

ANADA#200-291, Approved by FDA

Clinsol™

brand of clindamycin hydrochloride liquid

DESCRIPTION

Clinsol™ (clindamycin hydrochloride) Liquid 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*.

Clinsol (clindamycin hydrochloride) Liquid is a palatable formulation intended for oral administration to dogs and cats. Each mL of Clinsol (clindamycin hydrochloride) Liquid contains clindamycin hydrochloride equivalent to 25 mg clindamycin; and ethyl alcohol 8.64%.

ACTIONS

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: 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 gram negative bacilli, including: *Bacteroides* species, *Fusobacterium* species.

Anaerobic gram positive nonsporeforming bacilli, including: *Propionibacterium*, *Eubacterium*, *Actinomyces* species.

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 ? 3.2 ? g/mL	Resistant ? 4.0 ? 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 for the 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.

PHARMACOLOGY

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 hours 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.

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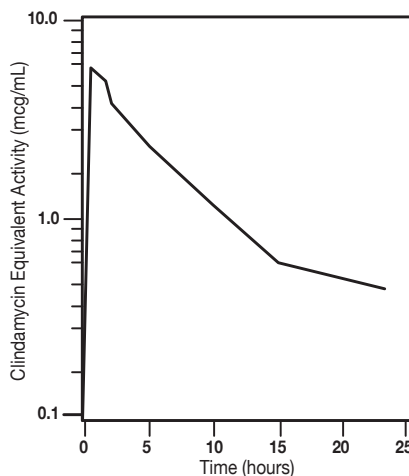
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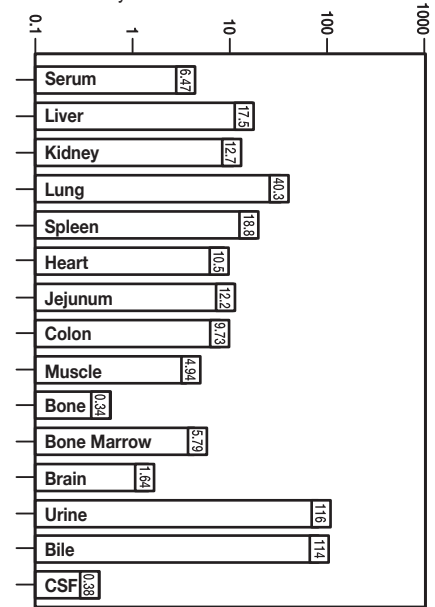
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Feline Serum Levels: Therapeutically effective serum levels of clindamycin can be maintained by oral dosing at the rate of 5 to 10 mg/lb body weight once every 24 hours. The average peak serum concentration of clindamycin occurs about 1 hour after 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.

Clindamycin Serum Concentrations
5 mg/lb (11 mg/kg) After Single Oral Dose of
Clindamycin Hydrochloride Liquid



Feline Tissue Levels: Tissue concentrations measured at 10 days (?g/g; means) of clindamycin hydrochloride liquid in cats 2 hours after oral administration at 10 mg/lb body weight 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 clindamycin hydrochloride 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.

TOXICOLOGY AND SAFETY

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 gestating bitches or breeding males has not been established.

Cat Data: The recommended daily therapeutic dose range for clindamycin hydrochloride liquid is 11 to 22 mg/kg/day (5 to 10 mg/lb/day) depending on the severity of the condition. Clindamycin hydrochloride 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.

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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.

INDICATIONS

Dogs: Aerobic bacteria: Clinsol (clindamycin hydrochloride) Liquid 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: Clinsol (clindamycin hydrochloride) Liquid is indicated for the treatment of soft tissue infections (deep wounds and abscesses), dental infections and osteomyelitis caused by or associated with susceptible strains of *Bacteroides fragilis*, *Bacteroides melaninogenicus*, *Fusobacterium necrophorum* and *Clostridium perfringens*. (See Microbiology section for additional information.)

Cats: Aerobic bacteria: Clinsol (clindamycin hydrochloride) Liquid 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: Clinsol (clindamycin hydrochloride) Liquid 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*. (See Microbiology section for additional information.)

IN VITRO SUSCEPTIBILITY TESTING

Susceptibility tests should be done on samples collected prior to initiation of therapy with Clinsol (clindamycin hydrochloride) Liquid. Clindamycin susceptibility testing is performed by using CLEOCIN Susceptibility Disks (clindamycin 2 mcg) and CLEOCIN Susceptibility Powder 20 mg. A standardized disk testing procedure* is recommended for determining susceptibility of aerobic bacteria to clindamycin. A description is contained in the CLEOCIN Susceptibility Disk insert. Using this method, the laboratory can designate isolates as resistant, intermediate, or susceptible. Tube or agar dilution methods may be used for aerobic and anaerobic bacteria. When the directions in the CLEOCIN Susceptibility Powder insert are followed, a MIC (minimal inhibitory concentration) of 1.6 mcg/mL may be considered susceptible; MICs of 1.6 to 4.8 mcg/mL may be considered intermediate and MICs greater than 4.8 mcg/mL may be considered resistant.

* Bauer, AW; Kirby, WM; Sherris, JC; Turck, M: Antibiotic susceptibility testing by a standardized single disk method. *Am. J. Clin. Path.*, 45: 493-496, 1966. Standardized Disk Susceptibility Test, *Federal Register*, 37: 20527-29, 1972.

CONTRAINDICATIONS

Clinsol (clindamycin hydrochloride) Liquid is contraindicated in animals with a history of hyper-sensitivity 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

Not for human use.

PRECAUTIONS

Clinsol (clindamycin hydrochloride) Liquid should be prescribed with caution in atopic animals.

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

The use of clindamycin hydrochloride occasionally results in overgrowth of non-susceptible organisms such as clostridia and yeasts. Therefore, the administration of clindamycin hydrochloride 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 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, clindamycin hydrochloride 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.

SIDE EFFECTS

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

DOSAGE AND ADMINISTRATION

Canine Infected Wounds, Abscesses and Dental Infections

Oral: 2.5 mg/lb body weight every 12 hours. **Duration:** Treatment with clindamycin hydrochloride 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:

Clinsol (clindamycin hydrochloride) Liquid, administer 1 mL/10 lbs body weight every 12 hours.

Canine Osteomyelitis

Oral: 5.0 mg/lb body weight every 12 hours. **Duration:** Treatment with Clinsol (clindamycin hydrochloride) Liquid 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:

Clinsol (clindamycin hydrochloride) Liquid, administer 2 mL/10 lbs body weight every 12 hours.

Feline Infected Wounds and Abscesses and Dental Infections

Oral: 5.0 to 10.0 mg/lb body weight once every 24 hours depending on the severity of the condition.

Duration: Treatment with Clinsol (clindamycin hydrochloride) 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:

Liquid

Clinsol (clindamycin hydrochloride) Liquid, to provide 5.0 mg/lb, administer 1 mL/5 lb body weight once every 24 hours; to provide 10.0 mg/lb, administer 2 mL/5 lb body weight once every 24 hours.

HOW SUPPLIED

Clinsol (clindamycin hydrochloride) Liquid is available as 20 mL filled in 30 mL bottles (25mg/mL) supplied in packers containing 12 cartoned bottles with direction labels and calibrated dosing droppers.

Store at controlled room temperature 15°-30°C (59°-86° F).

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

**Manufactured for: Virbac AH, Inc. • P.O. Box 162059
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