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ANTIROBE® / ANTIROBE AQUADROPS®



Pharmacia & Upjohn

clindamycin hydrochloride capsules, USP

clindamycin hydrochloride liquid

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

DESCRIPTION

ANTIROBE Capsules and ANTIROBE AQUADROPS Liquid contain 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*.

ANTIROBE Capsules (For Use in Dogs Only):

25 mg Capsule, each yellow and white capsule contains clindamycin hydrochloride equivalent to 25 mg of clindamycin.

75 mg Capsule, each green capsule contains clindamycin hydrochloride equivalent to 75 mg of clindamycin.

150 mg Capsule, each light blue and green capsule contains clindamycin hydrochloride equivalent to 150 mg of clindamycin.

300 mg Capsule, each light blue capsule contains clindamycin hydrochloride equivalent to 300 mg of clindamycin.

ANTIROBE AQUADROPS Liquid (For Use in Dogs and Cats) is a palatable formulation intended for oral administration. Each mL of ANTIROBE AQUADROPS Liquid contains clindamycin hydrochloride equivalent to 25 mg clindamycin; and ethyl alcohol, 8.64%.

CLINICAL PHARMACOLOGY

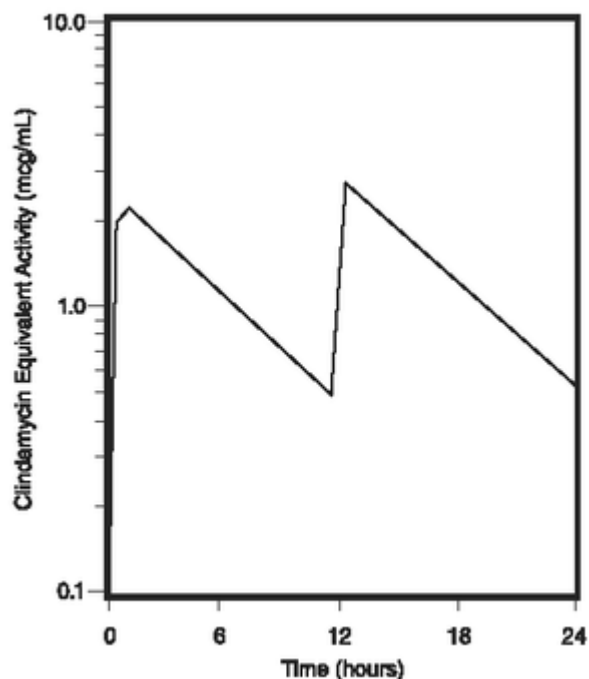
Absorption

Clindamycin hydrochloride is rapidly absorbed from the canine and feline gastrointestinal tract.

Dog Serum Levels

Serum levels at or above 0.5 µg/mL can be maintained by oral dosing at a rate of 2.5 mg/lb of clindamycin hydrochloride every 12 hours. This same study revealed that average peak serum concentrations of clindamycin occur 1 hour and 15 minutes after oral dosing. The elimination half-life for clindamycin in dog serum was approximately 5 hours. There was no bioactivity accumulation after a regimen of multiple oral doses in healthy dogs.

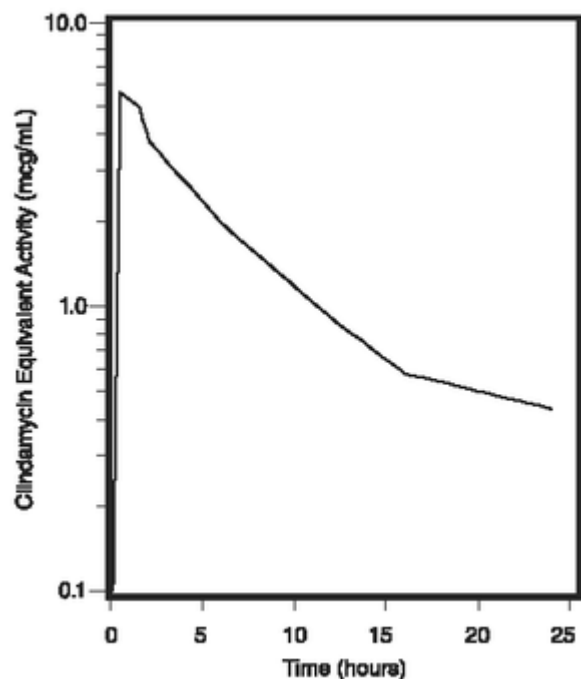
Clindamycin Serum Concentrations 2.5 mg/lb (5.5 mg/kg) After B.I.D. Oral Dose of Antirobe Capsules to Dogs



Cat Serum Levels

Serum levels at or above 0.5 µg/mL can be maintained by oral dosing at a rate of 5 mg/lb of clindamycin hydrochloride liquid every 24 hours. The average peak serum concentration of clindamycin occurs approximately 1 hour after oral dosing. The elimination half-life of clindamycin in feline serum is approximately 7.5 hours. In healthy cats, minimal accumulation occurs after multiple oral doses of clindamycin hydrochloride, and steady-state should be achieved by the third dose.

Clindamycin Serum Concentrations 5 mg/lb (11 mg/kg) After Single Oral Dose of Antirobe Aquadrops to Cats



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 product administration is due to the parent molecule (clindamycin). Urine bioactivity, however, reflects a mixture of clindamycin and active metabolites, especially N-demethyl clindamycin and clindamycin sulfoxide.

Site and Mode of Action

Clindamycin is an inhibitor of protein synthesis in the bacterial cell. The site of binding appears to be in the 50S sub-unit 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

Clindamycin is a lincosaminide antimicrobial agent with activity against a wide variety of aerobic and anaerobic bacterial pathogens. Clindamycin is a bacteriostatic compound that inhibits bacterial protein synthesis by binding to the 50S ribosomal sub-unit. The minimum inhibitory concentrations (MICs) of Gram-positive and obligate anaerobic pathogens isolated from dogs and cats in the United States are presented in Table 1 and Table 2. Bacteria were isolated in 1998-1999. All MICs were performed in accordance with the Clinical and Laboratory Standards Institute (CLSI).

Table 1. Clindamycin MIC Values ($\mu\text{g/mL}$) from Diagnostic Laboratory Survey Data Evaluating Canine Pathogens in the U.S. during 1998-99*

Organism	Number of Isolates	MIC ₅₀	MIC ₈₅	MIC ₉₀	Range
Soft Tissue/Wound ¹					

<i>Staphylococcus aureus</i>	17	0.5	0.5	≥4.0	0.25-≥4.0
<i>Staphylococcus intermedius</i>	28	0.25	0.5	≥4.0	0.125-≥4.0
<i>Staphylococcus</i> spp.	18	0.5	0.5	≥4.0	0.25-≥4.0
Beta-hemolytic streptococci	46	0.5	0.5	≥4.0	0.25-≥4.0
<i>Streptococcus</i> spp.	11	0.5	≥4.0	≥4.0	0.25-≥4.0
Osteomyelitis/Bone ²					
<i>Staphylococcus aureus</i>	20	0.5	0.5	0.5	0.5 ³
<i>Staphylococcus intermedius</i>	15	0.5	≥4.0	≥4.0	0.25-≥4.0
<i>Staphylococcus</i> spp.	18	0.5	≥4.0	≥4.0	0.25-≥4.0
Beta-hemolytic streptococci	21	0.5	2.0	2.0	0.25-≥4.0
<i>Streptococcus</i> spp.	21	≥4.0	≥4.0	≥4.0	0.25-≥4.0
Dermal/Skin ⁴					
<i>Staphylococcus aureus</i>	25	0.5	≥4.0	≥4.0	0.25-≥4.0
<i>Staphylococcus intermedius</i>	48	0.5	≥4.0	≥4.0	0.125-≥4.0
<i>Staphylococcus</i> spp.	32	0.5	≥4.0	≥4.0	0.25-≥4.0
Beta-hemolytic streptococci	17	0.5	0.5	0.5	0.25-0.5

*The correlation between the *in vitro* susceptibility data and clinical response has not been determined.

¹Soft Tissue/Wound: includes samples labeled wound, abscess, aspirate, exudates, draining tract, lesion, and mass

²Osteomyelitis/Bone: includes samples labeled bone, fracture, joint, tendon

³No range, all isolates yielded the same value

⁴Dermal/Skin: includes samples labeled skin, skin swab, biopsy, incision, lip

Table 2. Clindamycin MIC Values (µg/mL) from Diagnostic Laboratory Survey Data Evaluating Feline Pathogens from Wound and Abscess Samples in the U.S. during 1998*

Organism	Number of Isolates	MIC ₅₀	MIC ₉₀	Range
<i>Bacteroides/Prevotella</i>	30	0.06	4.0	≤0.015-4.0
<i>Fusobacterium</i> spp.	17	0.25	0.25	≤0.015-0.5
<i>Peptostreptococcus</i> spp.	18	0.13	0.5	≤0.015-8.0
<i>Porphyromonas</i> spp.	13	0.06	0.25	≤0.015-8.0

*The correlation between the *in vitro* susceptibility data and clinical response has not been determined.

INDICATIONS

ANTIROBE (brand of clindamycin hydrochloride) Capsules (for use in dogs only) and AQUADROPS Liquid (for use in dogs and cats) are indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the specific conditions listed below:

Dogs: Skin infections (wounds and abscesses) due to coagulase positive staphylococci (*Staphylococcus aureus* or *Staphylococcus intermedius*). **Deep wounds and abscesses** due to *Bacteroides fragilis*, *Prevotella melaninogenicus*, *Fusobacterium necrophorum* and *Clostridium perfringens*.

Dental infections due to *Staphylococcus aureus*, *Bacteroides fragilis*, *Prevotella melaninogenicus*, *Fusobacterium necrophorum* and *Clostridium perfringens*. **Osteomyelitis** due to *Staphylococcus aureus*, *Bacteroides fragilis*, *Prevotella melaninogenicus*, *Fusobacterium necrophorum* and *Clostridium perfringens*.

Cats: Skin infections (wounds and abscesses) due to *Staphylococcus aureus*, *Staphylococcus intermedius*, *Streptococcus* spp. **Deep wounds and infections** due to *Clostridium perfringens* and *Bacteroides fragilis*.

Dental infections due to *Staphylococcus aureus*, *Staphylococcus intermedius*, *Streptococcus* spp., *Clostridium perfringens* and *Bacteroides fragilis*.

CONTRAINDICATIONS

ANTIROBE Capsules and ANTIROBE AQUADROPS Liquid are contraindicated in animals with a history of hypersensitivity to preparations containing clindamycin or lincomycin.

Because of potential adverse gastrointestinal effects, do not administer to rabbits, hamsters, guinea pigs, horses, chinchillas or ruminating animals.

WARNINGS

Keep out of reach of children. Not for human use.

PRECAUTIONS

During prolonged therapy of one month or greater, periodic liver and kidney function tests and blood counts should be performed.

The use of ANTIROBE occasionally results in overgrowth of non-susceptible organisms such as clostridia and yeasts. Therefore, the administration of ANTIROBE should be avoided in those species sensitive to the gastrointestinal effects of clindamycin (see **CONTRAINDICATIONS**). Should superinfections occur, appropriate measures should be taken as indicated by the clinical situation.

Patients with very severe renal disease and/or very severe hepatic disease accompanied by severe metabolic aberrations should be dosed with caution, and serum clindamycin levels monitored during high-dose therapy. Clindamycin hydrochloride has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, ANTIROBE should be used with caution in animals receiving such agents.

Safety in gestating bitches and queens or breeding male dogs and cats has not been established.

ADVERSE REACTIONS

Side effects occasionally observed in either clinical trials or during clinical use were vomiting and diarrhea. To report a suspected adverse reaction call 1-800-366-5288.

DOSAGE AND ADMINISTRATION

Dogs

Infected Wounds, Abscesses, and Dental Infections

Oral

2.5-15.0 mg/lb body weight every 12 hours.

Duration

Treatment with ANTIROBE products 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

Capsules

ANTIROBE 25 mg, administer 1-6 capsules every 12 hours for each 10 pounds of body weight.

ANTIROBE 75 mg, administer 1-6 capsules every 12 hours for each 30 pounds of body weight.

ANTIROBE 150 mg, administer 1-6 capsules every 12 hours for each 60 pounds of body weight.

ANTIROBE 300 mg, administer 1-6 capsules every 12 hours for each 120 pounds of body weight.

Liquid

ANTIROBE AQUADROPS, administer 1-6 mL/10 lbs body weight every 12 hours.

Dogs

Osteomyelitis

Oral

5.0-15.0 mg/lb body weight every 12 hours.

Duration

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

Capsules

ANTIROBE 25 mg, administer 2-6 capsules every 12 hours for each 10 pounds of body weight.

ANTIROBE 75 mg, administer 2-6 capsules every 12 hours for each 30 pounds of body weight.

ANTIROBE 150 mg, administer 2-6 capsules every 12 hours for each 60 pounds of body weight.

ANTIROBE 300 mg, administer 2-6 capsules every 12 hours for each 120 pounds of body weight.

Liquid

ANTIROBE AQUADROPS, administer 2-6 mL/10 lbs body weight every 12 hours.

Cats

Infected Wounds, Abscesses, and Dental Infections

5.0 - 15.0 mg/lb body weight once every 24 hours depending on the severity of the condition.

Duration

Treatment with ANTIROBE AQUADROPS Liquid may be continued up to a maximum of 14 days if clinical judgment indicates. Treatment of acute infections should not be continued for more than three to four days if no clinical response to therapy is seen.

Dosage Schedule

ANTIROBE AQUADROPS, to provide 5.0 mg/lb, administer 1 mL/5 lbs body weight once every 24 hours; to provide 15.0 mg/lb, administer 3 mL/5 lbs body weight once every 24 hours.

ANIMAL SAFETY SUMMARY

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 capsules 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. At necropsy these dogs had erosive gastritis and focal areas of necrosis of the mucosa of the gallbladder.

Safety in gestating bitches or breeding males has not been established.

Cat Data

The recommended daily therapeutic dose range for clindamycin hydrochloride (ANTIROBE AQUADROPS Liquid) is 11 to 33 mg/kg/day (5 to 15 mg/lb/day) depending on the severity of the condition. Clindamycin hydrochloride (ANTIROBE AQUADROPS Liquid) 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; 5 mg/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; 5 mg/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.

STORAGE

Store at controlled room temperature 20° to 25°C (68° to 77°F).

HOW SUPPLIED

ANTIROBE Capsules are available as:

25 mg - bottles of 600	NDC 0009-3043-01
75 mg - bottles of 200	NDC 0009-3044-01
150 mg - bottles of 100	NDC 0009-3045-01
150 mg - blister packages of 100	NDC 0009-3045-08
300 mg - blister packages of 100	NDC 0009-5015-01

NADA #120-161, Approved by FDA

ANTIROBE AQUADROPS Liquid is available as 20 mL filled in 30 mL bottles (25 mg/mL) supplied in packers containing 12 cartoned bottles with direction labels and calibrated dosing droppers.	NDC 0009-3179-01.
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NADA #135-940, Approved by FDA

To request a material safety data sheet (MSDS), call 1-800-733-5500.

ANTIROBE AQUADROPS

Distributed by: **Pharmacia & Upjohn Company**, Division of Pfizer Inc, New York, NY 10017

ANTIROBE Capsules

Made in Canada

Distributed by: **Pharmacia & Upjohn Company**, Division of Pfizer Inc, New York, NY 10017

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