Baytril®
(enrofloxacin)
TECHNICAL BULLETIN

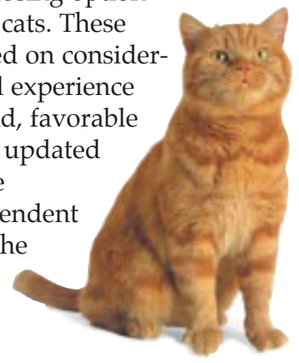
Baytril® Therapy for Cats
(enrofloxacin)

A Long Track Record

Baytril® (enrofloxacin) was the first fluoroquinolone developed and approved specifically for veterinary use. As a unique member of a novel antimicrobial class, Baytril is characterized by very rapid bactericidal activity and favorable pharmacokinetic features. Among these are extensive tissue distribution, prolonged post-antibiotic effects and a potent active metabolite with additive activity. Baytril has been proven to be highly effective for the treatment of a variety of small animal bacterial infections involving gram negative organisms, as well as gram positive bacteria such as *Staphylococcus* spp.

Baytril Tablets were first approved for cats in the United States in 1990. Since that time, over 10 million cats have safely been treated. Worldwide many more millions of cats have been treated over the past decade.

For many of these patients, therapy with Baytril has been a life-saving treatment. Baytril was initially labeled at a dosage of 2.5 mg/kg twice daily. In 1997, the Food and Drug Administration's Center for Veterinary Medicine (FDA-CVM) approved a flexible dosage range of 5-20 mg/kg/day and a once daily dosing option for both dogs and cats. These changes were based on considerable post-approval experience with the compound, favorable safety profile, and updated information on the concentration-dependent pharmacology of the fluoroquinolone class of drugs.



- **Millions of cats have been safely treated with Baytril over the past decade**
- **The revised Baytril Tablet label reflects the approved 5 mg/kg/day dosage for cats**
- **The vast majority of feline pathogens are effectively treated at 5 mg/kg/day**
- **Retinal effects are rare and appear to be dose related**

Bayer Corporation, Animal Health
Shawnee Mission, KS 66201

www.bayerus.com/ah

Bayer

B01249

Feline Safety

Enrofloxacin has proven to be a very well tolerated drug in a variety of species, including felines. Due to rare reports of acute vision impairment in cats temporally associated with the administration of Baytril® (enrofloxacin) in the recent past, notably at higher dosages, steps were taken to investigate any product relation.

In addition to thorough pharmacovigilance of reported cases, an extensive ocular safety study in cats was conducted. Bayer enlisted the expertise of a panel of independent board-certified veterinary ophthalmologists in the study design and investigation of this concern. Thirty-two cats were randomly assigned to one of four treatment groups and treated with either 0 (control), 5 mg/kg, 20 mg/kg or 50 mg/kg/day for 21 consecutive days. All study cats received pre- and post-treatment weekly ophthalmic examinations and electroretinographic (ERG) evaluations. Histopathology and electron microscopy were conducted on all ocular tissues at the conclusion of the study.

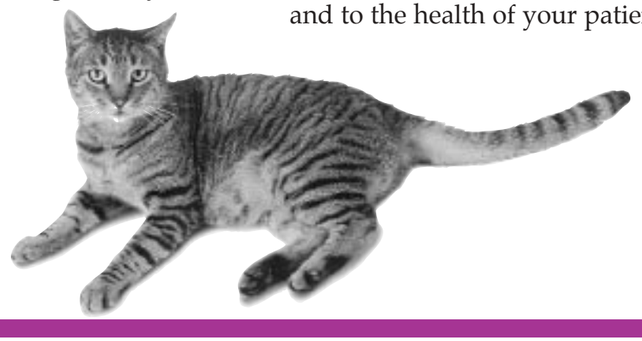
The study results indicated administration of Baytril at *elevated* dosages may result in mild to severe retinal changes in cats. No ocular changes were observed in either ophthalmic or histopathologic examinations in cats administered Baytril Tablets at 5 mg/kg once daily (2.27 mg/lb/day).

New Approved Label

Based on the study findings and post-approval experience, the Baytril Tablet label was revised in March 2001 to reflect an FDA-CVM approved oral dosage of **5 mg/kg/day in cats,** either once daily or divided and given BID. Due to the favorable pharmacokinetic profile of enrofloxacin in cats and the susceptibility of common feline pathogens, the vast majority of infections are effectively treated at this dose.

The revised label indicates that the use of fluoroquinolones in cats has been reported to adversely affect the retina in rare instances. Based on the number of cats treated with Baytril® (enrofloxacin) Tablets over the past decade, the incidence of vision-related reports to date is *extremely* rare. Of important note is that there is *no* evidence of ocular effects in canine species. This is underscored by the favorable tolerance even at markedly elevated dosages in excess of 20 mg/kg/day.

All drugs should be used rationally and after careful consideration of the benefits and risks of therapy. Baytril remains a safe and effective choice for the treatment of bacterial infections in cats when used according to label instructions. As a responsible manufacturer of human and veterinary pharmaceuticals and a leader in the animal health community, Bayer is committed to the safety of its products and to the health of your patients.



Baytril®

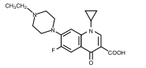
(enrofloxacin)

Antibacterial Tablets For Dogs and Cats

CAUTION:
Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.
Federal law prohibits the extralabel use of this drug in food-producing animals.

DESCRIPTION:
Enrofloxacin is a synthetic chemotherapeutic agent from the class of the quinolone carboxylic acid derivatives. It has antibacterial activity against a broad spectrum of Gram negative and Gram positive bacteria (See Tables I and II). It is rapidly absorbed from the digestive tract, penetrating into all measured body tissues and fluids (See Table III).
Tablets are available in three sizes (22.7, 68.0 and 136.0 mg enrofloxacin).

CHEMICAL NOMENCLATURE AND STRUCTURAL FORMULA:
1-cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid.



ACTIONS:
Microbiology: Quinolone carboxylic acid derivatives are classified as DNA gyrase inhibitors. The mechanism of action of these compounds is very complex and not yet fully understood. The site of action is bacterial gyrase, a synthesis promoting enzyme. The effect on *Escherichia coli* is the inhibition of DNA synthesis through prevention of DNA supercoiling. Among other things, such compounds lead to the cessation of cell respiration and division. They may also interrupt bacterial membrane integrity.[1]
Enrofloxacin is bactericidal, with activity against both Gram negative and Gram positive bacteria. The minimum inhibitory concentrations (MICs) were determined for a series of 39 isolates representing 9 genera of bacteria from natural infections in dogs and cats, selected principally because of resistance to one or more of the following antibiotics: ampicillin, cephalothin, colistin, chloramphenicol, erythromycin, gentamicin, kanamycin, penicillin, streptomycin, tetracycline, triple sulfa and sulfa/trimethoprim. The MIC values for enrofloxacin against these isolates are presented in Table I. Most strains of these organisms were found to be susceptible to enrofloxacin *in vitro* but the clinical significance has not been determined for some of the isolates.
The susceptibility of organisms to enrofloxacin should be determined using enrofloxacin 5 mcg disks. Specimens for susceptibility testing should be collected prior to the initiation of enrofloxacin therapy.

TABLE I—MIC Values for Enrofloxacin Against Canine and Feline Pathogens (Diagnostic laboratory isolates, 1984)

Organisms	Isolates	MIC Range (mcg/mL)
Bacteroides spp.	2	2
Bordetella bronchiseptica	3	0.125-0.5
Brucella canis	2	0.125-0.25
Clostridium perfringens	1	0.5
Escherichia coli	5*	≤0.016-0.031
Klebsiella spp.	11*	0.031-0.5
Proteus mirabilis	6	0.062-0.125
Pseudomonas aeruginosa	4	0.5-8
Staphylococcus spp.	5	0.125

*Includes feline isolates.

The inhibitory activity on 120 isolates of seven canine urinary pathogens was also investigated and is listed in Table II.

TABLE II—MIC Values for Enrofloxacin Against Canine Urinary Pathogens (Diagnostic laboratory isolates, 1985)

Organisms	Isolates	MIC Range (mcg/mL)
E. coli	30	0.06-2.0
P. mirabilis	20	0.125-2.0
K. pneumoniae	20	0.06-0.5
P. aeruginosa	10	1.0-8.0
Enterobacter spp.	10	0.06-1.0
Staph. (coag. +)	20	0.125-0.5
Strep. (alpha hemol.)	10	0.5-8.0

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 Tables I, II and III) are reached in most tissues by two hours after dosing at 2.5 mg/kg and are maintained for 8-12 hours after dosing. Particularly high levels of enrofloxacin are found in urine. A summary of the body fluid/tissue drug levels at 2 to 12 hours after dosing at 2.5 mg/kg is given in Table III.

TABLE III—Body Fluid/Tissue Distribution of Enrofloxacin in Dogs and Cats
Single Oral Dose = 2.5 mg/kg (1.13 mg/lb)

	Post-treatment Enrofloxacin Levels			
	Canine (n=2)		Feline (n=4)	
Body Fluids (mcg/mL)	**2 Hr.**	**8 Hr.**	**2 Hr.**	**12 Hr.**
Bile	-	-	2.13	1.97
Cerebrospinal Fluid	-	-	0.37	0.10
Urine	43.05	55.35	12.81	26.41
Eye Fluids	0.53	0.66	0.45	0.65
Whole Blood	1.01	0.36	-	-
Plasma	0.67	0.33	-	-
Serum	-	-	0.48	0.18
Tissues (mcg/g)				
Hematopoietic System				
Liver	3.02	1.36	1.84	0.37
Spleen	1.45	0.85	1.33	0.52
Bone Marrow	2.10	1.22	1.68	0.64
Lymph Node	1.32	0.91	0.49	0.21
Urogenital System				
Kidney	1.87	0.99	1.43	0.37
Bladder Wall	1.36	0.98	1.16	0.55
Testes	1.36	1.10	1.01	0.28
Prostate	1.36	2.20	1.88	0.55
Ovaries	-	-	0.78	0.56
Uterine Wall	1.59	0.29	0.81	1.05
Gastrointestinal and Cardiopulmonary Systems				
Lung	1.34	0.82	0.91	0.33
Heart	1.88	0.78	0.84	0.32
Stomach	3.24	2.16	3.26	0.27
Small Intestine	2.10	1.11	2.72	0.40
Large Intestine	-	-	0.94	1.10
Other				
Fat	0.52	0.40	0.24	0.11
Skin	0.66	0.48	0.46	0.17
Muscle	1.62	0.77	0.53	0.29
Brain	0.25	0.24	0.22	0.12
Mammary Gland	0.45	0.21	0.36	0.30
Feces	1.65	9.97	0.37	4.18

Pharmacokinetics: In dogs, the absorption and elimination characteristics of the oral formulation are linear (plasma concentrations increase proportionally with dose) when enrofloxacin is administered at up to 11.5 mg/kg, twice daily.[2] Approximately 80% of the orally administered dose enters the systemic circulation unchanged. 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. The absorption and elimination characteristics beyond this point are unknown. In cats, no oral absorption information is available at other than 2.5 mg/kg, administered orally as a single dose. Saturable absorption and/or elimination processes may occur at greater doses. When saturation of the absorption process occurs, the plasma concentration of the active moiety will be less than predicted, based on the concept of dose proportionality.
Following an oral dose in dogs of 2.5 mg/kg (1.13 mg/lb) enrofloxacin reached 50% of its maximum serum concentration in 15 minutes and peak serum level was reached in one hour. The elimination half-life in dogs is approximately 2 ½ - 3 hours at that dose, while in cats it is greater than 4 hours. In a study comparing dogs and cats, the peak concentration and the time to peak concentration were not different. A graph indicating the mean serum levels following a dose of 2.5 mg/kg (1.13 mg/lb) in dogs (oral and intramuscular) and cats (oral) is shown in Figure 1.

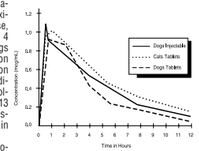


Figure 1 - Serum Concentrations of Enrofloxacin Following a Single Oral or Intramuscular Dose at 2.5 mg/kg in Dogs and a Single Oral Dose at 2.5 mg/kg in Cats.

Breakpoint: Based on pharmacokinetic studies of enrofloxacin in dogs and cats after a single oral administration of 2.5 mg enrofloxacin/kg BW (i.e. half of the lowest-end single daily dose range) and the data listed in Tables I and II, the following breakpoints are recommended for canine and feline isolates.

Zone Diameter (mm)	MIC (µg/mL)	Interpretation
≥ 21	≤ 0.5	Susceptible (S)
18-20	1	Intermediate (I)
≤ 17	≥ 2	Resistant (R)

A report of "Susceptible" indicates that the pathogen is likely to be inhibited by generally achievable plasma levels. A report of "Intermediate" is a technical buffer and isolates falling into this category should be retested. Alternatively the organism may be successfully treated if the infection is in a body site where drug is physiologically concentrated. A report of "Resistant" indicates that the achievable drug concentrations are unlikely to be inhibitory and other therapy should be selected.
Standardized procedures require the use of laboratory control organisms for both standardized disk diffusion assays and standardized dilution assays. The 5 µg enrofloxacin disk should give the following zone diameters and enrofloxacin powder should provide the following MIC values for reference strains.

QC strain	MIC (µg/mL)	Zone Diameter (mm)
E. coli ATCC 25922	0.008 - 0.03	32 - 40
P. aeruginosa ATCC 27853	1 - 4	15 - 19
S. aureus ATCC 25923		27 - 31
S. aureus ATCC 29213	0.03 - 0.12	

INDICATIONS:
Baytril® (brand of enrofloxacin) Antibacterial Tablets are indicated for the management of diseases associated with bacteria susceptible to enrofloxacin. Baytril Antibacterial Tablets are indicated for use in dogs and cats.

EFFICACY CONFIRMATION:
Dogs: Clinical efficacy was established in dermal infections (wounds and abscesses) associated with susceptible strains of *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis,* and *Staphylococcus intermedius;* respiratory infections (pneumonia, tonsillitis, rhinitis) associated with susceptible strains of *Escherichia coli* and *Staphylococcus aureus;* and urinary cystitis associated with susceptible strains of *Escherichia coli, Proteus mirabilis,* and *Staphylococcus aureus.*
Palatability: For Taste Tabs® free choice palatability in dogs was confirmed in a study in which 350 individual dosings resulted in a voluntary ingestion rate of 73%.
Cats: Clinical efficacy was established in dermal infections (wounds and abscesses) associated with susceptible strains of *Pasteurella multocida, Staphylococcus aureus,* and *Staphylococcus epidermidis.*

CONTRAINDICATIONS:
Enrofloxacin is contraindicated in dogs and cats known to be hypersensitive to quinolones.
Dogs: Based on the studies discussed under the section on Animal Safety Summary, the use of enrofloxacin is contraindicated in small and medium breeds of dogs during the rapid growth phase (between 2 and 8 months of age). The safe use of enrofloxacin has not been established in large and giant breeds during the rapid growth phase. Large breeds may be in this phase for up to one year of age and the giant breeds for up to 18 months. In clinical field trials utilizing a daily oral dose of 5.0 mg/kg, there were no reports of lameness or joint problems in any breed. However, controlled studies with histological examination of the articular cartilage have not been conducted in the large or giant breeds.

ADVERSE REACTIONS:
Dogs: Two of the 270 (0.7%) dogs treated with Baytril® (brand of enrofloxacin) Tablets at 5.0 mg/kg per day in the clinical field studies exhibited side effects, which were apparently drug related. These two cases of vomition were self-limiting.
Post Approval Experience: The following adverse experiences, although rare, are based on voluntary post-approval adverse drug experience reporting. The categories of reactions are listed in decreasing order of frequency by body system.
Gastrointestinal: Anorexia, diarrhea, vomiting, elevated liver enzymes
Neurologic: ataxia, seizures
Behavioral: Depression, lethargy, nervousness
Cats: No drug-related side effects were reported in 124 cats treated with Baytril® (brand of enrofloxacin) Tablets at 5.0 mg/kg per day for 10 days, in clinical field studies.
Post Approval Experience: The following adverse experiences, although rare, are based on voluntary post-approval adverse drug experience reporting. The categories of reactions are listed in decreasing order of frequency by body system.
Ocular: Mydriasis, retinal degeneration, (retinal atrophy, attenuated retinal vessels, and hyperreflective tapeta have been reported), loss of vision. Mydriasis may be an indication of impending or existing retinal changes.
Gastrointestinal: vomiting, anorexia, elevated liver enzymes, diarrhea
Neurologic: ataxia, seizures
Behavioral: Depression, lethargy, vocalization, aggression
To report adverse reactions or a suspected adverse reaction call 1-800-633-8405.

ANIMAL SAFETY SUMMARY:
Dogs: Adult dogs receiving enrofloxacin orally at a daily dosage rate of 52 mg/kg for 13 weeks had only isolated incidences of vomition and inappetence. Adult dogs receiving the tablet formulation for 30 consecutive days at a daily treatment of 25 mg/kg did not exhibit significant clinical signs nor were there effects upon the clinical chemistry, hematological or histological parameters. Daily doses of 125 mg/kg for up to 11 days induced vomition, inappetence, depression, difficult locomotion and death while adult dogs receiving 50 mg/kg/day for 14 days had clinical signs of vomition and inappetence.
Adult dogs dosed intramuscularly for three treatments at 12.5 mg/kg, followed by 57 oral treatments at 12.5 mg/kg, all at 12 hour intervals, did not exhibit either significant clinical signs or effects upon the clinical chemistry, hematological or histological parameters.
Oral treatment of 15 to 28 week old growing puppies with daily dosage rates of 25 mg/kg has induced abnormal carriage of the carpal joint and weakness in the hindquarters. 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. Clinical signs of difficult ambulation or associated cartilage lesions have not been observed in 29 to 34 week old puppies following daily treatments of 25 mg/kg for 30 consecutive days nor in 2 week old puppies with the same treatment schedule.
Tests indicated no effect on circulating microfilariae or adult heartworms (*Dirofilaria immitis*) when dogs were treated at a daily dosage rate of 15 mg/kg for 30 days. No effect on cholinesterase values was observed.
No adverse effects were observed on reproductive parameters when male dogs received 10 consecutive daily treatments of 15 mg/kg/day at 3 intervals (90, 45 and 14 days) prior to breeding or when female dogs received 10 consecutive daily treatments of 15 mg/kg/day at 4 intervals: between 30 and 0 days prior to breeding, early pregnancy (between 10th & 30th days), late pregnancy (between 40th & 60th days), and during lactation (the first 28 days).
Cats: Cats in age ranges of 3 to 4 months and 7 to 10 months received daily treatments of 25 mg/kg for 30 consecutive days with no adverse effects upon the clinical chemistry, hematological or histological parameters. In cats 7-10 months of age treated daily for 30 consecutive days, 2 of 4 receiving 5 mg/kg, 3 of 4 receiving 15 mg/kg, 2 of 4 receiving 25 mg/kg and 1 of 4 nontreated controls experienced occasional vomition. Five to 7 month old cats had no side effects with daily treatments of 15 mg/kg for 30 days, but 2 of 4 animals had articular cartilage lesions when administered 25 mg/kg/day for 30 days.
Doses of 125 mg/kg for 5 consecutive days to adult cats induced vomition, depression, incoordination and death while those receiving 50 mg/kg for 6 days had clinical signs of vomition, inappetence, incoordination and convulsions, but they returned to normal.
Enrofloxacin was administered to thirty-two (8 per group), six- to eight-month-old cats at doses of 0, 5, 20, and 50 mg/kg of body weight once a day for 21 consecutive days. There were no adverse effects observed in cats that received 5 mg/kg body weight of enrofloxacin. The administration of enrofloxacin at 20 mg/kg body weight or greater caused salivation, vomition, and depression. Additionally, dosing at 20 mg/kg body weight or greater resulted in mild to severe fundic lesions on ophthalmologic examination (change in color of the fundus, central or generalized retinal degeneration), abnormal electroretinograms (including blindness), and diffuse light microscopic changes in the retina.

DRUG INTERACTIONS:
Compounds that contain metal cations (e.g., aluminum, calcium, iron, magnesium) may reduce the absorption of some quinolone-class drugs from the intestinal tract. Concomitant therapy with other drugs that are metabolized in the liver may reduce the clearance rates of the quinolone and the other drug.
Dogs: Enrofloxacin has been administered to dogs at a daily dose rate of 10 mg/kg concurrently with a wide variety of other health products including anthelmintics (praziquantel, febantel), insecticides (pyrethrins), heartworm preventatives (diethylcarbamazine) and other antibiotics (ampicillin, gentamicin sulfate, penicillin, dihydrostreptomycin). No incompatibilities with other drugs are known at this time.
Cats: Enrofloxacin was administered at a daily dosage rate of 5 mg/kg concurrently with anthelmintics (praziquantel, febantel), an insecticide (propoxur) and another antibacterial (ampicillin). No incompatibilities with other drugs are known at this time.

WARNINGS:
For Use in Animals Only. In Rare Instances, Use of this Product in Cats has been associated with Retinal Toxicity. Do not exceed 5 mg/kg of body weight per day in cats. Safety in Breeding or Pregnant Cats has not been Established. Keep Out of Reach of Children.
Avoid contact with eyes. In case of contact, immediately flush eyes with copious amounts of water for 15 minutes. In case of dermal contact, wash skin with soap and water. Consult a physician if irritation persists following ocular or dermal exposure. Individuals with a history of hypersensitivity to quinolones should avoid this product. In humans, there is a risk of user photosensitization within a few hours after excessive exposure to quinolones. If excessive accidental exposure occurs, avoid direct sunlight.
For a copy of the Material Safety Data Sheet, call 1-800-633-8405.

PRECAUTION:
Quinolone-class drugs should be used with caution in animals with known or suspected Central Nervous System (CNS) disorders. In such animals, quinolones have, in rare instances, been associated with CNS stimulation which may lead to convulsive seizures.
Quinolone-class drugs have been associated with cartilage erosions in weight-bearing joints and other forms of arthropathy in immature animals of various species.
The use of fluoroquinolones in cats has been reported to adversely affect the retina. Such products should be used with caution in cats.

DOSAGE AND ADMINISTRATION:
Dogs: Administer orally at a rate to provide 5-20 mg/kg (2.27 to 9.07 mg/lb) of body weight. Selection of a dose within the range should be based on clinical experience, the severity of disease, and susceptibility of the pathogen. Animals which receive doses in the upper-end of the dose range should be carefully monitored for clinical signs that may include inappetence, depression, and vomition.

Weight of Dog	Once Daily Dosing Chart			
	5.0 mg/kg	10.0 mg/kg	15.0 mg/kg	20.0 mg/kg
9.1 kg (20 lb)	2 x 22.7 mg tablets	1 x 22.7 mg plus 1 x 68 mg tablets	1 x 136 mg tablet	1 x 136 mg plus 2 x 22.7 mg tablets
27.2 kg (60 lb)	1 x 136 mg tablet	2 x 136 mg tablets	3 x 136 mg tablets	4 x 136 mg tablets

All tablet sizes are double scored for accurate dosing.
Cats: Administer orally at 5 mg/kg (2.27 mg/lb) of body weight. The dose for dogs and cats may be administered either as a single daily dose or divided into two (2) equal daily doses administered at twelve (12) hour intervals. The dose should be continued for at least 2-3 days beyond cessation of clinical signs, to a maximum of 30 days. **In rare instances, use of this product in cats has been associated with retinal toxicity. Based on post approval experience, cats should be carefully monitored for clinical signs of mydriasis and/or changes in the retina.**

Weight of Cat	Once Daily Dosing Chart (5 mg/kg/day)
5 lb (2.27 kg)	1/2 x 22.7 mg tablet
10 lb (4.5 kg)	1 x 22.7 mg tablet
15 lb (6.8 kg)	1 and 1/2 x 22.7 mg tablets or 1/2 x 68 mg tablet

All tablet sizes are double scored for accurate dosing.
Palatability: Most dogs will consume Baytril® Taste Tabs® Tablets willingly when offered by hand. Alternatively the tablet(s) may be offered in food or hand-administered (pilled) as with other oral tablet medications. In cats, Baytril® Taste Tabs® Tablets should be pilled. After administration, watch the animal closely to be certain the entire dose has been consumed.
Dogs & Cats: The duration of treatment should be selected based on clinical evidence. Generally, administration of Baytril Tablets should continue for at least 2-3 days beyond cessation of clinical signs. For severe and/or complicated infections, more prolonged therapy, up to 30 days, may be required. If no improvement is seen within five days, the diagnosis should be reevaluated and a different course of therapy considered.
The lower limit of the dose range in dogs and the daily dose for cats was based on efficacy studies in dogs and cats where enrofloxacin was administered at 2.5 mg/kg twice daily. Target animal safety and toxicology were used to establish the upper limit of the dose range for dogs and treatment duration for dogs and cats.

STORAGE:
Dispense tablets in tight containers only.

HOW SUPPLIED:

Taste Tabs® Code Number	Film Coated Code Number	Baytril Tablets Tablet Size	Tablets/Bottle
0387	1868	22.7 mg	100 Double Scored
0388	1881	22.7 mg	500 Double Scored
0389	1869	68.0 mg	50 Double Scored
0390	1882	68.0 mg	250 Double Scored
0417	-	136.0 mg	50 Double Scored
0391	-	136.0 mg	200 Double Scored

U.S. Patent No. 4,670,444

REFERENCES:
[1]Dougherty, T.J. and Saukkonen, J.J.Membrane Permeability Changes Associated with DNA Gyrase Inhibitors in *Escherichia coli* Antimicrob. Agents and Chemoth., V. 28, Aug. 1985, 200-206.
[2]Walker, R.D. *et al*, Pharmacokinetic Evaluation of Enrofloxacin Administered Orally to Healthy Dogs. Am. J. Res. V. 53, No. 12, Dec. 1992; 2315-2319.

March, 2001

Bayer Corporation,
Agriculture Division, Animal Health,
Shawnee Mission, Kansas 66201, U.S.A.
B02048

NADA 140-441, Approved by FDA