Orbax® (Orbifloxacin)

For easy administration in Cats & Dogs

MERCK
Animal Health

Orbax®
(Orbifloxacin) Oral Suspension

Orbax® Oral Suspension. Once-a-day broad-spectrum antibiotic therapy ideal for cats.

- Tasty malt-flavored antibiotic for easy administration[1]
- Patented Ion Exchange taste-masking technology
  - *Orbifloxacin is bound to a taste-masking agent so it passes taste buds undetected, then is released in the low pH environment of the stomach.*

ION EXCHANGE TASTE-MASKING TECHNOLOGY

Convenient for pet owners

- ✓ Freely accepted by cats and dogs
- ✓ Administered once-a-day
- ✓ Mess-free dispensing system
  - Unique press-in syringe for easy and accurate dosing (3 mL with 0.25 markings)
- ✓ Ready to use, no reconstitution
- ✓ No refrigeration needed

Package sizes and dosing that work for cats and small dogs

Treatment	Dosage	Patient Weight	Daily Dose *mL / day*	Days of Treatment/Bottle
ORBAX® (orbifloxacin) 20 mL deliverable volume (30 mg/mL orbifloxacin)	7.5 mg/kg SID	cat or dog (4.5 kg; 10 lbs)	1.1 mL	18
	2.5 mg/kg SID	dog (9 kg; 20 lbs)	0.8 mL	25
	7.5 mg/kg SID	dog (9 kg; 20 lbs)	2.3 mL	9

Quinolones have been shown to cause arthropathy in immatu
quinolones have been associated with CNS stimulation, which
cats has been reported to adversely affect the

Convenient E-Z Break Tablets

Orbax® Tablets are easy and economical, delivering safe and effective broad-spectrum therapy for dogs.

- Once-a day dosing for better compliance
- Flexible dose range for cats and dogs based on the clinical severity of the condition
- Broad spectrum bactericidal activity for high first-treatment cure rates
- Color coded tablets for simplified dosing instructions
- E-Z Break scoring for breaking larger sized tablets without a pill cutter
- Low protein binding level
- Excellent treatment value

Coated E-Z break tablets for easy dosing and administration.

Explo-Tab technology for rapid and complete tablet dissolution.

DOSING CHART (2.5 mg/kg SID)									
Weight of dog or cat (lbs)									
	5	10	20	30	40	50	60	90	120
# of 5.7 mg tablets	**1**	**2**							
# of 22.7 mg tablets		**1/2**	**1**	**1 1/2**	**2**	**2 1/2**			
# of 68 mg tablets				**1/2**			**1**	**1 1/2**	**2**

re animals. In animals with known or suspected CNS disorders, may lead to convulsive seizures. The use of fluoroquinolones in retina and should be used with caution in cats.

NADA #141-305, Approved by FDA.

ORBAX® Oral Suspension (orbifloxacin)

For Oral Use in Cats Only.

Federal law prohibits the extra label use of this drug in food-producing animals

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Orbifloxacin is a synthetic broad-spectrum antibacterial agent from the class of fluoroquinolone carboxylic acid derivatives. Orbifloxacin is the international nonproprietary name for 1-cyclopropyl-5,6,8-trifluoro-1,4-dihydro-7-(*cis*-3,5-dimethyl-1-piperazinyl)-4-oxoquinoline-3-carboxylic acid. The chemical formula for orbifloxacin is $C_{19}H_{20}F_3N_3O_3$ and its molecular weight is 395.38. The compound is slightly soluble in water; however, solubility increases in both acidic and alkaline conditions. The compound has two dissociation constants (pKa's): 5.95 and 9.01. ORBAX® Oral Suspension is a malt flavored antibiotic suspension containing 30 mg/mL of orbifloxacin and sorbic acid as a preservative.

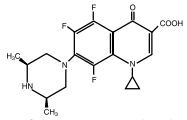

Figure 1. Chemical structure of orbifloxacin.

INDICATIONS: ORBAX® Oral Suspension is indicated for the treatment of skin infections (wounds and abscesses) in cats caused by susceptible strains of *Staphylococcus aureus, Escherichia coli,* and *Pasteurella multocida.*

DOSAGE AND ADMINISTRATION: Shake Well Before Use. BEFORE INITIAL USE, remove the cap and insert the syringe adaptor by pressing firmly into top of bottle. Insert the syringe tip into the adaptor opening and invert the bottle. Withdraw the required amount of medication with the calibrated syringe. After use, replace cap, leaving adaptor in the bottle, and rinse the syringe with water. In the cat, ORBAX® Oral Suspension and ORBAX® (orbifloxacin) Tablets are not bioequivalent. On a mg/kg basis, ORBAX® Oral Suspension provides lower and more variable plasma levels of orbifloxacin than ORBAX® (orbifloxacin) Tablets (See Clinical Pharmacology and Precautions). The dose of ORBAX® Oral Suspension in the cat is 3.4 mg/lb (7.5 mg/kg) of body weight administered once daily. DO NOT EXCEED 3.4 mg/lb (7.5 mg/kg) BODY WEIGHT PER DAY IN CATS. ORBAX® Oral Suspension should be given for two (2) to three (3) days beyond the cessation of clinical signs. Antibiotic susceptibility of the pathogenic organism(s) should be determined prior to use of this preparation. Therapy with ORBAX® Oral Suspension may be initiated before results of these tests are known. Once results become available, continue with appropriate therapy. If no improvement is seen within 3 to 4 days, the diagnosis should be re-evaluated and a different course of therapy considered.

CONTRAINDICATIONS: Orbifloxacin and other quinolones have been shown to cause arthropathy in immature animals of most species tested, the dog being particularly sensitive to this side effect. Orbifloxacin is contraindicated in immature dogs during the rapid growth phase (between 2 and 8 months of age in small and medium-sized breeds, and up to 18 months of age in large and giant breeds). Orbifloxacin is contraindicated in cats known to be hypersensitive to quinolones.

HUMAN WARNING: For use in animals only. Keep out of the reach of children. 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. 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.

PRECAUTIONS: Prescribing antibacterial drugs in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to treated animals and may increase the risk of the development of drug-resistant animal pathogens. The use of fluoroquinolones in cats has been reported to adversely affect the retina. Such products should be used with caution in cats. Blindness has also been reported post-approval in cats. In some cases, blindness has been temporary. DO NOT EXCEED 3.4 mg/lb (7.5 mg/kg) BODY WEIGHT PER DAY IN CATS. If higher blood levels of orbifloxacin are needed, ORBAX® (orbifloxacin) Tablets should be used at a dose of 2.3-3.4 mg/lb (5.0-7.5 mg/kg). On a mg/kg basis, ORBAX® (orbifloxacin) Tablets provide higher and less variable plasma levels of orbifloxacin than ORBAX® Oral Suspension. Quinolones 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. Quinolones have been shown to produce erosions of cartilage of weight-bearing joints and other signs of arthropathy in immature animals of various species. The safety of orbifloxacin in animals that are used for breeding or that are pregnant and/or lactating has not been demonstrated.

DRUG INTERACTIONS: Compounds (eg, sucralfate, antacids, and multivitamins) containing divalent and trivalent cations (eg, iron, aluminum, calcium, magnesium, and zinc) may substantially interfere with the absorption of quinolones resulting in a decrease in product bioavailability. Therefore, the concomitant oral administration of quinolones with foods, supplements, or other preparations containing these compounds should be avoided. The dosage of theophylline should be reduced when used concurrently with fluoroquinolones. Cimetidine has been shown to interfere with the metabolism of fluoroquinolones and should be used with care when used concurrently. Concurrent use of fluoroquinolones with oral cyclosporine is contraindicated. Concurrent administration of fluoroquinolones may increase the action of oral anticoagulants.

ADVERSE REACTIONS: In a field study, when the tablet formulation of orbifloxacin was administered at 2.5 mg/kg/day, no drug-related adverse reactions were reported. In a foreign field study using the oral suspension at 7.5 mg/kg/day, vomiting was reported for ORBAX® Oral Suspension and the comparator. Post Approval Experience with ORBAX® (orbifloxacin) Tablets (Rev. 2010): *The following adverse events are based on post-approval adverse drug experience reporting with ORBAX® Tablets. Not all adverse reactions are reported to FDA CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using this data. The following adverse events are listed in decreasing order of reporting frequency:* **CAT:** Blindness, mydriasis, anorexia, ataxia, depression/lethargy, vomiting, convulsions, abnormal retina, hypersalivation. In some cases, blindness has been temporary. *For a complete listing of adverse reactions for ORBAX® (orbifloxacin) Tablets reported to the CVM see:* http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm055394.html. For technical assistance or to report a suspected adverse reaction call 1-800-224-5318.

PALATABILITY: In a field palatability study, conducted in 101 cats, ORBAX® Oral Suspension was accepted by 95% of cats.

STORAGE CONDITIONS: Store between 2°C and 25°C (36°F and 77°F). ORBAX® Oral Suspension does not require refrigeration. Shake well before use. Store upright.

HOW SUPPLIED: ORBAX® Oral Suspension is supplied in a sealed bottle with a 20 mL deliverable volume.

Made in Friesoythe, Germany
Intervet Inc. January, 2010

NADA #141-305, Approved by FDA.

ORBAX® Oral Suspension (orbifloxacin)

For Oral Use in Dogs Only.

Federal law prohibits the extra label use of this drug in food-producing animals.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Orbifloxacin is a synthetic broad-spectrum antibacterial agent from the class of fluoroquinolone carboxylic acid derivatives. Orbifloxacin is the international nonproprietary name for 1-cyclopropyl-5,6,8-trifluoro-1,4-dihydro-7-(*cis*-3,5-dimethyl-1-piperazinyl)-4-oxoquinoline-3-carboxylic acid. The chemical formula for orbifloxacin is $C_{19}H_{20}F_3N_3O_3$ and its molecular weight is 395.38. The compound is slightly soluble in water; however, solubility increases in both acidic and alkaline conditions. The compound has two dissociation constants (pKa's): 5.95 and 9.01. ORBAX® Oral Suspension is a malt flavored antibiotic suspension containing 30 mg/mL of orbifloxacin and sorbic acid as a preservative.

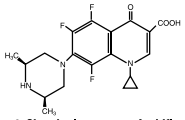

Figure 1. Chemical structure of orbifloxacin.

INDICATIONS: ORBAX® Oral Suspension is indicated for the treatment of urinary tract infections (cystitis) in dogs caused by susceptible strains of *Staphylococcus pseudintermedius, Proteus mirabilis, Escherichia coli* and *Enterococcus faecalis.* ORBAX® Oral Suspension is also indicated for skin and soft tissue infections (wounds and abscesses) in dogs caused by susceptible strains of *Staphylococcus pseudintermedius, Staphylococcus aureus, coagulase* positive staphylococci, *Pasteurella multocida, Proteus mirabilis, Pseudomonas* spp., *Klebsiella pneumoniae, Escherichia coli, Enterobacter* spp., *Citrobacter* spp., *Enterococcus faecalis,* β-hemolytic streptococci (Group G) and *Streptococcus equisimilis.*

DOSAGE AND ADMINISTRATION: Shake Well Before Use. BEFORE INITIAL USE, remove the cap and insert the syringe adaptor by pressing firmly into top of bottle. Insert the syringe tip into the adaptor opening and invert the bottle. Withdraw the required amount of medication with the calibrated syringe. After use, replace cap, leaving adaptor in the bottle, and rinse the syringe with water. The dose of ORBAX® Oral Suspension in the dog is 1.1 to 3.4 mg/lb (2.5 to 7.5 mg/kg) of body weight administered once daily (See Drug interactions and Animal Safety). The determination of dosage for any particular patient must take into consideration such factors as the severity and nature of the infection, the susceptibility of the causative organism, and the integrity of the patient's host-defense mechanisms. Antibiotic susceptibility of the pathogenic organism(s) should be determined prior to use of this preparation. Therapy with ORBAX® Oral Suspension may be initiated before results of these tests are known. Once results become available, continue with appropriate therapy. For the treatment of skin infections, ORBAX® Oral Suspension should be given for two (2) to three (3) days beyond the cessation of clinical signs to a maximum of 30 days. For the treatment of urinary tract infections, ORBAX® Oral Suspension should be administered for at least 10 consecutive days. If no improvement is seen within five (5) days, the diagnosis should be re-evaluated and a different course of therapy considered.

CONTRAINDICATIONS: Orbifloxacin and other quinolones have been shown to cause arthropathy in immature animals of most species tested, the dog being particularly sensitive to this side effect. Orbifloxacin is contraindicated in immature dogs during the rapid growth phase (between 2 and 8 months of age in small and medium-sized breeds, and up to 18 months of age in large and giant breeds). Orbifloxacin is contraindicated in dogs known to be hypersensitive to quinolones.

HUMAN WARNING: For use in animals only. Keep out of the reach of children. 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. 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.

PRECAUTIONS: Prescribing antibacterial drugs in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to treated animals and may increase the risk of the development of drug-resistant animal pathogens. Administer orbifloxacin with caution in the presence of hepatic insufficiency/impairment. Please refer to the cat side of this package insert for Precautions related specifically to cats. Quinolones 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. Quinolones have been shown to produce erosions of cartilage of weight-bearing joints and other signs of arthropathy in immature animals of various species. The safety of orbifloxacin in animals that are used for breeding or that are pregnant and/or lactating has not been demonstrated.

DRUG INTERACTIONS: Compounds (eg, sucralfate, antacids, and multivitamins) containing divalent and trivalent cations (eg, iron, aluminum, calcium, magnesium, and zinc) may substantially interfere with the absorption of quinolones resulting in a decrease in product bioavailability. Therefore, the concomitant oral administration of quinolones with foods, supplements, or other preparations containing these compounds should be avoided. The dosage of theophylline should be reduced when used concurrently with fluoroquinolones. Cimetidine has been shown to interfere with the metabolism of fluoroquinolones and should be used with care when used concurrently. Concurrent use of fluoroquinolones with oral cyclosporine is contraindicated. Concurrent administration of fluoroquinolones may increase the action of oral anticoagulants.

ADVERSE REACTIONS: In a field study, when the tablet formulation of orbifloxacin was administered at 2.5 mg/kg/day, no drug-related adverse reactions were reported. In a foreign field study using the oral suspension at 7.5 mg/kg/day, vomiting was reported for ORBAX® Oral Suspension and the comparator. Post Approval Experience with ORBAX® (orbifloxacin) Tablets (Rev. 2010): *The following adverse events are based on post-approval adverse drug experience reporting with ORBAX® (orbifloxacin) Tablets. Not all adverse reactions are reported to FDA CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using this data. The following adverse events are listed in decreasing order of reporting frequency:* **DOG:** Vomiting, convulsions, depression/lethargy, anorexia *For a complete listing of adverse reactions for ORBAX® (orbifloxacin) Tablets reported to the CVM see:* http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm055394.html. For technical assistance or to report a suspected adverse reaction call 1-800-224-5318.

PALATABILITY: In a field palatability study, conducted in 81 dogs, ORBAX® Oral Suspension was accepted by 96.3% of the dogs following oral administration.

STORAGE CONDITIONS: Store between 2°C and 25°C (36°F and 77°F). ORBAX® Oral Suspension does not require refrigeration. Shake well before use. Store upright.

HOW SUPPLIED: ORBAX® Oral Suspension is supplied in a sealed bottle with a 20 mL deliverable volume.

Made in Friesoythe, Germany
Intervet Inc. January, 2010

NADA #141-081, Approved by FDA.

ORBAX® Tablets (orbifloxacin)

For Oral Use in Dogs and Cats Only 81-497245

Brief Summary (For full Prescribing Information, see package insert.)

Federal law prohibits the extralabel use of this drug in food-producing animals.

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Orbifloxacin is a synthetic broad-spectrum antibacterial agent from the class of fluoroquinolone carboxylic acid derivatives. Orbifloxacin is the international nonproprietary name for 1-cyclopropyl-5,6,8-trifluoro-1,4-dihydro-7-(*cis*-3,5-dimethyl-1-piperazinyl)-4-oxoquinoline-3-carboxylic acid. The chemical formula for orbifloxacin is $C_{19}H_{20}F_3N_3O_3$ and its molecular weight is 395.38. The compound is slightly soluble in water; however, solubility increases in both acidic and alkaline conditions. The compound has two dissociation constants (pKa's): 5.95 and 9.01.

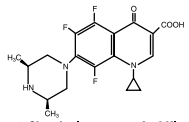

Figure 1. Chemical structure of orbifloxacin.

INDICATIONS: ORBAX® (orbifloxacin) Tablets are indicated for the management of diseases in dogs and cats associated with bacteria susceptible to orbifloxacin.

DOSAGE AND ADMINISTRATION: For routine out-patient treatment of infection caused by a susceptible organism, in an otherwise healthy dog or cat, the dose of ORBAX® (orbifloxacin) Tablets is 2.5 to 7.5 mg/kg of body weight administered once daily. (See **DRUG INTERACTIONS** and **TARGET ANIMAL SAFETY.**) The determination of dosage for any particular patient must take into consideration such factors as the severity and nature of the infection, the susceptibility of the causative organism, and the integrity of the patient's host-defense mechanisms. Antibiotic susceptibility of the pathogenic organism(s) should be determined prior to use of this preparation. Therapy with ORBAX® (orbifloxacin) Tablets may be initiated before results of these tests are known. Once results become available, continue with appropriate therapy.

For the treatment of skin and associated soft tissue infections, ORBAX® Tablets should be given for two (2) to three (3) days beyond the cessation of clinical signs to a maximum of 30 days. For the treatment of urinary tract infections, ORBAX® Tablets should be administered for at least 10 consecutive days. If no improvement is seen within five (5) days, the diagnosis should be re-evaluated and a different course of therapy considered.

To administer a total daily dose of 2.5 mg/kg, ORBAX® Tablets may be dispensed as indicated in Table 1.

Table 1: Dose Table for ORBAX® Tablets (2.5 mg/kg total daily dose)

	WEIGHT OF DOG/CAT (lbs)								
	5	10	20	30	40	50	60	90	120
No. of 5.7 mg tablets	1	2							
No. of 22.7 mg tablets		½	1	1½	2	2½			
No. of 68 mg tablets				½			1	1½	2

DRUG INTERACTIONS: Compounds (eg, sucralfate, antacids, and multivitamins) containing divalent and trivalent cations (eg, iron, aluminum, calcium, magnesium, and zinc) may substantially interfere with the absorption of quinolones resulting in a decrease in product bioavailability. Therefore, the concomitant oral administration of quinolones with foods, supplements, or other preparations containing these compounds should be avoided.

CONTRAINDICATIONS: Orbifloxacin and other quinolones have been shown to cause arthropathy in immature animals of most species tested, the dog being particularly sensitive to this side effect. Orbifloxacin is contraindicated in immature dogs during the rapid growth phase (between 2 and 8 months of age in small and medium-sized breeds, and up to 18 months of age in large and giant breeds).

Orbifloxacin is contraindicated in dogs and cats known to be hypersensitive to quinolones.

PRECAUTIONS: The use of fluoroquinolones in cats has been reported to adversely affect the retina. Such products should be used with caution in cats. Quinolones 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. Quinolones have been shown to produce erosions of cartilage of weight-bearing joints and other signs of arthropathy in immature animals of various species.

The safety of orbifloxacin in animals that are used for breeding or that are pregnant and/or lactating has not been demonstrated.

WARNINGS: For use in animals only. Do not exceed 7.5 mg/kg body weight per day in cats. Keep out of the 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.

ADVERSE REACTIONS: In clinical trials, when the drug was administered at 2.5 mg/kg/day, no drug-related adverse reactions were reported.

Post-Approval Experience – The following adverse reactions, although rare, are based upon voluntary post-approval reporting:

Hypersensitivity: facial edema, anaphylaxis/anaphylactoid reactions
Neurologic: seizures, ataxia
Behavioral: depression, lethargy
Gastrointestinal: vomiting, anorexia

HOW SUPPLIED: ORBAX® (orbifloxacin) Tablets are available in the following presentations:

5.7 mg:	Bottles of 250 yellow tablets	NDC 0061-1171-01
22.7 mg:	Bottles of 250 green, E-Z Break, single-scored tablets	NDC 0061-1141-01
68 mg:	Bottles of 100 blue, E-Z Break, single-scored tablets	NDC 0061-1174-01

STORAGE CONDITIONS: Store between 2° and 30°C (36° and 86°F). Protect from excessive moisture.

To report suspected adverse reactions, contact Schering-Plough Animal Health at 1-800-224-5318.

April 2006
Made in Canada.
Schering-Plough Animal Health Corp., Summit, NJ 07901

U.S. Patent No. 4,795,751

19335658-JBS

Orbax® (Orbifloxacin)

1. Data on file. Multi-clinic, randomized, controlled field trial evaluating the use of ORBAX® (orbifloxacin) Oral Suspension and Synulox® (amoxicillin/clavulanate) in the treatment of cats with skin and soft tissue infections (primarily post-traumatic wounds and abscesses) in France, Belgium, and Germany in 2001. Roseland, NJ: Intervet Inc.
2. Freedom of Information Summary. Original New Animal Drug Application (NADA 141-305). ORBAX® Oral Suspension. Roseland, NJ: Intervet Inc. July 1, 2009.

MERCK Animal Health

Intervet Inc. d/b/a Merck Animal Health, Summit, NJ, 07901 MAH-OR-97R