

PIONEER LABEL

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ACTIVE INGREDIENTS:

25 mg ANTIROBE capsule: Each capsule contains clindamycin hydrochloride equivalent to 25 mg of clindamycin

75 mg ANTIROBE capsule: Each capsule contains clindamycin hydrochloride equivalent to 75 mg of clindamycin

150 mg ANTIROBE capsule: Each capsule contains clindamycin hydrochloride equivalent to 150 mg of clindamycin

INDICATIONS:

Dogs: Aerobic bacteria: ANTIROBE is indicated for the treatment of soft tissue infections (wounds and abscesses), dental infections and osteomyelitis caused by susceptible strains of *Staphylococcus aureus*. Anaerobic bacteria: ANTIROBE is indicated for the treatment of soft tissue infections (wounds and abscesses), dental infections and osteomyelitis caused by or associated with susceptible strains of *Bacteroides fragilis*, *Bacteroides melaninogenicus*, *Fusobacterium necrophorum* and *Clostridium perfringens*.

Cats: Aerobic bacteria: ANTIROBE is indicated for the treatment of soft tissue infections (wounds and abscesses) and dental infections caused by or associated with susceptible strains of *Staphylococcus aureus*, *Staphylococcus intermedius* and *Streptococcus* spp. Anaerobic bacteria: ANTIROBE is indicated for the treatment of soft tissue infections (deep wounds and abscesses) and dental infections caused by or associated with susceptible strains of *Clostridium perfringens* and *Bacteroides fragilis*.

PHARMACOLOGY: ANTIROBE contains clindamycin hydrochloride which is the hydrated salt of clindamycin. Clindamycin is a semisynthetic antibiotic produced by a 7(S)-chlorosubstitution of the 7(R)-hydroxyl group of a naturally produced antibiotic produced by *Streptomyces lincolnensis* var. *lincolnensis*.

Actions: Site and mode of action: Clindamycin is an inhibitor of protein synthesis in the bacterial cell. The site of binding appears to be the 50S subunit of the ribosome. Binding occurs to the soluble RNA fraction of certain ribosomes, thereby inhibiting the binding of amino acids to those ribosomes. Clindamycin differs from cell wall inhibitors in that it causes irreversible modification of the protein synthesizing subcellular elements at the ribosomal level.

Microbiology: The following clindamycin *in vitro* data are available but their clinical significance is unknown. Clindamycin has been shown to

have *in vitro* activity against the following organisms isolated from animals: Aerobic gram-positive cocci including *Staphylococcus aureus* (penicillinase and non-penicillinase producing strains), *Staphylococcus intermedius*, *Staphylococcus simulans*, *Staphylococcus epidermidis*, Streptococci (except *Enterococcus faecalis*). Anaerobic and microaerophilic gram positive cocci, including: *Peptococcus* species, *Peptostreptococcus* species, Microaerophilic streptococci. Clostridia: Most *C. perfringens* are susceptible, but other species may be resistant to clindamycin. Overall susceptibility to clindamycin of anaerobes isolated from canine lesions. Data obtained from three veterinary diagnostic laboratories.

	Susceptible $\leq 3.2 \mu\text{g/ml}$	Resistant $\geq 4.0 \mu\text{g/ml}$
All isolates	122/137 (89%)	15/137 (11%)
<i>Clostridium</i> spp.	41/49 (84%)	8/49 (16%)
<i>Bacteroides</i> spp.	42/46 (91%)	4/46 (9%)
<i>Fusobacterium</i> spp.	16/16 (100%)	0/16 (0%)
<i>Peptostreptococcus</i> spp.	15/16 (94%)	1/16 (6%)
<i>Actinomyces</i> spp.	5/6 (83%)	1/6 (17%)
<i>Propionibacterium</i> spp.	3/4 (75%)	1/4 (25%)

The MIC values of anaerobes isolated from feline lesions are not different from the MIC values for the anaerobes isolated from canine lesions. *Mycoplasma* species: Most mycoplasma species are susceptible to clindamycin. Clindamycin and erythromycin show parallel resistance. Partial cross resistance has been demonstrated between clindamycin, erythromycin and macrolide antibiotics.

Absorption: Clindamycin hydrochloride is rapidly absorbed from the canine and feline gastrointestinal tract. Dogs and cats orally dosed with therapeutic amounts of clindamycin hydrochloride demonstrated antibacterial serum levels of the drug within 15 minutes post dosing. Canine serum levels: Therapeutically effective serum levels of clindamycin hydrochloride can be maintained by oral dosing at the rate of 2.5 mg/lb every 12 hours. Dogs orally dosed with clindamycin hydrochloride at 2.5 mg/lb every 12 hours during a 72-hour dosing regimen continuously maintained antibacterial serum levels of the drug. This same study revealed that average peak serum concentrations occurred 1 hour and 15 minutes after dosing. The biological half-life for clindamycin hydrochloride in dog serum was about 5 hours. There was no bioactivity accumulation after a regimen of multiple oral doses. Feline serum levels: Therapeutically effective serum levels of clindamycin can be maintained by oral dosing at the rate of 5 to 10 mg/lb body weight once every 24 hours. The average peak serum concentration of clindamycin occurs about 1 hour after oral administration. The terminal half-life of clindamycin in feline serum is approximately 7.5 hours. Minimal

accumulation occurs after multiple oral doses of clindamycin hydrochloride and steady-state should be achieved by the third dose. Feline tissue levels: Tissue concentrations measured at 10 days (mg/g; means) of clindamycin hydrochloride liquid in cats 2 hours after oral administration at 10 mg/lb bodyweight once every 24 hours for 10 days.

Metabolism and excretion: Extensive studies of the metabolism and excretion of clindamycin hydrochloride administered orally in animals and humans have shown that unchanged drug and bioactive and bioinactive metabolites are excreted in urine and feces. Almost all of the bioactivity detected in serum after ANTIROBE administration is due to the parent molecule (clindamycin). Urine bioactivity, however, reflects a mixture of clindamycin and active metabolites, especially N-dimethyl clindamycin and clindamycin sulfoxide.

DOSAGE AND ADMINISTRATION:

Canine infected wounds, abscesses and dental infections: 2.5 mg/lb, orally, twice a day. Treatment with ANTIROBE may be continued up to a maximum of 28 days if clinical judgment indicates. Treatment of acute infections should not be continued for more than three or four days if no response to therapy is seen.

Dosage schedule:

One 25 mg. ANTIROBE capsule per 10 lbs bodyweight, every 12 hours

One 75 mg. ANTIROBE capsule per 30 lbs bodyweight, every 12 hours.

One 150 mg. ANTIROBE capsule per 60 lbs. bodyweight, every 12 hours.

Canine osteomyelitis: 10 mg/lb bodyweight, orally, once a day. Treatment with ANTIROBE is recommended for a minimum of 28 days. Treatment should not be continued for longer than 28 days if no response to therapy is seen.

Dosage schedule:

One 25 mg. ANTIROBE capsule per 5 lbs. of bodyweight, every 12 hours.

One 75 mg ANTIROBE capsule per 15 lbs. of bodyweight, every 12 hours.

caution in animals receiving such agents. Safety in gestating bitches and queens or breeding male dogs and cats has not been established.

WARNINGS: Not for human use.

TOXICOLOGY:

Rat and dog data: One year oral toxicity studies in rats and dogs at doses of 30, 100 and 300 mg/kg/day (13.6, 45.5 and 136.4 mg/lb/day) have shown clindamycin hydrochloride to be well tolerated. Differences did not occur in the parameters evaluated to assess toxicity when comparing groups of treated animals with contemporary controls. Rats administered clindamycin hydrochloride at 600 mg/kg/day (272.7 mg/lb/day) for six months tolerated the drug well; however, dogs orally dosed at 600 mg/kg/day (272.7 mg/lb/day) vomited, had anorexia and subsequently lost weight. Safety in bitches or breeding males has not been established.

Cat data: The recommended daily therapeutic dose range for clindamycin hydrochloride is 11 to 22 mg/kg/day (5 to 10 mg/lb/day) depending on the severity of the condition. Clindamycin hydrochloride was tolerated with little evidence of toxicity in domestic shorthair cats when administered orally at 10X the minimum recommended therapeutic daily dose (11 mg/kg; 5mg/lb) for 15 days, and at doses up to 5X the minimum recommended therapeutic dose for 42 days. Gastrointestinal tract upset (soft feces to diarrhea) occurred in control and treated cats with emesis occurring at doses 3X or greater than the minimum recommended therapeutic dose (11 mg/kg/day; 5mg/lb/day). Lymphocytic inflammation of the gallbladder was noted in a greater number of treated cats at the 110 mg/kg/day (50 mg/lb/day) dose level than for control cats. No other effects were noted. Safety in gestating queens or breeding male cats has not been established.

SIDE EFFECTS: Side effects occasionally observed in either clinical trials or during clinical use were vomiting and diarrhea.

REFERENCES: Bauer, AW; Kirby, WM; Sherris, JC; Turck, M: Antibiotic susceptibility testing by a standardized single disk method, Am. J. Clin. Path., 45:493-496, 1996. Standardized Disk Susceptibility Test, Federal Register, 37:20527-29, 1972.

PRESENTATION: ANTIROBE capsules are available as:

25 mg, bottles of 600
75 mg, bottles of 200
150 mg, bottles of 100

MANUFACTURED BY: Global Pharm, Inc., CANADA