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ENRO 50mg/mL INJECTION

For the treatment of diseases caused by susceptible bacterial pathogens in dogs and cats.

ACTIVE CONSTITUENT:

ENROFLOXACIN 50 mg/mL

NET CONTENTS: 50mL

DESCRIPTION

Enrofloxacin is a synthetic drug from the class of the quinolone carboxylic acid derivatives, also known as fluoroquinolones. It has antibacterial activity against a broad spectrum of Gram negative and Gram positive bacteria, including Mycoplasma. (See Table 1). It is rapidly absorbed from the digestive tract, penetrating into all measured body tissues and fluids (See Table 2). Enrofloxacin has the chemical name 1-cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1, 4- dihydro-4-oxo-3- quinoline carboxylic acid. It is presented as an injection.

MICROBIOLOGY

Enrofloxacin exerts bactericidal activity by interaction with the A subunit of DNA gyrase in the target bacteria. The DNA gyrase is a topoisomerase which controls bacterial replication, i.e., it catalyses supercoiling by rewinding and rejoining of chromosomal DNA strands. The fluoroquinolones also possess activity against bacteria in the stationary phase by an alteration of the permeability of the outer membrane phospholipid layer of the cell wall. These mechanisms of action explain the rapid loss of viability of susceptible bacteria. With enrofloxacin, inhibitory and bactericidal concentrations are closely correlated. They are identical or differ in many cases within one or two dilution steps at maximum. Enrofloxacin possesses antimicrobial activity at low concentration against most Gram negative bacteria, many Gram positive bacteria and against mycoplasmas. Enrofloxacin is therefore active against the micro-organisms that are primarily or secondarily involved in many of the infectious diseases which occur in small animals.

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TABLE 1. Minimum Inhibitory Concentrations for enrofloxacin against pathogens isolated from dogs and cats.

DISTRIBUTION AND METABOLISM

Organism	No. of Strains	MIC 1,1g/mL
Gram negative organisms *E.coli* *Salmonella spp.* *Klebsiella spp.* *Proteus spp.* *Pseudomonas aeruginosa* *Brucella canis* *Bordetella bronchiseptica*	 *180* *115* *48* *55* *43* *3* *31*	 *0.01 - 0.5* *0.003 - 0.5* *<0.03- 0.5* *0.03 - 0.5* *0.156 - 5.0* *0.1 - 0.25* *0.1 - 4.0*
Gram positive organisms *Staph. aureus* *Staph. intermedius* *Streptococcus spp* *Actinomyces (Corynebacterium) pyogenes*	 *135* *2* *62* *29*	 *0.03-1.0* *0.039 - 0.3125* *0.06 - 4.0* *0.06 - 4.0*
Mycoplasmas *Mycoplasma spp.*	*92*	*0.01 - 1.0*

DISTRIBUTION IN THE BODY

Enrofloxacin penetrates into all canine and feline tissues and body fluids. Concentrations of drug equal to or greater than the MIC for many pathogens (See Table 1) are reached in most tissues within two hours of dosing and are maintained for eight hours after dosing. Particularly high levels of enrofloxacin are found in urine.

A summary of the body fluid/tissue drug levels at 1 and 8 hours after dosing is given in Table 2 for a 5 mg/kg oral dose in dogs and cats.

TABLE 2. Enrofloxacin body fluid and tissue levels at 1 and 8 hours after oral treatment in dogs and cats at 5 mg/kg.

TISSUE	DOG		CAT	
	Average Concentration µg/mL or g at:-			
	1 hour	8 hours	1 hour	8 hours
Serum	*0.9*	*0.3*	*2.2*	*1.3*
Lung *Liver* *Kidney* *Spleen* *Heart* *Adrenal*	*2.5* *5.8* *3.5* *2.8* *3.1* *2.1*	*0.7* *1.1* *1.0* *0.9* *1.0* *0.6*	*4.5* *6.5* *5.4* *3.0* *5.0* -	*2.1* *2.6* *2.5* *1.6* *2.2* -

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TISSUE	DOG		CAT	
	Average Concentration µg/mL or g at:-			
	1 hour	8 hours	1 hour	8 hours
Serum	*0.9*	*0.3*	*2.2*	*1.3*
Muscle *Skin* *Fat* *Rib bone*	*2.3* *0.7* *1.4* *0.7*	*1.2* *0.7* *1.4* *0.7*	*2.8* *1.9* *1.3* *2.2*	*2.3* *1.1* *0.4* *2.0*
Brain *Eye-humour* *Eye-iris*	*0.4* *0.09* *0.2*	*0.1* *0.1* *0.3*	*1.6* *0.5* -	*0.7* *1.2* -
Uterus *Ovary* *Testes*	*0.2* *0.3* *1.9*	*0.8* *0.9* -	*2.2* *2.4* -	*1.1* *1.2* -
Bile *Urine* *CSF*	*30.0* *25.0* *0.9*	*57.0* *49.0* *0.1*	*39.0* *30.1* *1.0*	- - *0.7*

- = not tested

PHARMACOKINETICS

Following an oral dose in dogs, enrofloxacin reaches its peak serum level in one hour. The elimination half-life is greater than three hours at 2.5 mg/kg. The eliminating organs, based on the drug's body clearance time, can readily remove the drug with no indication that the eliminating mechanisms are saturated. The primary route of excretion is via the urine.

Table 3 below shows typical blood levels for dogs and cats after oral and parenteral administration at the recommended dose.

TABLE 3. Enrofloxacin serum levels at various times after administration at 5 mg/kg in dogs and cats. Levels are a mean of 4-8 dogs per group and 3 cats per group

	ROUTE	MEAN SERUM LEVEL µg/mL at hours							
		0.5	1	2	4	6	8	12	24
DOG	*Oral* *SC*	*0.6* *1.0*	*1.25* *1.1*	*1.19* *1.0*	*0.74* *0.7*	*0.46* *0.4*	*0.36* -	*0.14* -	*<0.04* *Nd*
CAT	*Oral* *SC*	- -	*1.51* *1.19*	*1.9* *1.31*	*1.72* *1.09*	*1.07* *0.79*	- -	*0.41* *0.22*	*0.04* *0.02*

= not tested nd = not detected

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CLINICAL APPLICATIONS (INDICATIONS)

PRIMARY INDICATIONS FOR USE IN THE DOG AND CAT ARE:

- Urinary tract infections including infections with E.coli, Proteus spp., Klebsiella spp., Pseudomonas aeruginosa, Staph spp., and Group D Streptococcus.
- Respiratory infections, including infections with E.coli, Streptococcus spp., Pasteurella spp., Klebsiella spp., Pseudomonas spp., Bordetella bronchiseptica, Staphylococcus spp.
- Deep pyodermas caused by Staph. intermedius including those infected with secondary invaders.
- Wounds, abscesses and discharging sinuses.
- Enro 50mg/mL Injection is especially useful in cats for treating serious antibiotic resistant infections of the respiratory tract or genito-urinary system, particularly chronic urinary tract infections. In cats it is also useful for deep pyodermas, osteomyelitis and Gram negative septicaemias.

Enro 50mg/mL Injection may also be used in exotic animals (small mammals, reptiles and avian species) for the treatment of bacterial infections of the alimentary and respiratory tracts where clinical experience, supported where possible by sensitivity testing of the causal organism, indicates enrofloxacin as the drug of choice.

DOSAGE AND ADMINISTRATION

DOGS & CATS

The optimum dose of Enro 50mg/mL Injection in dogs and cats is 5 mg/kg of body weight (1 ml per 10 kg bodyweight) administered once daily.

Enro 50mg/mL Injection should be administered subcutaneously, and normal sterile precautions should be taken.

In simple infections, Enro 50mg/mL Injection should be given for 2-3 days beyond the cessation of clinical signs. Enro 50mg/mL Injection may be used as the initial dose. If no improvement is seen within five days, the diagnosis should be re-evaluated, and a different course of therapy considered. In deep or complex infections, eg pyodermas and discharging sinuses, extended courses may be required and progress should be regularly reviewed.

EXOTIC ANIMALS

Species	Dosage	Route	Dose Frequency	Treatment Duration
Small mammals	5 mg/kg	s.c.	Twice daily	7 days
Reptiles	5 mg/kg	i.m.	24 - 48-hour intervals	6 days
Avian spp.	10 mg/kg	i.m.	Twice daily	7 days

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DRUG INTERACTIONS

DOGS: Enrofloxacin has been administered to dogs concurrently with a wide variety of other products including anthelmintics (praziquantel, febantel, sodium disophenol), insecticides (fenthion, pyrethrins), heartworm preventatives (diethylcarbamazine), and other antibiotics (ampicillin, gentamicin sulfate, penicillin, dihydrostreptomycin). No incompatibilities with other drugs are known at this time except that fluoroquinolones may interfere with the metabolism of theophylline and related drugs (e.g., aminophylline) so the dosage of theophylline may need to be reduced.

CATS: Enrofloxacin was administered concurrently with anthelmintics (praziquantel, febantel), a carbamate insecticide (propoxur), and another antibacterial (ampicillin). No incompatibilities with other drugs are known at this time.

ANIMAL SAFETY

DOGS

1) ADULTS

Dogs receiving enrofloxacin at 12.5 mg/kg (2.5X) twice daily or 25 mg/kg (5X) daily for 28 and 30 days respectively showed no abnormalities. Dogs dosed at 52 mg/kg (10X) for 13 weeks showed only isolated incidences of vomiting and inappetance. Dosages of 125 mg/kg (25X) are toxic and may be lethal if given repeatedly.

2) GROWING DOGS

Oral treatment of 15- to 28-week-old growing puppies with daily dosages of 25 mg/kg has induced abnormal carriage of the carpal joint and weakness in the hindquarters. However significant improvement of clinical signs is observed following drug withdrawal. Microscopic studies have identified lesions of the articular cartilage following 30 day treatments at either 5, 15 or 25 mg/kg in this age group.

3) GENERAL SAFETY

Tests indicated no effect on circulating microfilariae or adult heartworms (Dirofilaria immitis). Enro 50mg/mL Injection has no effect on cholinesterase levels.

4) REPRODUCTION

No abnormalities in reproductive parameters were observed when male dogs received 10 consecutive daily treatments of 15 mg/kg/day at 3 intervals (90, 45 and 14 days) prior to breeding. Nor when female dogs received 10 consecutive daily treatments of 15mg/kg/day at 4 intervals: between 30 and O days prior to breeding, early pregnancy (between 10th and 30th days), late pregnancy (between 40th and 60th days), and during lactation (the first 28 days).

CATS

1) ADULTS

Cats receiving 50 mg/kg (1OX) of enrofloxacin for 6 days showed clinical signs of vomition, inappetance, incoordination and convulsions, but returned to normal on withdrawal of the drug. Dosages of 125 mg/kg (25X) for 5 consecutive days induced vomition, depression, incoordination, and lead to death.

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2) GROWING CATS

Cats in age ranges of 3 to 4 months and 7 to 10 months received daily treatments of 25 mg/kg (5X) for 30 consecutive days with no adverse effects. Occasional vomiting was seen in 7- to 10-month-old cats during 30 days of consecutive dosing at 5, 15, or 25 mg/kg.

Growing kittens 5 to 7 months old showed articular cartilage lesions when dosed with 25 mg/kg (5X) for 30 days but no lesions were seen at 15 mg/kg (3X) for 30 days.

EXOTIC SPECIES:

In the absence of data on its use in some exotic species, caution should be used when prescribing during pregnancy or lactation in small mammals and a careful risk/benefit assessment made.

CONTRAINDICATIONS

DOGS: Based on the studies of animal safety, the use of enrofloxacin is contraindicated in dogs during the rapid growth phase. Enro 50mg/mL Injection should not be used in dogs under one year of age. Giant breeds may be in the rapid growth phase for up to 18 months. Care should be used in treating individuals of these breeds with Enro 50mg/mL Injection when they are younger than 18 months.

CATS: Enro 50mg/mL Injection should not be used in cats less than 12 weeks of age. The safe use of enrofloxacin in breeding female cats has not been established.

STORAGE

Store below 25°C (Air conditioning). Protect from light.

APVMA Approval No. 89196