC).{R-9} A post-antibiotic effect, in which growth of pathogens may remain inhibited for varying periods after fluoroquinolone concentrations fall below inhibitory concentrations, has been demonstrated with enrofloxacin and orbifloxacin in some bacteria.{R-9; 82}

Absorption: Oral absorption of fluoroquinolones is high for most animals studied.{R-1; 10; 97; 98} It is not affected by administration with food, although absorption may be delayed.{R-95} Divalent and trivalent cations can affect absoprtion (see the *Drug interactions* section in this monograph).{R-96} In cats, dogs, and pigs, oral absorption of fluoroquinolones approaches 100%, but in ruminants, it is generally less.{R-95}

The horse may be unique regarding oral bioavailability patterns in that enrofloxacin, marbofloxacin, and orbifloxacin are considered to have clinically adequate bioavailabilities (65%, 62%, and 68%,

respectively), but ciprofloxacin has been shown to have an oral bioavailability of 7%.{R-27; 144; 171; 174}

Absorption from parenteral administration of fluoroquinolones is rapid and often nearly complete.{R-9; 11; 22; 28; 29; 32; 41; 45; 151} In some animals, there is delayed absorption from intramuscular or subcutaneous administration, producing longer half-lives from these routes compared to intravenous absorption.{R-95}

Enrofloxacin—Oral administration: Rapidly absorbed in monogastric species and preruminant calves.{R-1; 10} Absorption in adult ruminants is variable and has ranged from 10 to 50%.{R-86}

Distribution: Fluoroquinolones achieve concentrations that are at least as high as plasma in a wide range of tissues, with the exception of the central nervous system and the eye.{R-1; 26; 95-98; 162} This is true in many species, including cats, cattle, chickens, dogs, horses, pigs, and rabbits.{R-1; 5; 15; 18; 26; 31; 32; 162}

Differences in volume of distribution among the fluoroquinolones however, account for a range of maximum plasma concentrations among the drugs. Drugs with the lowest volume of distribution are diluted less in body fluid and produce higher plasma concentrations than drugs with a higher volume. The consequence of this difference is reflected in the dose administered; to achieve the same peak serum concentration, drugs with a high volume of distribution require a higher dose.{R-95}

Fluoroquinolones are rapidly accumulated in macrophages and neutrophils. Unlike other antibiotics that concentrate in subcellular sites within phagocytic cells, the quinolones are distributed into the cytosol where they can reach intracellular pathogens.{R-20} This concentration in leukocytes may explain the higher fluoroquinolone concentrations in infected tissue compared to healthy tissue.{R-95}

Because of renal elimination, urine concentration of fluoroquinolones occurs in many species. Enrofloxacin concentration in canine prostate tissue matches that in the serum and concentration in urine reaches about 100 times that in the serum.{R-18; 19} After administration of multiple oral doses of enrofloxacin to horses, urine concentrations are higher than serum concentrations.{R-27} The orbifloxacin concentration in canine prostate tissue exceeds that in serum and concentration in urine reaches about 50 times that in serum.{R-82} Although less than 5% of a difloxacin dose is renally eliminated in the dog, urine concentrations that are 10 times plasma concentration are achieved after a single dose of 10 mg per kg of body weight (mg/kg).{R-96}

Danofloxacin—

Cattle: Danofloxacin is extensively distributed. High concentrations are achieved in healthy lung tissue, pneumonic lung tissue, bronchial mucosa, and bronchial secretions.{R-151; 153; 157-161; 163}

Pigs: Danofloxacin has been shown to reach a high concentration in lung tissue and gastrointestinal tissue, including mucosa.{R-162; 164}

Sheep: Danofloxacin quickly reaches high tissue concentrations. One hour after intramuscular administration, the concentration peaks in lung tissue and interdigital skin.{R-166} It peaks in duodenal contents, lymph nodes, and brain 2 to 4 hours after administration, and in ileal and colonic contents, 4 to 8 hours after administration.{R-166}

Difloxacin—*Horses:* After an intragastric dosage of 7.5 mg/kg a day for five doses, highest mean cerebrospinal fluid, endometrial tissue, peritoneal fluid, synovial fluid, and urine concentrations were 0.87 ± 0.52 mcg/mL at 99 hours, 0.78 ± 0.48 mcg/gram at 97.5 hours, 1.50 ± 0.56 at 98 hours, 1.26 ± 0.49 mcg/mL at 100 hours, and 92.05 ± 30.35 mcg/mL at 104 hours, respectively.{R-183}

Marbofloxacin—*Dogs:* Tissue concentrations of marbofloxacin were determined in healthy male beagle dogs at 2, 18, and 24 hours after a single oral dose (2.75 or 5.5 mg/kg). Based on the terminal elimination half-life and the dosing interval, steady-state levels are reached after the third dose and are expected to be approximately 25% greater than those achieved after a single dose.

Marbofloxacin administered to dogs as a single intravenous dose of 2 mg/kg before cataract surgery produced a mean peak concentration in the aqueous humor of 0.41 ± 0.17 mcg/mL at 3.5 hours after administration and a mean aqueous-humor-to-serum ratio of 0.38.{R-179} This dose was predicted to inhibit Enterobacteriaceae and some staphylococci in the eye, while a higher dose of 5.5 mg/kg may be sufficient to inhibit growth of *Pseudomonas aeruginosa* and staphylococci, but not streptococcal infections.{R-179}

Orbifloxacin—*Dogs:* With oral administration of 7.5 mg/kg a day for at least 4 days, the average skin to plasma ratio of orbifloxacin concentration is 0.96 ± 0.24 in dogs with normal skin and 1.44 ± 0.65 in dogs with pyoderma.{R-180}

Protein binding:

Ciprofloxacin—*Dogs:* 18.48 ± 2.98%, with an antibiotic concentration of 1 to 2 mcg/mL;{R-175} 44 ± 3% (antibiotic concentration not reported).{R-12}

Danofloxacin—

Cattle:{R-160; 163}

50 ± 3%, with an antibiotic concentration of 50 nanograms per mL (ng/mL).

42 ± 3%, with a concentration of 100 ng/mL.

34 ± 1%, with a concentration of 250 ng/mL.

29 ± 1%, with a concentration of 500 ng/mL.

26 ± 1%, with a concentration of 1000 ng/mL.

Goats: 13.55 ± 1.78%.{R-169}

Pigs:{R-164}

Healthy animals—44 ± 8%.

With induced gastrointestinal infection (*Salmonella typhimurium*)—53 ± 8%.

Difloxacin—

Dogs: 46 to 52%.{R-97}

Goats: 13.79 ± 1.02%.{R-185}

Rabbits: 22%.{R-184}

Enrofloxacin—

Camels: Concentration dependent—

1.7% at 1.8 mcg of enrofloxacin per mL of serum (mcg/mL).{R-45}

5% at 0.6 mcg/mL.{R-45}

24.2% at 0.33 mcg/mL.{R-45}

Cattle, lactating: 36 to 45%.{R-11}

Chickens: 24 ± 2%;{R-30} 21 ± 0.1.{R-12}

Dogs: 34.74 ± 2.33%, with a concentration of 1 to 2 mcg/mL;{R-175} 72% at 1 mcg/mL.{R-86}

Horses: 22 ± 2%.{R-12}

Pigs: 27 ± 3%.{R-12}

Rabbits:

Up to 30 days of age—40 to 50%.{R-34; 35}

Adult—53 ± 1%.{R-12}

Does, pregnant—35 ± 5%.{R-63}

Marbofloxacin—

Cats: 7.3%.{R-97}

Dogs: 21.81 ± 6.26%, with a concentration of 1 to 2 mcg/mL;{R-175} 9.1%.{R-97}

Orbifloxacin—

Dogs: 7.7 to 14.5%.{R-82}

Horses: 20.64%.{R-174}

Biotransformation:

Difloxacin—In the dog, difloxacin is metabolized to an ester glucuronide and the desmethyl derivative.{R-96}

Enrofloxacin—Enrofloxacin is de-ethylated to form ciprofloxacin, an antimicrobically active metabolite in many species.{R-11; 13; 18; 22; 24; 28; 29; 31; 39; 42; 46; 71; 72} Therefore, microbiologic assays in pharmacokinetic studies are likely to measure the activity of both enrofloxacin and ciprofloxacin combined. Because minimum inhibitory concentrations for some pathogens are lower for ciprofloxacin than for enrofloxacin,{R-13} therapeutic

concentrations of ciprofloxacin can be reached with dosing calculated to achieve effective enrofloxacin concentrations.{R-16; 25; 28} Ciprofloxacin can be considered an important contributor to the activity of enrofloxacin.{R-16; 28} Evaluations of enrofloxacin activity based on serum or tissue concentrations should consider the contributions of both enrofloxacin and ciprofloxacin. It is also possible that other as yet undiscovered metabolites have antimicrobial activity.{R-16}

Cats: After oral administration, the half-time for conversion of enrofloxacin to ciprofloxacin is about 13 minutes.{R-22} Ciprofloxacin is about 20% of the enrofloxacin concentration in the serum at any one time; about 10% at maximum serum concentrations.{R-22; 72; 86}

Cattle, lactating: The serum concentration of ciprofloxacin is 35% that of enrofloxacin during the elimination phase, after an intravenous dose of 5 mg/kg.{R-11}

Chickens: Enrofloxacin is extensively metabolized to ciprofloxacin.{R-31}

Dogs: Overall, 40% of the oral or intravenous enrofloxacin dose administered is metabolized to ciprofloxacin.{R-23} Ciprofloxacin makes up about 20% of the total serum concentration of enrofloxacin and ciprofloxacin after enrofloxacin administration; ciprofloxacin makes up about 35% of the total body concentration when calculated based on the area under the concentration-time curve (AUC).{R-16; 18; 86}

Ducks: Less than 10% of the administered enrofloxacin dose is converted to ciprofloxacin after a 10 mg/kg dose.{R-42}

Horses: The concentration of ciprofloxacin in the serum reaches 20 to 35% of the enrofloxacin concentration in adult horses.{R-24} In foals, the amount of ciprofloxacin measured is negligible.{R-85}

Llamas: Approximately 36% of enrofloxacin administered is converted to ciprofloxacin in llamas.{R-46}

Macaques, long-tailed: Ciprofloxacin makes up about 22% of the total amount of active drug measured in the serum after intramuscular administration of 5 mg/kg of enrofloxacin.{R-71}

Parrots, African grey: Ciprofloxacin concentration in the serum reaches 3 to 78% of the enrofloxacin dose administered.{R-39} The ratio of ciprofloxacin to enrofloxacin in the serum increases with multiple dosing over 10 days.{R-39}

Pigs: The concentration of ciprofloxacin in the plasma comprises less than 10% of the amount of enrofloxacin present in the plasma.{R-29}

Sheep: In one study, the concentration of ciprofloxacin in the plasma reached 35 and 55% of the serum enrofloxacin concentrations, with intravenous and intramuscular administration, respectively, of a 2.5 mg/kg dose.{R-28} Another study found the concentration of ciprofloxacin in the plasma to be 10 to 20% of the serum drug concentration.{R-86}

Marbofloxacin—*Dogs:* 10 to 15% of the dose is metabolized in the liver.{R-97}

Elimination:

Danofloxacin—

Cattle: Because danofloxacin is rapidly eliminated, only negligible drug accumulation is expected when it is administered at the labeled dose with a 48-hour dosing interval.{R-151; 153} In the first twenty-four hours after an intramuscular dose of 2 mg/kg, 38% of the dose is eliminated in the urine.{R-162}

Pigs: In the first twenty-four hours after an intramuscular dose of 2 mg/kg, 43% of the dose is eliminated in the urine.{R-162}

Difloxacin—*Dogs:* Primarily eliminated through glucuronidation and subsequent biliary secretion. The glucuronide metabolite may be hydrolyzed back to the parent compound and reabsorbed in the gastrointestinal tract. After intravenous administration, 80% of the dose is eliminated in the feces while renal clearance accounts for less than 5% of difloxacin elimination.{R-96}

Enrofloxacin—Renal. Primarily by glomerular filtration and tubular secretion.{R-10}

Marbofloxacin—

Cats: Primarily renal. 70% of an oral dose is excreted into the urine as parent drug and metabolites.{R-97}

Dogs: 40% of an oral or subcutaneous dose is excreted as parent drug into the urine. Elimination of parent drug into the feces is also a significant route of elimination.{R-97; 115}

Orbifloxacin—

Calves: In the first 72 hours after a single intramuscular dose of 5 mg/kg, 37% was recovered in the urine and 5% in the feces.{R-181} After intramuscular administration, 94% of orbifloxacin eliminated in the urine was unchanged parent drug, 1% was glucuronide metabolite, and 5% was an oxidative metabolite.{R-181}

Cats: In the first 72 hours after a single subcutaneous dose of 5 mg/kg, 28% was recovered in the urine and 15% in the feces.{R-181} After subcutaneous administration, 96% of the orbifloxacin eliminated in urine was unchanged parent drug and 4% was N-hydroxy orbifloxacin, an active metabolite with somewhat higher minimum inhibitory concentrations (MICs) for pathogens sensitive to orbifloxacin.{R-111}

Dogs: In the first 72 hours after a single subcutaneous dose of 5 mg/kg, 45% was recovered in the urine and 18% in the feces.{R-181} With oral administration, 40% of the dose was excreted as parent drug into the urine.{R-97} After a subcutaneous dose, 87% of the orbifloxacin eliminated in the urine was parent compound and 13% was glucuronide metabolite.{R-111}

Pigs: In the first 72 hours after a single intramuscular dose of 5 mg/kg, 71% was recovered in the urine and 9% in the feces.{R-181} After intramuscular administration, 97% of the orbifloxacin eliminated in urine was unchanged parent drug and 3% was glucuronide metabolite.{R-181}

Precautions to Consider

Bacterial resistance

Concerns about the risk of increasing resistance of human pathogens to fluoroquinolones as well as the ability of infections in animals to resist treatment should be considered by health practitioners when prescribing these medications. There have been warnings by infectious disease experts that widespread use of fluoroquinolones may lead to increased resistance, and transfer of resistance to humans has been suggested for *Campylobacter* species and *Salmonella typhimurium* type DT-104. Increased resistance in *Campylobacter jejuni* infecting people was reported after 1995, the same period in which fluoroquinolones were first approved for use in poultry. The United States Food and Drug Administration withdrew drug approval for the administration of enrofloxacin to poultry in 2005 because of the emergence of resistance in *Campylobacter* species.{R-3} There has also been discussion about the appearance of resistant strains of *Salmonella typhimurium* during the time fluoroquinolones have been used in livestock. However, some resistant strains have been traced to farms that were not administering fluoroquinolones, leading to the suggestion that the resistance may have arisen spontaneously.{R-95} As scientists continue to uncover evidence pertaining to the potential for transfer of fluoroquinolone-resistant pathogens from animals to man, fluoroquinolones have had limited approval for use in food-producing animals and extra-label use in these animals is prohibited in the United States.{R-95; 106}

Species sensitivity

Cats: Because of the risk of retinal degeneration associated with enrofloxacin administration at high doses (20 mg per kg of body weight [mg/kg] a day),{R-1} it has been recommended that administration of high doses of all fluoroquinolones be avoided in cats whenever possible. It may be that not all fluoroquinolones have the same potential to cause retinal damage. Limited studies showed that marbofloxacin caused no visible retinal changes with fundiscopic or histologic examination when the medication was

administered to 8-month-old cats at 10 times the highest recommended dosage for 2 weeks,[R-97] whereas enrofloxacin has been shown to cause ocular lesions at 4 times the recommended dosage.[R-1] No retinal changes were visible with fundoscopic or histologic examination when orbifloxacin was administered to cats at a dose of 15 mg/kg a day for 30 days (2 times the highest labeled dose), while much higher doses (45 to 75 mg/kg) produced tapetal hyperreflectivity in the area centralis and minimal photoreceptor degeneration.[R-146]

Carcinogenicity

Danofloxacin and enrofloxacin—No evidence of carcinogenicity has been found in studies of laboratory animal models.[R-2; 151]

Pregnancy/Reproduction

The attributes of fluoroquinolones make them likely to cross the placenta in many species; however, adverse effects have not yet been reported when fluoroquinolones have been administered to pregnant animals.[R-95]

Adequate and well-controlled studies of the effects of fluoroquinolones in pregnant human beings have not been done; however, administration during human pregnancy is generally not recommended, based on reports of arthropathy in immature animals.[R-107]

Ciprofloxacin—Ciprofloxacin crosses the human placenta.[R-107] Intravenous doses of ciprofloxacin of up to 20 mg per kg of body weight (mg/kg) in pregnant rats and mice have not shown evidence of maternal toxicity, embryotoxicity, or teratogenic effects.[R-107]

Danofloxacin—

Cattle: Safety in breeding or pregnant cattle has not been determined.[R-151; 152]

Mice and *rats:* No teratogenic effects were reported in rats given up to 50 mg/kg a day from days 6 to 15 of gestation or in mice given up to 100 mg/kg a day for eight days of gestation.[R-153] A reproductive study in three generations of rats established a no observable effect level (NOEL) of 6.25 mg/kg a day.[R-151]

Rabbits: Although maternal toxicity (decreased appetite and subsequent abortion) occurred in rabbits given up to 15 mg/kg a day, no teratogenic effects in their fetuses were reported.[R-151; 153]

Difloxacin, marbofloxacin, and orbifloxacin—Safety in breeding or pregnant animals has not been determined.[R-96-98]

Enrofloxacin—

Cats and *cattle:* Effect on reproduction or pregnancy has not been established.[R-1; 2]

Chickens: No adverse effects were noted in measured reproductive parameters when male and female chickens were given an enrofloxacin dose of 150 parts per million in the drinking water for 7 days. This regimen was repeated at five different ages between 1 day and 206 days of age with no reproductive effect noted. The parameters measured included egg production, egg weight, hatchability, chick viability, and reproductive histology of treated birds and their hatched chicks.[R-4]

Dogs:

No adverse effects were noted in measured reproductive parameters, including libido, successful pregnancy, and number of pups per litter, when male dogs were administered 5 to 15 mg/kg a day for 10 days beginning at 90, 45, or 14 days before breeding.[R-1; 5]

No adverse effects were noted in female dogs administered 15 mg/kg a day for 10 days in the last 30 days before breeding, between the 10th and 30th days of gestation, between the 40th and 60th days of gestation, or during the first 28 days of lactation.[R-1; 5; 6]

Rabbits: Enrofloxacin is transferred across the placenta in rabbits;[R-63] adverse effects on pups have not been reported. Ciprofloxacin also crosses the placenta but at a much slower pace (6% of the rate of enrofloxacin).[R-63]

Lactation

Because of the risk of producing arthropathies in immature animals, it has been recommended that significant levels of fluoroquinolones in the milk of nursing animals be avoided.[R-95; 107] Fluoroquinolones can be distributed into milk, sometimes at a higher concentration than in plasma,[R-11-14; 34] but it is not known under what conditions significant amounts might be absorbed by nursing animals.[R-86]

Mastitis—It has not been shown that fluoroquinolones are effective in treating mastitis,[R-95] perhaps because of factors in milk that inhibit activity.[R-11]

Cattle: United States federal law prohibits the extra-label use of fluoroquinolones in food-producing animals (see the *Regulatory Considerations* section).

Danofloxacin appears rapidly in milk after parenteral administration. In one study, milk concentration equaled plasma concentration 90 minutes after intravenous injection and 120 minutes after intramuscular injection.[R-161] Three to four hours after intravenous administration of 1.25 mg/kg, milk concentration was 4 to 15 times the serum concentration; it peaked at 0.8 mcg/mL at 4 hours. Danofloxacin continued to be measured in milk for at least 24 hours but was no longer found in serum 6 and 12 hours after intravenous and intramuscular administration, respectively (limit of detection, 0.02 mcg/mL).[R-161]

Enrofloxacin appears rapidly in milk after parenteral administration, reaching a peak concentration 30 to 60 minutes after intravenous injection, followed by a gradual decline in milk concentration similar to that occurring in serum concentration.[R-11; 14] Approximately 0.2% of a 5 mg per kg of body weight dose of enrofloxacin is measured in milk in the first 24 hours; therapeutic antimicrobial concentrations can be reached.[R-11]

The ciprofloxacin metabolite of enrofloxacin also appears rapidly in milk, but this occurs 4 to 8 hours after parenteral administration. It concentrates to a higher peak than enrofloxacin itself.[R-11; 14]

Horses: Following an oral dose of 5 mg/kg to lactating mares, concentration of ciprofloxacin and enrofloxacin in milk ranged from 0.25 to 0.78 mcg per mL. At this concentration, a nursing foal would ingest a dose of less than 0.1 mg per kg of body weight a day, producing plasma concentrations below detection limits in the foal.[R-86]

Rabbits: United States federal law prohibits the extra-label use of fluoroquinolones in food-producing animals (see the *Regulatory Considerations* section). The following information is included in case of accidental dosing.

Therapeutic concentrations of enrofloxacin are reached in milk following a dose of 7.5 mg per kg of body weight.[R-34]

Sheep: United States federal law prohibits the extra-label use of fluoroquinolones in food-producing animals (see the *Regulatory Considerations* section). The following information is included in case of accidental dosing.

With intramuscular or intravenous administration of danofloxacin, milk concentration exceeds serum concentration within 60 to 90 minutes. Danofloxacin continues to be present in milk after the drug and its active metabolites can no longer be measured in the serum by microbiological assay.[R-167]

Similarly, with intramuscular or intravenous administration of enrofloxacin, milk concentrations reached are much higher than serum concentrations.[R-147]

Pediatrics

See also the *Side/Adverse Effects* section for information on risk of arthropathies in immature animals.

Enrofloxacin—

Calves: Until at least 1 week of age, the elimination of enrofloxacin is slower in calves than in adult cattle.[R-13]

Adjustment of dosage, including increased dosing interval, may be necessary.[R-13]

Foals: Elimination of enrofloxacin in foals (half-life = 18 hrs) is slower than in adult horses and oral absorption in foals is approximately 42%.[R-86] Administering enrofloxacin at a dose of 10 mg per kg a day caused every one of five healthy foals to have lesions on articular cartilage.[R-85]

Rabbits: Elimination of enrofloxacin is significantly less in neonates until at least 16 days of age compared with that in adult rabbits.[R-34] The ease of penetration of enrofloxacin into milk should be considered when treating lactating does that continue to nurse.[R-35] Enrofloxacin pharmacokinetics in 30-day-old rabbits are similar to those in adult rabbits.[R-35]

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Digoxin: A small study investigating the effect of enrofloxacin administration on digoxin clearance and serum concentrations in dogs showed no effect with concurrent administration.[R-59]

Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Antacids, aluminum-, calcium-, or magnesium-containing or
Laxatives, magnesium-containing or
Multivitamins or
Sucralfate or
Zinc

(compounds containing divalent or trivalent cations, such as aluminum, calcium, iron, magnesium, or zinc, administered concurrently with a fluoroquinolone, may reduce the absorption of the fluoroquinolone)[R-1; 96-98]

Diclofenac[R-189]
Flunixin[R-176]
Tolfenamic acid[R-177]

(the coadministration of nonsteroidal anti-inflammatory drugs with fluoroquinolones may affect the pharmacokinetics of one or both drugs; the clinical significance of these changes is not known)

Theophylline[R-61] or
Hepatically metabolized drugs, other[R-1]

(in dogs, the clearance of theophylline was reduced by 43% with concurrent administration of enrofloxacin [5 mg per kg of body weight every 24 hours]; peak serum concentration of theophylline was significantly increased; the pharmacokinetics of enrofloxacin were unaffected)[R-62]

(the concurrent administration of a fluoroquinolone with other drugs metabolized by hepatic enzymes may affect the pharmacokinetics of one or both drugs;[R-1] enrofloxacin has been shown to inhibit liver microsomal mixed-function oxidases in broiler chicks, including aniline hydroxylase and aminopyrine *N*-demethylase;[R-60] cytochrome P450 activity was not significantly affected in chickens;[R-60] in mice, there is indirect evidence that cytochrome P450 enzymes may be affected by enrofloxacin administration;[R-62] the effect of these enzyme inhibitions on specific drugs has not yet been demonstrated)

Human drug interactions and/or related problems[R-107]

In addition to the above drug interactions reported in animals, the following drug interactions have been reported in humans, and are included in the human monograph *Fluoroquinolones (Systemic)* in *USP DI Volume I;* these drug interactions are intended for informational purposes only and may or may not be applicable to the use of fluoroquinolones in animals:

Note: There are no danofloxacin, difloxacin, enrofloxacin, marbofloxacin, or orbifloxacin products labeled for use in human beings.

Anticonvulsants, hydantoin, especially:
Phenytoin

(concurrent administration of ciprofloxacin with phenytoin has resulted in a 34 to 80% decrease in the plasma concentration of phenytoin)

Antidiabetic agents, sulfonylurea, especially:
Glyburide or
Insulin

(concurrent use of ciprofloxacin with glyburide or other antidiabetic agents has, on rare occasions, resulted in hypoglycemia; also, hyperglycemia and hypoglycemia have been reported in patients taking quinolone antibiotics and antidiabetic agents concurrently; the mechanism is not understood and similar effects with other sulfonylurea antidiabetic agents may be expected when these medications are used with fluoroquinolones)

Anti-inflammatory drugs, nonsteroidal (NSAIDs)

(fluoroquinolones are competitive inhibitors of gamma-aminobutyric acid receptor binding, and some NSAIDs have been shown to enhance this effect; concurrent administration of NSAIDs with quinolone antibiotics may increase the risks of CNS stimulation and convulsions)

Cyclosporine

(concurrent use with ciprofloxacin has been reported to elevate serum creatinine and serum cyclosporine concentrations; other studies have not found ciprofloxacin to alter the pharmacokinetics of cyclosporine)

Probenecid

(concurrent use of probenecid decreases the renal tubular secretion of fluoroquinolones, resulting in decreased urinary excretion of the fluoroquinolone, prolonged elimination half-life, and increased risk of toxicity; this interaction is more significant with fluoroquinolones excreted largely unchanged in the urine)

Warfarin

(concurrent use of warfarin with ciprofloxacin has been reported to increase the anticoagulant effect of warfarin, increasing the chance of bleeding; other studies have not found fluoroquinolones to alter the prothrombin time [PT] significantly)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

With diagnostic test results
Coombs' test

(positive reactions for the Coombs' test may be seen in animals receiving cephalosporins;[R-110] this may be due to changes in the red blood cells, but hemolytic anemia usually is not occurring[R-2])

Glucose, urine

(in dogs, enrofloxacin administered at a dose of 5 to 10 mg/kg has been shown to produce false-positive urine glucose results with one commercial product tested [*Clinitest* tablets] while the strips tested were not affected [*Chemstrips 10 SG, Multistix 10 SG,* and *Urispec 9-way*]; other than being test-dependent, this problem is probably also dosage-dependent [more common with the higher dose of 10 mg/kg every 12 hours] and dependent on the timing of collection after drug administration [with the lower dose, it occurred at 6 hours but not at 24 hours])[R-178]

Human laboratory value alterations[R-107]

The following laboratory value alterations have been reported in humans, and are included in the human monograph *Fluoroquinolones (Systemic)* in *USP DI Volume I;* these

laboratory value alterations are intended for informational purposes only and may or may not be applicable to the use of fluoroquinolones in the treatment of animals:

Note: There are no danofloxacin, difloxacin, enrofloxacin, marbofloxacin, or orbifloxacin products labeled for use in human beings.

With physiology/laboratory test values
Alanine aminotransferase (ALT [SGPT]) and
Alkaline phosphatase and
Amylase and
Aspartate aminotransferase (AST [SGOT]) and
Lactate dehydrogenase (LDH)
(serum values may be increased)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problems exist:

Hypersensitivity to quinolones
(animals with a history of hypersensitivity to quinolones are at risk for developing reactions to them)[R-1; 97; 98; 200]

Immature animals in some species
(fluoroquinolone administration during rapid growth has been associated with arthropathies and cartilage erosions in weight-bearing joints in immature cats, dogs, and horses;[R-1; 5; 25; 26; 85; 96-98] in dogs, enrofloxacin has been shown to cause abnormal carriage of the carpal joint and hindlimb weakness, as well as cartilage lesions; administration of enrofloxacin should be avoided in small and medium breed dogs during rapid growth, typically 2 to 8 months of age; large or giant breeds may rapidly grow until 18 months of age)[R-1]

Risk-benefit should be considered when the following medical problems exist:

Central nervous system (CNS) disorders[R-1; 150]

Seizures, history of
(fluoroquinolones have been associated with CNS stimulation that may lead to seizures in a few rare cases and should be used with caution;[R-1; 2; 151] the clinical significance of a report of increased seizure incidence with enrofloxacin administration to dogs with phenobarbital-controlled seizures is not known)[R-10]

Hepatic disease, severe

Renal failure
(fluoroquinolones are primarily eliminated by a combination of renal clearance and hepatic metabolism, sometimes with significant biliary secretion; the predominance of one route over another depends on the quinolone and the animal species; there is little research information on changes in elimination in various disease states in animals; the induction of moderate renal impairment in dogs [glomerular filtration rate decreased 37% and serum creatinine values increased 85% from normal controls] had only a minor effect on the clearance of marbofloxacin)[R-108]

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; » = major clinical significance):

Culture and sensitivity *in vitro* and
Minimum inhibitory concentration (MIC)
(*in vitro* cultures and MIC tests should be done on samples collected prior to fluoroquinolone administration to determine pathogen susceptibility)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs in parentheses where appropriate)—not necessarily inclusive:

Those indicating need for medical attention

Incidence unknown

Multiple species

Arthropathy—in immature animals, especially dogs and foals

Note: The risk of arthropathy increases with increasing dose but has been reported to occur at recommended dosages in young dogs.

Danofloxacin—Articular cartilage lesions consistent with fluoroquinolone chondropathy have not been demonstrated in growing *calves* when danofloxacin is administered at the labeled dose. The typical cartilage lesions were reported at necropsy and histopathology of calves given 18 mg per kg of body weight (three times the labeled dose) or more, with a shortened dosing interval or lengthened duration of treatment compared to the labeled dosage.[R-151]

Difloxacin—Articular cartilage lesions were seen in 15- to 16-week-old *puppies* administered difloxacin at 5, 25, or 35 mg per kg of body weight (mg/kg) a day for 90 days.[R-96] Lameness, in addition to cartilage lesions, was observed in puppies administered 50 or 125 mg/kg a day.[R-96]

Enrofloxacin—Cartilage damage has been observed in 10- to 28-week-old *puppies* with an oral enrofloxacin dose of 5 to 25 mg/kg a day for 30 days and 5- to 7-month-old *kittens* with an oral dose of 25 mg/kg a day for 30 days;[R-1; 5] changes include splitting of the articular cartilage surface and, in some cases, necrosis of the hyaline cartilage.[R-4] Arthropathy has been reported in growing horses.[R-25; 26] In manufacturer-generated data, a dose of 5 mg/kg administered to *foals* once a day was reported to cause cartilage lesions and signs of arthropathy after 6 days;[R-25] however, studies have shown no effect on cartilage in adult horses when used continuously for up to 21 days.[R-86; 136] In 23-day-old *calves,* a dose of 25 mg/kg a day for 15 days had no measurable effect on articular cartilage in the stifle joint at 2 and 9 days after the end of treatment.[R-2]

Marbofloxacin—Lameness and articular cartilage lesions were reported in large breed, 3- to 4-month-old dogs administered 11 mg/kg a day for 14 days.[R-97]

Orbifloxacin—Microscopic cartilage lesions typical of fluoroquinolone arthropathy have also been reported with orbifloxacin administration; in one of eight, 8- to 10-week-old puppies given 12.5 mg/kg a day and all 8 puppies given 25 mg/kg a day.[R-98] Cats appear to be resistant to this affect, showing no cartilage lesions after one month of 25 mg/kg a day.[R-98]

Cats

Retinal degeneration (acute blindness, mydriasis)—reported with enrofloxacin at doses higher than 5 mg/kg a day

Note: Administering enrofloxacin to cats at a dose of 20 mg/kg can cause *retinal degeneration,*[R-1; 103] often manifested as temporary or permanent blindness with mydriasis.[R-1; 103; 119] Mild to severe fundic lesions are observed on ophthalmologic exam of affected cats, including changes in the color of the fundus and central or generalized retinal degeneration. There are also abnormal electroretinogram results and diffuse light microscopic changes in the retinas.[R-1] Caution is recommended when considering high dose therapy of any fluoroquinolone in cats.

Cats and *dogs*

Anorexia, decreased appetite, diarrhea, or vomiting—with difloxacin and orbifloxacin; ***ataxia***—with enrofloxacin and orbifloxacin; ***hypersensitivity reactions*** (anaphlaxis or anapylactoid reactions, facial edema)—with orbifloxacin;

seizures—with enrofloxacin and orbifloxacin

Note: The above effects were not observed during preapproval clinical field trial but were noted as part of voluntary postapproval adverse drug experience reporting.{R-1; 96; 200}

Horses

Oral erosions or ulcers—with oral administration of enrofloxacin injection{R-201}

Note: Some practitioners have administered enrofloxacin injection (100 mg/mL) orally to horses because of the relatively high cost of administering multiple tablets sized for cats and dogs. However, it is not unusual for horses to develop serious *oral erosions or ulcers* during this treatment. Even when the injection was compounded into a oral gel formulation, oral lesions were noted in about 10% of the horses treated.{R-201}

Parrots, African grey

Appetite, decreased;{R-40} ***polydipsia and polyuria***—with an enrofloxacin dose of 30 mg/kg every 12 hours for 10 days{R-39} or in drinking water with 1.5 to 3 mg of enrofloxacin per mL of water;{R-40} may resolve within 2 or 3 days of treatment cessation{R-39}

Incidence less frequent

Calves

Lameness

Note: Transient lameness was reported in one out of forty-one calves during a field trial in which calves were given 6 mg/kg every forty-eight hours. Two of thirty-eight calves became lame four days after a single dose of 8 mg/kg; one was still lame at the end of the study six days later.{R-151}

Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Cats

Vomiting—with enrofloxacin, occasional vomiting was observed in up to 75% of 7- to 10-month-old cats administered a 5- to 15-mg/kg dose for 30 days; however, 25% of untreated cats also vomited occasionally.{R-1}

Incidence less frequent

Cats

Diarrhea—reported with marbofloxacin (2.1% of cats in one report){R-97}

Dogs

Decreased activity—reported with marbofloxacin (4.4% of dogs in one report);{R-97} ***decreased appetite***—reported with marbofloxacin (5.4%);{R-97} ***vomiting***—reported with marbofloxacin (2.9%){R-97}

Incidence rare

Cats

Vomiting—with marbofloxacin (<1%){R-97}

Dogs

Vomiting—with enrofloxacin (0.7% of dogs){R-1}

Incidence unknown

Cats and *dogs*

Depression; lethargy—with orbifloxacin{R-200}

Cattle,{R-2} *horses,*{R-24} and *rabbits*{R-68; 69}

Local tissue reaction, transient—with injection; in cattle, can cause trim loss of edible tissue at slaughter{R-2; 151}

Human side/adverse effects{R-107}

In addition to the above side/adverse effects reported in animals, the following side/adverse effects have been reported in humans and are included in the human monograph *Fluoroquinolones (Systemic)* in *USP DI Volume I;* these side/adverse effects are intended for informational purposes only and may or may not be applicable to the use of fluoroquinolones in the treatment of animals:

Note: The following human side/adverse effects are those pertaining to ciprofloxacin or to fluoroquinolones in general. Danofloxacin, difloxacin, enrofloxacin, marbofloxacin, and orbifloxacin are not available as products labeled for human use.

Note: The relative insolubility of ciprofloxacin at an alkaline pH has resulted in *crystalluria,* usually when the urinary pH exceeds 7. *Seizures* have been reported very rarely with ciprofloxacin therapy; however, the patients who did have seizures either had a previous seizure history, were alcoholic, or were taking ciprofloxacin concurrently with theophylline.

Incidence more frequent

Central nervous system (CNS) toxicity; gastrointestinal reactions; vaginitis

Incidence less frequent or rare

Arthralgia; back pain; cardiovascular reactions such as palpitation, vasodilation, or tachycardia; central nervous system (CNS) stimulation; change in sense of taste; dysuria; hematuria; hepatotoxicity; hypersensitivity reactions; interstitial nephritis; moniliasis, oral; moniliasis, vaginal; myalgia; phlebitis—for intravenous ciprofloxacin; ***photosensitivity; phototoxicity; pseudomembranous colitis; Stevens-Johnson Syndrome*** (blistering, itching, loosening, peeling, or redness of skin; diarrhea); ***tendinitis or tendon rupture; vision, abnormal***

Indicating possible phototoxicity, pseudomembranous colitis, or tendinitis or tendon rupture and the need for medical attention if they occur after medication is discontinued:

Abdominal or stomach cramps and pain, severe; abdominal tenderness; blisters; diarrhea, watery and severe, which may also be bloody; fever; pain in calves, radiating to heels; sensation of skin burning; skin rash, itching, or redness; swelling of calves or lower legs

Overdose

For more information in cases of overdose or unintentional ingestion, **contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center** (888-426-4435 or 900-443-0000; a fee may be required for consultation) **and/or the drug manufacturer.**

Reported lethal dose of danofloxacin—*Mice* and *rats:* >2000 mg per kg of body weight (mg/kg).{R-151}

Reported lethal doses of enrofloxacin—

Cats: 125 mg/kg a day for 5 days.{R-1}

Dogs: Oral—125 mg/kg a day for up to 11 days.{R-1; 5}

Mice: Oral—LD_{50} for female mice is 4335 mg/kg and for male mice is 5000 mg/kg.{R-4}

Rabbits: Oral—LD_{50} for male and female rabbits is 500 to 800 mg/kg.{R-4}

Rats: Oral—LD_{50} for male and female rats is more than 5000 mg/kg.{R-2}

Turkey poults, 1-day-old: Oral—626 parts of enrofloxacin per million parts of drinking water administered for 21 days caused the death of 11 out of 40 birds in the first 10 days.{R-4} Surviving birds showed signs of listlessness and decreased body weight gain.{R-3}

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance—not necessarily inclusive:

For danofloxacin

Note: United States federal law prohibits the extra-label use of fluoroquinolones in food-producing animals (see the *Regulatory Considerations* section).

Calves, 21-day-old, with a dose of 18 mg/kg, administered twice, forty-eight hours apart{R-151}

Nasal pad erythema

Calves, feeder, with a dose of 30 mg/kg a day for 6 consecutive days{R-151}

Ataxia; exophthalmos; inappetance; lameness, transient; nystagmus; recumbency; tremors

For difloxacin

Dogs, with doses of 5, 15, or 25 mg/kg a day for 30 consecutive days[R-96]
Decreased appetite; diarrhea; erythema/edema on the facial area, transient; weight loss

For enrofloxacin

Calves, feeder, with a dose of 15 or 25 mg/kg a day for 10 to 15 days or a dose of 50 mg/kg a day for 3 days[R-2]
Note: United States federal law prohibits the extra-label use of fluoroquinolones in food-producing animals (see the *Regulatory Considerations* section).
Depression; decreased appetite; incoordination; muscle fasciculations

Cats, with a dose of 20 mg/kg a day for 21 days[R-1]
Depression; retinal degenerative effects; salivation; vomiting

Cats, with a dose ≥ 50 mg/kg a day for 6 days[R-1]
Convulsions; depression; incoordination; loss of appetite; retinal degenerative effects; vomiting

Chicks, 1-day-old, with a dose in drinking water of 625 ppm for 21 to 28 days[R-4]
Decreased water consumption; decreased weight

Dogs, with an oral dose of 50 to 125 mg/kg a day for 11 to 14 days[R-1; 5; 8]
Convulsions; depression or excitation; incoordination; loss of appetite; muscle tremors; salivation; vomiting

For marbofloxacin

Cats, with a dose of 5.5, 16.5, or 27.5 mg/kg a day for 42 days
Dermatitis, perivascular to diffuse (often reddened pinnae); ***excessive salivation; softened stools***

Cats, with a dose of 55 mg/kg a day for 14 days
Decreased activity; decreased food consumption; dermatitis, perivascular to diffuse (often reddened pinnae); ***excessive salivation; vomiting, occasional***

Dogs, with a dose of 5.5, 16.5, or 27.5 mg/kg a day for 42 days
Decreased food consumption; reddened mucous membranes; reddened skin (usually involving the ears); ***vomiting; weight loss***

Dogs, with a dose of 55 mg/kg a day for 12 days
Decreased food consumption; dehydration; decreased activity; excessive salivation; facial swelling; reddened skin (usually the ears); ***tremors; vomiting; weight loss***

For orbifloxacin

Cats, with a dose of 22.5 and 37.5 mg/kg a day[R-98]
Softened stools

Cats, with a dose of 75 mg/kg a day for 10 days[R-98]
Decreased food consumption; diarrhea, ***vomiting***

Treatment of overdose

Although there is no specific information available on treatment of fluoroquinolone overdose in animals, treatment of human overdose includes induction of vomiting or use of gastric lavage, observation, and supportive care, including hydration and dialysis.

Client Consultation

Care should be exercised to avoid contact of medication with the eyes or skin while handling solutions.[R-2]

General Dosing Information

Flouroquinolone antibiotics have concentration-dependent bactericidal activity.[R-21] Serum and tissue concentrations must be high enough for a long enough period of time to be effective against the target pathogen. Fortunately, minimum inhibitory concentrations (MIC) for fluoroquinolones are relatively low. Depending on many variables, such as the organism treated and the presence of neutrophils, fluoroquinolones can also produce a post-antibiotic effect, suppressing bacterial growth after local drug concentrations have fallen.[R-21; 112]

Product labeling for veterinary fluoroquinolone products include a dosage range and MIC data for bacterial pathogens for specific indications in which efficacy has been confirmed.[R-1; 96-98] It is recommended that the dose be chosen based on clinical experience, the type and severity of infection, and susceptibility of the pathogen.[R-1] The effective treatment of canine infections caused by *Pseudomonas aeruginosa*[R-17] and *Staphylococcus* species[R-21] may require the high end of the dosage range.

Cats: Because of the risk of retinal damage associated with high dosages of enrofloxacin, it is recommended that caution be used when considering administering fluoroquinolone at dosages higher than those recommended for cats.

Breakpoints determined for ciprofloxacin by the Clinical and Laboratory Standards Institute (CLSI; formerly the National Committee for Clinical Laboratory Standards)[R-95]

MIC (mcg/mL)	Interpretation
≤ 1.0	Susceptible
2.0	Intermediacate
≥ 4	Resistant

Note: Be aware that ciprofloxacin may not be appropriate for use as a representative of veterinary fluoroquinolones in susceptibility testing. Use of specific antibiotic MIC ranges has been recommended.[R-110]

Breakpoints (provisional) determined by CLSI for danofloxacin in the treatment of bovine respiratory disease (*Mannheimia haemolytica* and *Pasteurella multocida*)[R-152; 156]

Zone diameter (millimeters)	MIC (mcg/mL)	Interpretation
≥ 22	≤ 0.25	Susceptible
—	—	Intermediate
—	—	Resistant

Note: The disk content is 5 mcg.[R-152; 156] There are insufficient data available to establish breakpoints for the intermediate and resistant categories.[R-152] The CLSI describes this as "susceptible only," a category used for populations of organisms (usually one species) for which regression analysis (disk vs. MIC) cannot be performed.[R-156] The single breakpoint allows detection of strains with decreased susceptibility compared to the population originally tested.[R-156]

Breakpoints determined by CLSI for difloxacin in the treatment of dermal and urinary tract infections in dogs, including those caused by Enterobacteriaceae and *Staphylococcus* species[R-156]

Zone diameter (millimeters)	MIC (mcg/mL)	Interpretation
≥ 21	≤ 0.5	Susceptible
18–20	1–2	Intermediate
≤ 17	≥ 4	Resistant

Note: The disk content is 10 mcg.

Breakpoints determined by CLSI for enrofloxacin in the treatment of dermal infections in cats and in the treatment of dermal, respiratory, and urinary tract infections in dogs, including those caused by Enterobacteriaceae and *Staphylococcus* species.[R-156]

Zone diameter (millimeters)	MIC (mcg/mL)	Interpretation
≥ 23	≤ 0.5	Susceptible
17–22	1–2	Intermediate
≤ 16	≥ 4	Resistant

Note: The disk content is 5 mcg.

Breakpoints recommended by the manufacturer for enrofloxacin in the treatment of *Mannheimia haemolytica* and *Pasteurella multocida* infections in cattle[R-150] and listed by CLSI for bovine respiratory disease caused by *Pasteurella multocida* or *Histophilus somnus*[R-156]

Zone diameter	MIC	Interpretation

(millimeters)	(mcg/mL)	
≥ 21	≤ 0.25	Susceptible
17–20	0.5–1	Intermediate
≤ 16	≥ 2	Resistant

Note: The disk content is 5 mcg.

Breakpoints recommended by CLSI for marbofloxacin in the treatment of dermal infections in cats and in the treatment of dermal and urinary tract infections in dogs, including those caused by Enterobacteriaceae and *Staphylococcus* species{R-156}

Zone diameter (millimeters)	MIC (mcg/mL)	Interpretation
≥ 20	≤ 1	Susceptible
15–19	2	Intermediate
≤ 14	≥ 4	Resistant

Note: The disk content is 5 mcg.

Breakpoints recommended by CLSI for orbifloxacin in the treatment of dermal infections in cats and in the treatment of dermal and urinary tract infections in dog, including those caused by Enterobacteriaceae and *Staphylococcus* species{R-156}

Zone diameter (millimeters)	MIC (mcg/mL)	Interpretation
≥ 23	≤ 1	Susceptible
18–22	2–4	Intermediate
≤ 17	≥ 8	Resistant

Note: The disk content is 10 mcg.

CIPROFLOXACIN

Summary of Differences

General considerations: Expected to be more active than other quinolones against some gram-negative bacilli, especially *Pseudomonas aeruginosa*.{R-174; 199}

Regulatory considerations: Ciprofloxacin is not labeled for use in animals.

Oral Dosage Forms

Note: The text between EL[US] and EL describes uses not included in U.S. product labeling. Text between EL[CAN] and EL describes uses that are not included in Canadian product labeling.

The EL[US] or EL[CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CIPROFLOXACIN FOR ORAL SUSPENSION

Usual dose:

Note: EL[US,CAN]*Dogs*—Although the safety and efficacy have not been established, an oral dose of 10 to 20 mg per kg of body weight every twenty-four hours has been recommended in the treatment of susceptible *bacterial infections,* based on pharmacokinetic data.{R-95; 118; 134}

For empiric treatment of infections in dogs caused by probable *Pseudomonas aeruginosa* or *Staphylococcus* infections, the higher end of the dosage range may be preferable, pending susceptibility results.EL

EL[US,CAN]*Horses*EL—Due to poor bioavailability,{R-144} oral ciprofloxacin should not be used in horses.

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

250 mg per 5 mL (5%) (Rx) [*Cipro*].

500 mg per 5 mL (10%) (Rx) [*Cipro*].

Canada—

Not commerically available.

Packaging and storage: Prior to reconsitution, store below 25 ºC (77 ºF). Protect from freezing. After reconstitution, store below 30 ºC (86 ºF). Protect from freezing.

Preparation of dosage form: To prepare the oral suspension, the small bottle containing the microcapsules should be emptied into the large bottle containing the diluent. **Water should not be added to the suspension.** The large bottle should be closed and shaken vigorously for about 15 seconds.

Stability: The suspension is stable for 14 days when stored in a refrigerator or at room temperature (below 30 ºC [86 ºF]).

USP requirements: Not in USP.{R-105}

CIPROFLOXACIN TABLETS USP

Usual dose: See *Ciprofloxacin for Oral Suspension.*

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

100 mg (base) (Rx) [*Cipro*].

250 mg (base) (Rx) [*Cipro;* GENERIC].

500 mg (base) (Rx) [*Cipro;* GENERIC].

750 mg (base) (Rx) [*Cipro;* GENERIC].

Canada—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

100 mg (base) (Rx) [*Cipro*].

250 mg (base) (Rx) [*Cipro;* GENERIC].

500 mg (base) (Rx) [*Cipro;* GENERIC].

750 mg (base) (Rx) [*Cipro;* GENERIC].

Packaging and storage: Store below 30 ºC (86 ºF), in a well-closed container, unless otherwise specified by manufacturer.

USP requirements: Preserve in well-closed containers. Contain an amount of ciprofloxacin hydrochloride equivalent to the labeled amount of ciprofloxacin, within ±10%. Meet the requirements for Identification, Dissolution (80% in 30 minutes in 0.01 *N* hydrochloric acid in Apparatus 2 at 50 rpm), Uniformity of dosage units, and Residual solvents.{R-105}

Parenteral Dosage Forms

Note: The text between EL[US] and EL describes uses not included in U.S. product labeling. Text between EL[CAN] and EL describes uses that are not included in Canadian product labeling.

The EL[US] or EL[CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

CIPROFLOXACIN INJECTION USP

Usual dose:

Note: EL[US,CAN]*Dogs*—Although the safety and efficacy have not been established, an intravenous dose of 10 to 15 mg per kg of body weight, administered slowly every twenty-four hours has been recommended in the treatment of susceptible *bacterial infections.*EL{R-81}

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

Not commercially available.

Human-labeled product(s):

200 mg per 20 mL (Rx) [*Cipro I.V.* (in sterile water for injection; requires dilution prior to administration); GENERIC].

200 mg per 100 mL (Rx) [*Cipro I.V.* (in 5% dextrose injection; premixed)].

400 mg per 40 mL (Rx) [*Cipro I.V.* (in sterile water for injection; requires dilution prior to administration); GENERIC].

400 mg per 200 mL (Rx) [*Cipro I.V.* (in 5% dextrose injection; premixed)].

1200 mg per 120 mL (Rx) [*Cipro I.V.* (in sterile water for injection; requires dilution prior to administration); GENERIC].

Canada—

Veterinary-labeled product(s):

Not commerically available.

Human-labeled product(s):

200 mg per 20 mL (Rx) [*Cipro I.V.* (in sterile water for injection; requires dilution prior to administration)].

400 mg per 40 mL (Rx) [*Cipro I.V.* (in sterile water for injection; requires dilution prior to administration)].

Packaging and storage: Store in a cool place (between 8 and 15 ºC [46 and 59 ºF]) or at controlled room temperature (between 20 and 25 ºC [68 and 77 ºF]), unless otherwise specified by manufacturer. Protect from light and freezing.

Preparation of dosage form: To prepare a solution for intravenous infusion, the concentrate in sterile water for injection should be withdrawn aseptically from the vial and diluted to a final concentration of 1 to 2 mg per mL with a suitable intravenous solution (see manufacturer's package insert). *Solutions that come from the manufacturer in 5% dextrose injection should not be diluted prior to intravenous infusion.* The resulting solution should be infused over a period of at least 60 minutes by direct infusion or through a Y-type intravenous infusion set. It is recommended that administration of any other solutions be discontinued during infusion of ciprofloxacin.

Stability: When diluted with appropriate intravenous fluids (see manufacturer's package insert) to concentrations from 0.5 to 2 mg per mL, solutions retain their potency for up to 14 days when refrigerated or stored at room temperature.

Incompatibilities: Ciprofloxacin is incompatible with aminophylline, amoxicillin, cefepime, clindamycin, dexamethasone, floxacillin, furosemide, heparin, and phenytoin.

If ciprofloxacin is to be given concurrently with another medication, each medication should be administered separately according to the recommended dosage and route of administration for each medication.

USP requirements: Preserve in single-dose containers, preferably of Type I glass, in a cool place or at controlled room temperature. Avoid freezing and exposure to light. A sterile solution of Cipofloxacin or Ciprofloxacin Hydrochloride in Sterile Water for Injection, in 5% Dextrose Injection, or in 0.9% Sodium Chloride Injection prepared with the aid of Lactic Acid. The label indicates whether the vehicle is Sterile Water for Injection, 5% Dextrose Injection, or 0.9% Sodium Chloride Injection. Label the Injection that has Sterile Water for Injection as the vehicle to indicate that it is a concentrated form that must be diluted to appropriate strength (1 to 2 mg per ml) with 5% Dextrose Injection or 0.9% Sodium Chloride Injection before administration, and that the resulting solution is stable for up to 14 days when stored in a cool place or at controlled room temperature. Contains the labeled amount, within ±10%. Meets the requirements for Color (where it is labeled as being a concentrated form), Identification, Bacterial endotoxins, Sterility, pH (3.5–4.6, except that where the Injection is labeled as being a concentrated form, its pH is between 3.3 and 3.9), Particulate matter, Limit of ciprofloxacin ethylenediamine analog (not more than 0.5%), Lactic acid content (0.288—0.352 mg per mg of ciprofloxacin claimed on label, except that where the Injection is labeled as being a concentrated form, it contains between 0.335 and 0.409 mg per mg of ciprofloxacin claimed on the label), Dextrose content (if present), and Sodium chloride content (if present), Residual solvents, and for Volume in Container under Injections.{R-105}

DANOFLOXACIN

Parenteral Dosage Forms

DANOFLOXACIN MESYLATE INJECTION

Usual dose: Pneumonia—*Cattle:* Subcutaneous, 6 mg per kg of body weight, administered twice, forty-eight hours apart.{R-151; 152}

Withdrawal times—*Cattle:* US—Meat: 4 days.{R-151} Canada—Meat: 7 days.{R-152} US and Canada—Not labeled for use in cattle intended for dairy production or in calves to be processed for veal.{R-151; 152} Subcutaneous injection can cause a local tissue reaction that is transient but can cause trim loss of edible tissue at slaughter.{R-151; 152}

Note: Product labeling recommends not administering more than 15 mL per injection site.{R-151}

Strength(s) usually available:

U.S.—{R-151}

Veterinary-labeled product(s):

180 mg per mL (Rx) [*A180*].

Canada—{R-152}

Veterinary-labeled product(s):

180 mg per mL (Rx) [*A180*].

Packaging and storage: Store at or below 30 ºC (86 ºF), in a tightly closed container, unless otherwise specified by manufacturer. Protect from light. Protect from freezing.{R-151; 152; 154}

Caution: Keep out of the reach of children and animals.{R-151; 152}

Those who administer this medication should avoid contact with their eyes and skin. If contact occurs, immediately flush eyes with copious amounts of water for 15 minutes. In case of dermal contact, wash skin with soap and water. A physician should be consulted if irritation persists following exposure. In human beings, there is a risk of user photosensitization within a few hours of significant exposure to quinolones. If significant accidental exposure occurs, avoid direct sunlight.{R-151}

USP requirements: Not in USP.{R-105}

DIFLOXACIN

Oral Dosage Forms

DIFLOXACIN HYDROCHLORIDE TABLETS

Usual dose: Bacterial infections—*Dogs:* Oral, 5 to 10 mg per kg of body weight every twenty-four hours.{R-96; 99}

Note: The 5 mg per kg dose was found to be clinically effective in the treatment of susceptible skin, soft tissue, and urinary tract infections.{R-99}

For empiric treatment of probable *Pseudomonas aeruginosa* or *Staphylococcus* infections in dogs, the higher end of the dosage range may be preferable, pending susceptibility results.

Strength(s) usually available:

U.S.—[R-96]

Veterinary-labeled product(s):

11.4 mg (Rx) [*Dicural Tablets*].
45.4 mg (Rx) [*Dicural Tablets*].
136 mg (Rx) [*Dicural Tablets*].

Canada—[R-99]

Veterinary-labeled product(s):

11.4 mg (Rx) [*Dicural Tablets*].
45.4 mg (Rx) [*Dicural Tablets*].
136 mg (Rx) [*Dicural Tablets*].

Packaging and storage: Store below 40 ºC (104 ºF), preferably between 15 and 30 ºC (59 and 86 ºF), unless otherwise specified by manufacturer.

USP requirements: Not in USP.[R-105]

ENROFLOXACIN

Summary of Differences

Pharmacology/pharmacokinetics: Biotransformation—Enrofloxacin is de-ethylated to form ciprofloxacin; therapeutic concentrations of ciprofloxacin can be reached with dosing calculated to achieve effective enrofloxacin concentrations.

Side/adverse effects: *Cats*—Retinal degeneration (acute blindness, mydriasis) has been reported with enrofloxacin at doses higher than 5 mg per kg of body weight a day.

Oral Dosage Forms

Note: The text between [EL]US and [EL] describes uses not included in U.S. product labeling. Text between [EL]CAN and [EL] describes uses that are not included in Canadian product labeling.

The [EL]US or [EL]CAN designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

ENROFLOXACIN TABLETS

Usual dose: Bacterial infections—

Cats: Oral, 5 mg per kg of body weight a day.[R-1] The dose may be administered as a single daily dose or divided into two equal doses administered every twelve hours.[R-1]

Note: The above dose recommendation is based on risk of retinal damage in cats administered doses higher than 5 mg/kg.[R-1]

Dogs: Oral, 5 to 20 mg per kg of body weight a day.[R-1] The dose may be administered as a single daily dose or divided into two equal doses administered every twelve hours.[R-1]

Note: For empiric treatment of probable *Pseudomonas aeruginosa* or *Staphylococcus* infections in dogs, the higher end of the dosage range may be preferable, pending susceptibility results.

Note: [EL]US,CAN*Bustards*—Although the safety and efficacy have not been established, an oral dose of 10 mg per kg of body weight every twelve hours has been suggested for the treatment of susceptible *bacterial infections,* based on pharmacokinetic data.[EL][R-41]

Cats—Although the efficacy has not been established, if enrofloxacin is used in the treatment of [EL]US,CAN*Bartonella henselae*[EL] infection or [EL]US,CAN*hemobartonellosis*[EL] in cats, the USP Veterinary Medicine Committee currently recommends the administration of 5 mg per kg of body weight a day. Limited research studies on the treatment of these infections have sometimes led to recommendations for higher dosages;[R-72; 148] however, there is concern about the occurrence of retinal degeneration with doses higher than those recommended on product labeling.

Dogs—[EL]US,CANAn oral dose of 3 mg per kg of body weight every twelve hours for seven days has been used in the treatment of *Rocky Mountain spotted fever* in dogs, based on a controlled therapeutic trial using disease models.[EL][R-84]

[EL]US,CAN*Ducks,* pet or research—In the U.S., extra-label use is banned in ducks: Although the safety and efficacy have not been established, an oral dose of 10 mg per kg of body weight a day has been suggested for the treatment of susceptible *bacterial infections* in Muscovy ducks, based on pharmacokinetic data.[EL][R-42]

[EL]US,CAN*Foals*—Although the safety and efficacy have not been established, an oral dose of 2.5 mg per kg of body weight once a day for eight days has been recommended in the treatment of susceptible bacterial infections in foals. Because of the potential for arthropathy in immature animals, use is recommended in foals only when other antimicrobials are inappropriate.[EL][R-85]

[EL]US,CAN*Horses*—In the U.S., for use only in animals not to be used for food production—Although the safety and efficacy have not been established, an oral dose of 7.5 to 10 mg per kg of body weight every twenty-four hours has been recommended.[R-24-27; 93] Tablets have been crushed and suspended in water for administration[R-27] or ground into a powder and mixed in sugar syrup.[EL][R-25]

[EL]US,CAN*Pacu,* red—Although the safety and efficacy have not been established, administration of enrofloxacin by immersion of fish in a bath of a 2.5 mg per liter solution of enrofloxacin for five hours, every twenty-four to forty-eight hours, has been suggested for the treatment of susceptible *bacterial infections* in red pacu fish, based on pharmacokinetic data.[EL][R-44]

[EL]US,CAN*Parrots,* African grey—Although the safety and efficacy have not been established, an oral dose of 7.5 to 30 mg per kg of body weight every twelve hours has been suggested in the treatment of susceptible *bacterial infections* in African grey parrots, based on pharmacokinetic data.[R-39] The risk of side effects increases with higher doses; polyuria and polydipsia have been reported with the dose of 30 mg per kg of body weight.[EL][R-39]

[EL]US,CAN*Rabbits,* pet or research—In the U.S., extra-label use is banned in rabbits: Although the safety and efficacy have not been established, an oral dose of 5 mg per kg of body weight every twelve hours for fourteen days has been recommended in the treatment of *pasteurellosis* in rabbits, based on clinical efficacy studies.[EL][R-67-69]

Strength(s) usually available:

U.S.—[R-1]

Veterinary-labeled product(s):

22.7 mg (Rx) [*Baytril Tablets* (film-coated); *Baytril Taste Tabs*].
68 mg (Rx) [*Baytril Tablets* (film-coated); *Baytril Taste Tabs*].
136 mg (Rx) [*Baytril Taste Tabs*].

Canada—[R-102]

Veterinary-labeled product(s):

15 mg (Rx) [*Baytril Tablets*].
50 mg (Rx) [*Baytril Tablets*].
150 mg (Rx) [*Baytril Tablets*].

Packaging and storage: Store below 40 ºC (104 ºF), preferably between 15 and 30 ºC (59 and 86 ºF), unless otherwise specified by the manufacturer. Store in a tight container.

USP requirements: Not in USP.{R-105}

Parenteral Dosage Forms

Note: The text between [EL-US] and [EL] describes uses not included in U.S. product labeling. Text between [EL-CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL-US] or [EL-CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

ENROFLOXACIN INJECTION

Usual dose:

Bacterial infections—

Dogs:

Intramuscular, 2.5 mg per kg of body weight.{R-86} U.S. product labeling recommends that this be an initial single dose, to be followed by a dosage regimen using enrofloxacin tablets; this was based on studies establishing the efficacy of 2.5 mg per kg of body weight every twelve hours.{R-104} Canadian product labeling recommends a maximum of six doses.{R-102}

[EL-US,CAN] Intravenous, 5 to 20 mg per kg of body weight a day. The dose may be administered as a single daily dose or divided into two equal doses administered every twelve hours. To avoid adverse effects, the drug should be diluted in a 2X volume of saline and infused over 15 to 20 minutes. Mixing enrofloxacin in magnesium-containing fluids or injecting enrofloxacin into the fluid line while administering magnesium-containing fluids should be avoided, as these actions can increase the precipitation of enrofloxacin.[EL]{R-203}

Note: For empiric treatment of probable *Pseudomonas aeruginosa* or *Staphylococcus* infections, the higher end of the dosage range may be preferable, pending susceptibility results.

[EL-US,CAN] *Cats*: Intramuscular, 2.5 mg per kg of body weight. For dogs, U.S. product labeling recommends that this be an initial single dose, to be followed by a dosage regimen using enrofloxacin tablets; this was based on studies establishing the efficacy of 2.5 mg per kg of body weight every twelve hours.[EL]{R-104}

Bacterial pneumonia—*Cattle:* Subcutaneous, 7.5 to 12.5 mg per kg of body weight as a single dose, or 2.5 to 5 mg per kg of body weight every twenty-four hours for three to five days.{R-2; 150}

Withdrawal times—*Cattle:* US—Meat: 28 days.{R-2} Canada—Meat: 36 days.{R-150} US and Canada—Not labeled for use in cattle intended for dairy production or in calves to be processed for veal. Subcutaneous injection can cause a local tissue reaction that is transient but can cause trim loss of edible tissue at slaughter.{R-2; 150}

Note: The volume of injection at one site should be 10 mL or less.{R-150}

Up to at least 1 week of age, calves eliminate enrofloxacin and the active metabolite ciprofloxacin more slowly than do adult cattle.{R-13}

Note: [EL-US,CAN] *Bustards*—Although the safety and efficacy have not been established, a parenteral dose of 10 mg per kg of body weight every twelve hours or 15 mg per kg of body weight every twenty-four hours has been suggested for the treatment of susceptible *bacterial infections*, based on pharmacokinetic data.[EL]{R-41}

[EL-US,CAN] *Camels*—Although the safety and efficacy have not been established, an intramuscular or subcutaneous dose of 2.5 mg per kg of body weight every twelve hours has been suggested for the treatment of susceptible *bacterial infections* in camels, based on pharmacokinetic data.[EL]{R-45}

[EL-US,CAN] *Ducks,* pet or research—In the U.S., extra-label use is banned in ducks: Although the safety and efficacy have not been established, a parenteral dose of 10 mg per kg of body weight every twenty-four hours has been suggested for the treatment of susceptible *bacterial infections*, based on pharmacokinetic data.[EL]{R-42}

[EL-US,CAN] *Emus,* pet or research—In the U.S., for use only in animals not to be used for food production: Although the safety and efficacy have not been established, a parenteral dose of 2.2 mg per kg of body weight every twelve hours has been suggested for the treatment of susceptible *bacterial infections* in emus, based on pharmacokinetic data.[EL]{R-43}

[EL-US,CAN] *Horses*—In the U.S., for use only in animals not to be used for food production: Although the safety and efficacy have not been established, an intravenous dose of 5 mg per kg of body weight every twenty-four hours has been used in the treatment of susceptible *bacterial infections* in horses.{R-93; 188} If a dose higher than 5 mg per kg of body weight is administered, slow injection by indwelling catheter is recommended to avoid adverse effects; dilution in 500 mL of sterile saline solution may also be necessary.[EL]{R-136}

Oral administration of enrofloxacin injection (100 mg/mL) to horses is not recommended because of the risk of developing serious oral erosions or ulcers during this treatment. Even when the injection was compounded into a oral gel formulation, oral lesions were noted in about 10% of the horses treated.{R-201}

[EL-US,CAN] *Llamas,* pet or research—In the U.S., for use only in animals not to be used for food production: Although the safety and efficacy have not been established, an intramuscular or subcutaneous dose of 5 mg per kg of body weight every twelve hours has been suggested for the treatment of susceptible *bacterial infections* in llamas, based on pharmacokinetic data.[EL]{R-45}

[EL-US,CAN] *Oryx*—Although the safety and efficacy have not been established, a parenteral dose of 1.6 mg per kg of body weight every six to eight hours has been suggested for the treatment of susceptible *bacterial infections* in oryx, based on pharmacokinetic data.[EL]{R-45}

[EL-US,CAN] *Pacu,* red—Although the safety and efficacy have not been established, an intramuscular dose of 5 mg per kg of body weight every forty-eight hours has been suggested for the treatment of susceptible *bacterial infections* in the red pacu, based on pharmacokinetic data.[EL]{R-44}

[EL-US,CAN] *Parrots,* African grey—Although the safety and efficacy have not been established, an intramuscular dose of 7.5 to 30 mg per kg of body weight every twelve hours has been suggested in the treatment of susceptible *bacterial infections* in African grey parrots, based on pharmacokinetic data.{R-39} The risk of side effects increases with higher doses; polyuria and polydipsia have been reported with administration of 30 mg per kg of body weight.[EL]{R-39}

[EL-US,CAN] *Pigs,* potbellied and miniature—In the U.S., extra-label use is banned in pigs: Although the safety and efficacy have not been established, an oral dose of 10 mg per kg of body weight every 24 hours has been recommended for pigs in the treatment of susceptible *bacterial infections*, based on pharmacokinetic data.{R-25} See also the *Regulatory considerations* section.[EL]

[EL-US,CAN] *Pythons*—Although the safety and efficacy have not been established, an intramuscular dose of 10 mg per kg of body weight as a loading dose followed by 5 mg per kg of body weight every forty-eight hours has been suggested for the treatment of susceptible *bacterial infections* in pythons.{R-48} For the treatment of *Pseudomonas* species infections, 10 mg per kg of body weight every forty-eight hours has been suggested, based on pharmacokinetic data.[EL]{R-48}

[EL][US,CAN]*Rabbits,* pet or research—In the U.S., extra-label use is banned in rabbits: Although the safety and efficacy have not been established, a subcutaneous dose of 5 mg per kg of body weight every twelve hours for fourteen days has been recommended in the control of *pasteurellosis* in rabbits.[EL]{R-33; 67-69}

[EL][US,CAN]*Sheep,* pet or research—In the U.S., extra-label use is banned in sheep: Although the safety and efficacy have not been established, an intramuscular or intravenous dose of 2.5 to 5 mg per kg of body weight every twenty-four hours has been recommended for sheep in the treatment of susceptible *bacterial infections*,{R-28} based on pharmacokinetic data. See also the *Regulatory considerations* section.[EL]

Strength(s) usually available:

U.S.—

Veterinary-labeled product(s):

22.7 mg per mL (Rx) [*Baytril Injectable Solution 2.27%*].{R-104}

100 mg per mL (Rx) [*Baytril 100 Injectable Solution*].{R-2}

Note: The more concentrated enrofloxacin injection, 100 mg per mL, is labeled only for use in cattle,{R-2} while the less concentrated injection, 22.7 mg per mL, is labeled for use in dogs.{R-104} The excipients in the two products are different; the safety of using the cattle product in other species has not been demonstrated.{R-2}

Canada—

Veterinary-labeled product(s):

50 mg per mL (Rx) [*Baytril Injectable Solution*].{R-102}

100 mg per mL (Rx) [*Baytril 100 Injectable Solution*].{R-150}

Packaging and storage: Store below 40 ºC (104 ºF), preferably between 15 and 30 ºC (59 and 86 ºF), unless otherwise specified by manufacturer. Protect from direct sunlight. Do not freeze.{R-1; 2}

Caution: Those who administer medication should avoid contact with their eyes and skin. If contact occurs, immediately flush eyes with copious amounts of water for 15 minutes. In case of dermal contact, wash skin with soap and water. A physician should be consulted if irritation persists following exposure. In human beings, there is a risk of user photosensitization within a few hours of significant exposure to quinolones.

USP requirements: Not in USP.{R-105}

MARBOFLOXACIN

Summary of Differences

General considerations: Expected to be more active than other quinolones against *Pseudomonas aeruginosa*.{R-199}

Oral Dosage Forms

MARBOFLOXACIN TABLETS

Usual dose: Bacterial infections—*Cats* and *dogs:* Oral, 2.75 to 5.5 mg per kg of body weight every twenty-four hours.{R-97; 101}

Note: The 2.75-mg-per-kg dose was found to be clinically effective in the treatment of susceptible skin, soft tissue, and urinary tract infections.{R-97}

For empiric treatment of probable *Pseudomonas aeruginosa* or *Staphylococcus* infections, the higher end of the dosage range may be preferable, pending susceptibility results.

Note: [EL][US,CAN]*Horses*—In the U.S., for use only in animals not to be used for food production: Although the safety and efficacy have not been established, an oral dose of 2 mg per kg of body weight every twenty-four hours has been recommended for the treatment of susceptible *bacterial infections* in adult horses.{R-172-173} Infections susceptible at this dosage may include gram-negative infections caused by susceptible Enterobacteriaceae; however, the dose is not considered adequate for many infections caused by gram-positive bacteria, such as *Staphylococcus* species with MIC values ≥ 0.25 mcg/mL.{R-172-173}

Strength(s) usually available:

U.S.—{R-97}

Veterinary-labeled product(s):

25 mg (Rx) [*Zeniquin Tablets*].

50 mg (Rx) [*Zeniquin Tablets*].

100 mg (Rx) [*Zeniquin Tablets*].

200 mg (Rx) [*Zeniquin Tablets*].

Canada—{R-101}

Veterinary-labeled product(s):

25 mg (Rx) [*Zeniquin Tablets*].

50 mg (Rx) [*Zeniquin Tablets*].

100 mg (Rx) [*Zeniquin Tablets*].

200 mg (Rx) [*Zeniquin Tablets*].

Packaging and storage: Store below 40 ºC (104 ºF), preferably between 15 and 30 ºC (59 and 86 ºF), unless otherwise specified by manufacturer.

USP requirements: Not in USP.{R-105}

ORBIFLOXACIN

Oral Dosage Forms

Note: The text between [EL][US] and [EL] describes uses not included in U.S. product labeling. Text between [EL][CAN] and [EL] describes uses that are not included in Canadian product labeling.

The [EL][US] or [EL][CAN] designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

ORBIFLOXACIN TABLETS

Usual dose: Bacterial infections—*Cats* and *dogs:* Oral, 2.5 to 7.5 mg per kg of body weight every twenty-four hours.{R-98}

Note: Product labeling states that the high end of the dosage range, 7.5 mg per kg of body weight, should not be exceeded for cats.{R-200}

For empiric treatment of probable *Pseudomonas aeruginosa* or *Staphylococcus* infections, the higher end of the dosage range may be preferable, pending susceptibility results.

Note: [EL][US,CAN]*Horses*—In the U.S., for use only in animals not to be used for food production: Although the safety and efficacy have not been established, pharmacokinetic data suggest an oral dose of 5 mg per kg of body weight every twenty-four hours may be effective for the treatment of susceptible *bacterial infections* in adult horses.{R-133; 174} Tablets have been crushed and suspended in water for administration.[EL]{R-133}

Strength(s) usually available:

U.S.—{R-98}

Veterinary-labeled product(s):

5.7 mg (Rx) [*Orbax Tablets*].

22.7 mg (Rx) [*Orbax Tablets*].

68 mg (Rx) [*Orbax Tablets*].

Canada—{R-100}

Veterinary-labeled product(s):

5.7 mg (Rx) [*Orbax Tablets*].

22.7 mg (Rx) [*Orbax Tablets*].
68 mg (Rx) [*Orbax Tablets*].

Packaging and storage: Store between 2 and 30 ºC (36 and 86 ºF),[R-98] unless otherwise specified by manufacturer.

USP requirements: Not in USP.[R-105]

Developed: 02/17/00
Revised: 11/6/06
Interim revision: 03/28/03

Table I. Pharmacology/Pharmacokinetics—Intravenous administration

CIPROFLOXACIN

Species	Dose (mg/kg)	Elimination half-life (hours)	Vol_D, area (L/kg)	Vol_D, steady state (L/kg)	Clearance (mL/min/kg)
Cats[R-182]	10	4.53 ± 0.74		3.85 ± 1.34	10.7 ± 4.67
Dogs[R-117]	2.5	3.00 ± 0.64	4.88 ± 0.68		
	5	2.16 ± 0.78	3.06 ± 0.75		
	10	2.55 ± 0.62	2.96 ± 0.43		

DANOFLOXACIN

Species	Dose (mg/kg)	Elimination half-life (hours)	Vol_D, area (L/kg)	Vol_D, steady state (L/kg)	Clearance (mL/min/kg)
Calves, 4 to 6 weeks of age[R-160]	1.25	7.4 ± 1.8		4.3 ± 0.8	9.1 ± 3.3
Calves, 4 months of age[R-155]	1.25	2.65 ± 0.16	3.90 ± 0.30	3.12 ± 0.13	17 ± 1
Calves, 112 kg body weight[R-162]	5	2.9			
Calves, 180 kg body weight, with acute pneumonia[R-158]	1.25	6.26 ± 2.27	3.99 ± 1.49	3.44 ± 1.13	7.5 ± 1.3
Calves[R-151; 153]					
Heifers	6	4.2 ± 0.29		2.6 ± 0.10	
Steers	6	4.8 ± 0.86		2.7 ± 0.19	
Cattle, lactating[R-161]	1.25	0.91 ± 0.19		2.04 ± 1.10	
Camels[R-49]	1.25	5.37 ± 0.50		2.53 ± 0.18	7.33 ± 0.33
Chickens[R-170]	5	6.73		10.2	23.5
Goats[R-168]	1.25	4.67 ± 0.45		3.02 ± 0.28	9.5 ± 0.3
[R-169]	1.25	1.35 ± 0.06		1.41 ± 0.15	9.8 ± 0.6
Pigs, 10 kg body weight[R-162]	5	8			
Pigs, 25 to 39 kg body weight[R-164]					
Healthy	2.4	6.7 ± 0.8		5.2 ± 0.9	9.5 ± 1.2
With induced gastrointestinal infection*	2.5	9.4 ± 0.5		3.8 ± 0.4	4.8 ± 0.3
Sheep[R-165]	1.25	3.39 ± 0.75		2.76 ± 0.17	11.8 ± 2.2
[R-166]	1.25	3.35 ± 0.23		2.76 ± 0.16	10.5 ± 0.7
[R-167]	1.25	2.08 ± 0.64		1.9 ± 0.7	11.1 ± 3.4

DIFLOXACIN

Species	Dose (mg/kg)	Elimination half-life (hours)	Vol_D, area (L/kg)	Vol_D, steady state (L/kg)	Clearance (mL/min/kg)
Goats[R-185]	5	6.30 ± 0.11		1.1 ± 0.01	2.16 ± .002
Rabbits[R-184]	5	3.25 ± 0.03		1.51 ± 0.16	9.83 ± 1.58

ENROFLOXACIN

Species	Dose (mg/kg)	Compound measured	Elimination half-life (hours)	Vol_D, area (L/kg)	Vol_D, steady state (L/kg)	Clearance (mL/min/kg)
Alligators, American[R-	5	Enrofloxacin	21.1 ± 11.8	3.71 ± 0.97	3.39 ± 0.84	0.78 ± 0.35

87}						
Alpacas{R-88}	5	Enrofloxacin	13.04	1.61	0.44	1.41
Birds						
Bustards{R-41}	10	Enrofloxacin	5.63 ± 0.54	2.82 ± 0.37	2.98 ± 0.32	5.71 ± 0.41
Chickens{R-30}	10	Enrofloxacin	4.16 ± 0.19	2.20 ± 0.17	2.43 ± 0.19	2.2 ± 0.09
{R-31}	10	Enrofloxacin	10.29 ± 0.45	4.31 ± 0.15	2.77 ± 0.09	4.8 ± 0.17
{R-170}	10	Enrofloxacin	5.56		3.9	10.3
Emus{R-43}	2.2	Enrofloxacin	3.33	1.49 ± 0.52	1.62 ± 1.04	6.00 ± 3.17
Rheas, greater, 4 months of age{R-192}	15	Enrofloxacin	2.66 ± 0.46		5.01 ± 1.18	65.8 ± 17.8
Calves{R-13}						
One day of age	2.5	Enrofloxacin	6.61 ± 1.12		1.81 ± 0.1	3.16 ± 0.5
	2.5	Ciprofloxacin	9.19 ± 1.46			
One week old	2.5	Enrofloxacin	4.87 ± 0.68		2.28 ± 0.14	6.5 ± 1
	2.5	Ciprofloxacin	8.19 ± 0.85			
Cattle, lactating{R-11}	5	Active drug†	1.68 ± 0.18		> 1	
{R-15}	5	Enrofloxacin	1.09		2.1	21
	5	Ciprofloxacin	2.67			
Camels{R-45}	2.5	Active drug	3.6 ± 0.89		1.13 ± 0.126	4.61 ± 1.03
Cats{R-190}	5	Enrofloxacin				
2 weeks of age			4.2	1.8	1.8	4.88
4 weeks of age			6.3	1.8	1.7	3.23
6 weeks of age			4.1 ± 2.2	4.4 ± 2.6	3.9 ± 1.6	12.6 ± 3.7
8 weeks of age			3.7 ± 1.4	3.9 ± 0.8	3.5 ± 0.7	13.5 ± 4.3
Adult			6.7 ± 0.8	2.5 ± 0.5	2.4 ± 0.4	4.3 ± 0.9
Cats{R-22}	5	Enrofloxacin	6.7 ± 2.3		4.0 ± 0.3	
		Ciprofloxacin	6.1 ± 1.3			9.5 ± 0.7
Cuttlefish, European{R-193}	5	Enrofloxacin	1.81		0.39	4.71
Dogs{R-5}	1.25 to 5	Enrofloxacin	> 3			9
{R-16}	5	Enrofloxacin	2.4 ± 0.87		7.0 ± 6.4	27.1 ± 16.2
	5	Ciprofloxacin	3.9 ± 1.3			
{R-18}	5.8	Enrofloxacin	4.4 ± 1		3.7 ± 0.6	10.88 ± 0.68
	5.8	Ciprofloxacin	5.2 ± 0.4			
Fish						
Salmon{R-37}	10	Enrofloxacin	34.2		6.1	2.3
Trout, rainbow{R-36}	5	Active drug	24.4	3.22	2.77	1.52
	10	Active drug	30.4	2.56	2.34	0.97
Goats{R-195}	5	Active drug	2.73 ± 0.29		1.94 ± 0.46	11.72 ± 2.82
Foals{R-85}	5	Enrofloxacin	17.10 ± 0.09	2.49 ± 0.43	2.47 ± 0.04	1.73 ± 0.001
Horses{R-27}	2.5	Active drug	5.94	1.22 ± 0.07		2.33 ± 0.17
	5	Active drug	6.09	0.77 ± 0.11		1.50 ± 0.17
{R-24}	5	Enrofloxacin	4.4		2.3 ± 0.5	0.51 ± 0.11
		Ciprofloxacin	5.1 ± 2.1			
Mares{R-188}	5	Enrofloxacin	6.68 ± 2.93	1.91 ± 0.41	1.66 ± 0.45	3.70 ± 1.45
Llamas{R-46}	5	Enrofloxacin	3.38 ± 2.13		3.46 ± 0.98	11.7 ± 3.5
Oryx (antelope){R-47}	1.3	Enrofloxacin	0.69 ± 0.46	0.80 ± 0.3		12.07 ± 7.12
Pigs{R-29}	5	Enrofloxacin			3.9 ± 0.5	6.17 ± 1.83
Neonatal rabbits{R-35}						
1 day of age	7.5 (IP)	Enrofloxacin	5.01	2.03		4.7
8 days	7.5 (IP)	Enrofloxacin	8.5	2.02		2.7
16 days	7.5 (IP)	Enrofloxacin	6.1	2.52		4.8
30 days	7.5 (IP)	Enrofloxacin	2	6.52		33.8
Rabbits{R-32}	5	Enrofloxacin	2.19 ± 0.29	4.4 ± 1.4	3.4 ± 0.9	22.8 ± 6.8
{R-33}	5	Active drug	2.5	2.12	0.93	10.1
	7.5	Active drug	1.9	3.97 ± 0.9		23.9 ± 3.5
Sheep{R-28}	2.5	Enrofloxacin	3.73 ± 0.44		3.02 ± 0.22	9.17 ± 2.3
{R-195}	5	Active drug	3.26 ± 0.37		2.27 ± 0.57	8.86 ± 1.54
{R-196}	5	Enrofloxacin	4.77	1.15	0.97	3.37
Sheep, lactating{R-147}	2.5	Active drug	3.30 ± 0.36	2.91 ± 0.17	2.82 ± 0.21	10.05 ± 0.43

MARBOFLOXACIN

Species	Dose (mg/kg)	Elimination half-life (hours)	Vol_D, area (L/kg)	Vol_D, steady state (L/kg)	Clearance (mL/min/kg)
Calves, 7 months of	2	4.23 ± 0.12		1.09 ± 0.06	3.5 ± 0.33

age[R-187]					
Dogs[R-108]	2	10.8 ± 1.3		1.33 ± 0.10	1.60 ± 0.21
[R-115]	2	12.4 ± 2.6	1.90 ± 0.76	1.37 ± 0.19	
[R-97]	5.5	9.5 ± 0.7		1.19 ± 0.08	1.56 ± 0.13
Goats[R-186]					
1 week of age	2	9.66 ± 1.28		0.92 ± 0.24	1.30 ± 0.33
3 weeks of age	2	8.25 ± 2.35		0.95 ± 0.25	1.62 ± 0.50
6 weeks of age	2	6.44 ± 0.99		1.00 ± 0.24	3.00 ± 0.67
Adult	2	7.18 ± 1.09		1.31 ± 0.15	3.83 ± 0.50
Horses[R-172]	2	4.74 ± 0.81		1.17 ± 0.18	3.17 ± 0.67
[R-171]	2	7.56 ± 1.99	2.83 ± 0.75	1.48 ± 0.30	4.15 ± 0.75

ORBIFLOXACIN

Species	Dose (mg/kg)	Elimination Half-life (hours)	Vol_D, area (L/kg)	Vol_D, steady state (L/kg)	Clearance (mL/min/kg)
Cats[R-98]	2.5	4.5 ± 1.8		1.3 ± 0.13	
Dogs[R-98]	2.5	5.4 ± 1.1		1.2 ± 0.2	
Horses[R-174]	2.5	5.08		1.58	4.67

Note: IP = Intraperitoneal

*Pigs were given an inoculum of *Salmonella typhimurium*.

†Agar-well diffusion microbiological assays use a test organism, such as *Bacillus subtilis, Escherichia coli,* or *Klebsiella pneumoniae,* and, therefore, measure enrofloxacin, ciprofloxacin, and any other unidentified metabolites with specific antimicrobial activity.

Table II. Pharmacology/Pharmacokinetics: Other systemic data

CIPROFLOXACIN

Species	Dose (mg/kg)/Route, Water temperature	Number of doses	Absorption half-life (hours)	Peak serum concentration (mcg/mL)	Time to peak serum concentration (hours)	Half-life, terminal (hours)	Bioavailability (%)
Cats[R-182]	10/PO	Every 12 hours for 7 doses		1.04 ± 0.27	1.63 ± 0.93	2.41 ± 0.46	33
Dogs[R-134]	10/PO	Single		1.4 (fr. graph)	2(fr. graph)	4.91 ± 1.26	
	20/PO	Single		2.8 (fr. graph)	2(fr. graph)	5.30 ± 1.15	
	40/PO	Single		6.6 (fr. graph)	6(fr. graph)	8.86 ± 2.78	
[R-118]	11/PO	Single				4.65	
		Every 12 hours for 7 doses				7.48	
	23/PO	Single				3.95	
		Every 12 hours for 7 doses		5.68 ± 0.54	1.53 ± 0.52	4.48	

DANOFLOXACIN

Species	Dose (mg/kg)/Route, Water temperature	Number of doses	Absorption half-life (hours)	Peak serum concentration (mcg/mL)	Time to peak serum concentration (hours)	Half-life, terminal (hours)	Bioavailability (%)
Calves, 112 kg body weight[R-162]	5/SC	Single		0.63 ± 0.09	1.0 ± 0.0	4.3	72
Calves, 190 kg body weight, with acute pneumonia[R-158]	1.25/IM	Single		0.25	0.80	6.73	91
Calves, 217 to 286 kg body weight[R-153]							
Female	6/SC	Single		1.3 ± 0.17	1.6 ± 0.50	4.0 ± 0.16	87
Male	6/SC	Single		1.2 ± 0.19	3.4 ± 1.43	4.6 ± 0.83	92
Calves, 4 months							

of age[R-155]	1.25/SC	Single	0.19 ± 0.04	0.21 ± 0.01	0.83 ± 0.11	4.03 ± 0.29	76
Heifers, 6 months of age[R-153]	1.25/SC	Single		0.34 ± 0.04	1.6 ± 0.54	3.6 ± 0.47	
	6/SC	Single		1.35 ± 0.24	1.6 ± 0.54	3.8 ± 0.11	
	10/SC	Single		2.07 ± 0.25	2.2 ± 1.1	3.7 ± 0.19	
Calves, 10 months of age[R-157]	1.25/SC	Single		0.23 ± 0.05	1.25 ± 0.66		
Camels[R-49]	1.25/IM	Single		0.49 ± 0.06	0.70 ± 0.06	5.71 ± 0.92	100
Chickens[R-170]	5/PO	Single		0.47	1.5	6.62	99
Pigs, 10 kg[R-162]	5/IM	Single		0.80 ± 0.02	0.8 ± 0.3	6.8	76
Goats[R-168]	1.25/IM	Single		0.33 ± 0.02	0.74 ± 0.15	4.41 ± 0.23	100
[R-169]	1.25/IM	Single		0.33 ± 0.01	0.58 ± 0.04	2.37 ± 0.17	66
Sheep[R-166]	1.25/IM	Single		0.32 ± 0.02	1.23 ± 0.34		96
[R-167]	1.25/IM	Single		1.2 ± 1,0	0.5 ± 0.0	3.49 ± 0.94	100

DIFLOXACIN

Species	Dose (mg/kg)/Route, Water temperature	Number of doses	Absorption half-life (hours)	Peak serum concentration (mcg/mL)	Time to peak serum concentration (hours)	Half-life, terminal (hours)	Bioavailability (%)
Dogs[R-96]	5/PO	Single		1.8	2.8	9.3	>80
[R-113]	5/PO	Single		1.11 ± 0.07	2.84 ± 0.31	6.94 ± 0.54	
[R116]	5/PO	Every 24 hours for 5 days		1.79 ± 0.11	2.17 ± 0.26	8.52 ± 0.84	
Goats[R-185]	5/IM	Single		3.76 ± 0.22	1.71 ± 0.05	6.60 ± 0.06	95
Horses[R-183]	7.5/IG	Single		2.25 ± 0.70	3.12 ± 2.63		
		Every 24 hours for 5 doses		2.41 ± 0.86	97.86 ± 1.45	8.75 ± 2.77	
Rabbits[R-184]	5/IM	Single		3.85 ± 0.21	1.61 ± 0.04	3.82 ± 0.06	95

ENROFLOXACIN

Species	Dose (mg/kg)/ Route, Water temperature	Number of doses	Compound measured	Absorption half-life (hours)	Peak serum concentration (mcg/mL)	Time to peak serum concentration (hours)	Half-life, terminal (hours)	Bioavailability (%)
Alligators, American[R-87]	5/PO	Single	Enrofloxacin		0.50 ± 0.27	55 ± 29	77.7 ± 4.8	
Alpacas[R-88]	10/PO	Single	Enrofloxacin		1.42	4.0	15.32	29
	5/SC	Single	Enrofloxacin		4.16	6.0	7.83	90
Birds								
Bustards[R-41]	10/IM	Single	Enrofloxacin	0.23 ± 0.07	2.75 ± 0.11	1.72 ± 0.19	6.39 ± 1.49	97
	10/PO	Single	Enrofloxacin	0.17 ± 0.02	1.84 ± 0.16	0.66 ± 0.05	6.80 ± 0.79	62
Chickens[R-30]	10/IM	Single	Enrofloxacin	1.83 ± 0.04	2.45 ± 0.1	1.43 ± 0.02	4.06 ± 0.06	88
	10/PO	Single	Enrofloxacin	0.92 ± 0.05	1.69 ± 0.08	2.52 ± 0.08	4.29 ± 0.1	60
	10/SC	Single	Enrofloxacin	0.36 ± 0.02	2.41 ± 0.06	1.46 ± 0.06	4.48 ± 0.04	81
[R-31]	10/PO	Single	Enrofloxacin	0.67 ± 0.05	2.44 ± 0.64	1.64 ± 0.04	14.23 ± 0.46	64
Ducks[R-42]	10/IM	Single	Enrofloxacin		1.67 ± 0.29	0.94 ± 0.18		
	10/PO	Single	Enrofloxacin		0.99 ± 0.08	1.38 ± 0.18		
Parrots[R-39]	15/IM	Single	Enrofloxacin		3.87 ± 0.27	1	2.31 ± 0.09	
	3/PO	Single	Enrofloxacin		0.31 ± 0.11	4	2.59 ± 0.36	48
	15/PO	Single	Enrofloxacin		1.12 ± 0.11	2	2.52 ± 0.33	
	30/PO	Single	Enrofloxacin		1.69 ± 0.23	4	2.74 ± 0.37	
Calves, 10 months of age[R-157]	2.5/SC	Single	Enrofloxacin		0.24 ± 0.08	1.75 ± 1.04		
			Ciprofloxacin		0.11 ± 0.03	3.25 ± 1.04		
Calves[R-150]	2.5/SC	Single	Enrofloxacin		0.37	3.4	5.4	
	5/SC	Single	Enrofloxacin		0.69	3.3	5.9	
	7.5/SC	Single	Enrofloxacin		0.83	5.8	6.4	
			Ciprofloxacin		0.32	6.5		
Cattle, lactating	5/IM	Single	Active drug		0.73 ± 0.12	2.40 ± 0.68	5.90 ± 1.44	82
[R-11]	5/SC	Single	Active drug		0.98 ± 0.20	3.20 ± 1.09	5.55 ± 0.52	137
Camels[R-45]	2.5/IM	Single	Active drug	0.76 ± 0.46	1.44 ± 0.8	1	6.36 ± 2.03	85

	2.5/PO	Single	Active drug		Not detected			
	2.5/SC	Single	Active drug	0.5 ± 0.12	1.23 ± 0.27	1	10.58 ± 6.78	92
Cats[R-190]	5/PO	Single	Enrofloxacin					
2 weeks of age					0.50		4.8	33.7
4 weeks of age					1.19		8.4	49.4
6 weeks of age					0.48 ± 0.22		6.0 ± 3.1	70.9
8 weeks of age					1.01 ± 0.46		3.5 ± 1.4	72.8
Adult								
Cats[R-190]	5/SC	Single	Enrofloxacin					
2 weeks of age					2.5		4.6	85.1
4 weeks of age					1.3		7.3	27.9
6 weeks of age					0.9 ± 0.1		6.1 ± 2.6	77.6
8 weeks of age					11 ± 0.3		5.7 ± 3.1	107.7
Adult								
Cats[R-22]	5/PO	Every 24 hours for 10 days	Enrofloxacin	0.2 ± 0	1.67 ± 0.11	0.6 ± 0.1		
	5/PO	Every 24 hours for 10 days	Ciprofloxacin		0.13 ± 0.01	2.3 ± 0.5		
Dogs[R-8]	1.25/IM	Single	Active drug		1.09	0.5		
[R-5]	1.25/PO	Single	Enrofloxacin		0.4 (from graph)	1	> 3	
	2.5/PO	Single	Enrofloxacin		1 (from graph)	1	> 3	
	5/PO	Single	Enrofloxacin		1.5 (from graph)	1	> 3	
[R-175]	5/PO	Single	Enrofloxacin		1.24 ± 0.39	0.94 ± 0.53	2.23 ± 0.89	63
	5/PO	Single	Ciprofloxacin		0.36 ± 0.10	3.00 ± 1.41	3.41 ± 0.70	
[R-16]	5/PO	Single	Enrofloxacin		1.16 ± 0.6	0.9 ± 0.8	2.4 ± 0.5	
	5/PO	Single	Ciprofloxacin		0.29 ± 0.19	3.6 ± 0.3	3.9 ± 3.2	
[R-194]	7.5/PO	Single	Enrofloxacin		2.12 ± 0.59	2.17 ± 1.07	5.23 ± 0.96	
			Ciprofloxacin		1.35 ± 0.31	2.75	8.81 ± 3.03	
	10/PO	Single	Enrofloxacin		2.10 ± 0.34	2.83 ± 1.13	5.05 ± 0.60	
			Ciprofloxacin		1.30 ± 0.24	2.33	9.81 ± 2.96	
	20/PO	Single	Enrofloxacin		4.74 ± 1.05	2.33 ± 0.98	4.65 ± 1.16	
			Ciprofloxacin		2.00 ± 0.34	3.08	10.73 ± 4.01	
[R-17]	2.75/PO	Every 12 hours for 7 doses	Enrofloxacin		1.03 ± 0.28	1.88 ± 0.72	3.07 ± 1	83
	5.5/PO	Every 12 hours for 7 doses	Enrofloxacin		2.45 ± 0.84	1.55 ± 0.56	4.04 ± 0.78	
	11/PO	Every 12 hours for 7 doses	Enrofloxacin		4.56 ± 0.49	2.31 ± 0.82	4.26 ± 1.03	
[R-18]	5.8/PO	Every 12 hours for 15 days	Enrofloxacin		1.43 ± 0.12	1.8 ± 0.2		
	5.8/PO	Every 12 hours for 15 days	Ciprofloxacin		0.36 ± 0.03	2.2 ± 0.3		
[R-21]	2.5/SC	Single	Active drug*					
	25/SC	Single	Active drug		0.6 ± 0.03	2.25 ± 0.09	2.61 ± 0.15	
					5.77 ± 0.41	3.92 ± 0.16	6.42 ± 0.29	
Elephants[R-191]	2.5/PO	Single	Enrofloxacin		1.31 ± 0.40	5.0 ± 4.2	18.4	
Fish								
Pacu[R-44]	5/IM	Single	Enrofloxacin		1.64 ± 0.92	4	28.9	
			Ciprofloxacin		0.05 ± 0.01	4	53	
	5/PO	Single	Enrofloxacin		0.8 ± 1.17	36		
			Ciprofloxacin		0.02 ± 0.008	36		
	2.5 mg per Liter/bath immersion	Single 5 hour dose	Enrofloxacin		0.17 ± 0.04	2		
			Ciprofloxacin		0.024 ± 0.001	2		
Salmon[R-38]	5/PO, 9.7 ºC	Single	Active drug		0.53	2.87	48.2	46
	10/PO, 9.7 ºC	Single	Active drug		0.27	0.42	105.1	49
[R-37]	10/PO (in feed), 10 ºC	Single	Enrofloxacin		1.54	6		56
Trout[R-36]	5/PO, 10 ºC	Single	Active drug		0.37	24	44.2	35
	10/PO, 10 ºC	Single	Active drug		0.55	6	29.5	24

	50/PO, 10 ºC	Single	Active drug		1.93	6	29.5	17
Goats{R-195}	5/IM	Single	Active drug		1.33 ± 0.17	1.85 ± 0.41	2.62 ± 0.38	98
{R-198}	5/IM	Single	Enrofloxacin		2.80 ± 0.29	0.88 ± 0.06	1.39 ± 0.19	
			Ciprofloxacin		0.64 ± 0.04	1.25 ± 0.11	1.82 ± 0.21	
{R-197}	7.5/SC	Single	Active drug		2.91 ± 0.39	2.9 ± 0.51	2.84 ± 0.57	
Foals{R-85}	10/PO	Single	Enrofloxacin		2.12 ± 0.51	2.20 ± 2.17	18.4 ± 0.06	42
Horses{R-24}	5/IM	Single	Enrofloxacin				9.9	
{R-27}	2.5/PO	Every 12 hours for 3 days	Active drug	0.89	2.62 ± 0.61	1 ± 0.35		57
{R-27}	5/PO	Every 12 hours for 3 days	Active drug	0.8	5.97 ± 1.56	1.25 ± 0.43		63
	5/PO	Single	Active drug		1.85 ± 0.86	0.92 ± 0.59	7.75	
Mice{R-21}	1.56/SC	Single	Active drug		0.57 ± 0.06	0.37 ± 0.02	0.3 ± 0.03	
	25/SC	Single	Active drug		6.44 ± 0.46	0.54 ± 0.06	0.54 ± 0.04	
Pigs{R-29}	10/PO	Single	Enrofloxacin		1.4 ± 0.5	4.8 ± 1.9		83
Pythons{R-48}	5/IM	Single	Enrofloxacin		1.66 ± 0.42	5.75 ± 1.47	6.37	
	5/IM	Single	Ciprofloxacin		0.35 ± 0.21	13 ± 5.9		
Rabbits{R-32}	5/IM	Single	Enrofloxacin	0.07 ± 0.02	3.04 ± 0.34	0.17	1.81 ± 0.3	92
{R-33}	5/PO	Single	Active drug		0.452	2.3	2.41	61
	5/SC	Single	Active drug		2.07	0.9		72
Sheep{R-28}	2.5/IM	Single	Enrofloxacin		0.78 ± 0.07	1.25 ± 0.11	3.65 ± 0.31	85
	2.5/IM	Single	Ciprofloxacin		0.14 ± 0.02	5 ± 0.45	9.98 ± 2.33	
{R-195}	5/IM	Single	Active drug		1.29 ± 0.14	1.96 ± 0.42	3.53 ± 0.51	83
{R-196}	5/Drench	Single	Enrofloxacin		1.61	5.50	14.80	48
	5/Crushed tablets in feed	Single	Enrofloxacin		2.69	8.00	10.80	98
	5/Solution in feed	Single	Enrofloxacin		2.26	8.00	13.07	94
Sheep, lactating {R-147}	2.5/IM	Single	Active drug		0.74 ± 0.07	0.83 ± 0.12	3.87 ± 0.10	75

MARBOFLOXACIN

Species	Dose (mg/kg)/Route, Water temperature	Number of doses	Absorption half-life (hours)	Peak serum concentration (mcg/mL)	Time to peak serum concentration (hours)	Half-life, terminal (hours)	Bioavailability (%)
Calves{R-187}	2/IM	Single	0.09 ± 0.00	1.50 ± 0.08	0.51 ± 0.01	4.33 ± 0.19	104
Cats{R-97}	6.2/PO	Single		4.8 ± 0.7	1.2 ± 0.6	12.7 ± 1.1	
Dogs{R-115}	1/PO	Single	0.38 ± 0.35	0.83 ± 0.26	1.7 ± 1.2	14.7 ± 4.9	~100
	2/PO	Single	0.53 ± 0.24	1.38 ± 0.40	2.5 ± 1.2	14.0 ± 4.9	
	4/PO	Single	0.68 ± 0.59	2.93 ± 0.58	2.0 ± 1.1	12.5 ± 2.7	
	1/SC	Single	0.20 ± 0.11	0.78 ± 0.08	1.0 ± 0.6	11.5 ± 1.9	~100
	2/SC	Single	0.20 ± 0.07	1.52 ± 0.13	0.9 ± 0.2	13.0 ± 3.3	
	4/SC	Single	0.25 ± 0.12	3.04 ± 0.24	1.3 ± 0.6	13.4 ± 2.8	
{R-113}	2/PO	Single		1.47 ± 0.09	1.83 ± 0.17	9.07 ± 1.90	
{R-108}	2/PO	Every 24 hours for 8 days		1.37 ± 0.21	1.97 ± 0.97		
{R-175}	5/PO	Single		3.63 ± 0.85	1.95 ± 1.16	7.63 ± 3.70	105
{R-97}	2.7/PO	Single		2.0 ± 0.2	1.5 ± 0.3	10.7 ± 1.6	
	5.6/PO	Single		4.2 ± 0.5	1.8 ± 0.3	10.9 ± 0.6	94
Horses{R-172}	2/IM	Single		1.42 ± 0.33	0.95 ± 0.37	5.47 ± 1.33	88
{R-171}	2/PO	Single	0.16 ± 0.20	1.07 ± 0.30	0.72 ± 0.31	10.4 ± 4.3	98
	2/SC	Single	0.06 ± 0.10	0.89 ± 0.14	0.58 ± 0.20	8.78 ± 2.70	62

ORBIFLOXACIN

Species	Dose (mg/kg)/Route, Water temperature	Number of doses	Absorption half-life (hours)	Peak serum concentration (mcg/mL)	Time to peak serum concentration (hours)	Half-life, terminal (hours)	Bioavailability (%)
Cats{R-98}	2.5/PO	Single		2.06 ± 0.6	1 ± 0.45	5.52 ± 2.66	
Dogs{R-98}	2.5/PO	Single		2.3 ± 0.3	0.77 ± 0.45	5.6 ± 1.1	97
{R-113}	2.5/PO	Single		1.37 ± 0.01	2.42 ± 0.36	7.14 ± 0.42	

Horses[R-174]	2.5/PO	Single	1.25	1.21	3.42	68
Mares[R-133]	7.5/PO	Single	2.41 ± 0.03	1.5	9.06 ± 1.33	

Note: IG = Intragastric administration, IM= Intramuscular administration, PO = Oral administration, SC = Subcutaneous administration
*Agar-well diffusion microbiological assays use a test organism, such as *Bacillus subtilis, Escherichia coli,* or *Klebsiella pneumoniae,* and, therefore, measure enrofloxacin, ciprofloxacin, and any other unidentified metabolites with specific antimicrobial activity.

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