ANADA 200-291, Approved by FDA

CLINSOL® Liquid

brand of clindamycin hydrochloride liquid

DESCRIPTION

CLINSOL® 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 Liquid (For Use in Dogs and Cats) is a palatable formulation intended for oral administration. Each mL of CLINSOL 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: 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 National Committee for Clinical Laboratory Standards (NCCLS).

Table 1. Clindamycin MIC Values (µg/mL) from Diagnostic Laboratory Survey Data Evaluating Canine Pathogens in the U.S. during 1998-99[1]

Organism	Number of Isolates	MIC_{50}	MIC_{85}	MIC_{90}	Range
Soft Tissue/Wound[2]					
Staphylococcus aureus	17	0.5	0.5	≥4.0	0.25-≥4.0
Staphylococcus intermedius	28	0.25	0.5	≥4.0	0.125-≥4.0
Staphylococcus spp.	18	0.5	0.5	≥4.0	.025-≥4.0
Beta-hemolytic streptococci	46	0.5	0.5	≥4.0	0.25-≥4.0
Streptococcus spp.	11	0.5	≥4.0	≥4.0	0.25-≥4.0
Osteomyelitis/Bone[3]					
Staphylococcus aureus	20	0.5	0.5	0.5	0.5[4]
Staphylococcus intermedius	15	0.5	≥4.0	≥4.0	0.25-≥4.0
Staphylococcus 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
Streptococcus spp.	21	≥4.0	≥4.0	≥4.0	0.25-≥4.0
Dermal/Skin[5]					
Staphylococcus aureus	25	0.5	≥4.0	≥4.0	0.25-≥4.0
Staphylococcus intermedius	48	0.5	≥4.0	≥4.0	0.125-≥4.0
Staphylococcus 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

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

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

[3] Osteomyelitis/Bone: includes samples labeled bone, fracture, joint, tendon

[4] No range, all isolates yielded the same value

[5] Dermal/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[1]

Organism	Number of Isolates	MIC_{50}	MIC_{90}	Range
Bacteroides/ Prevotella	30	0.06	4.0	≤0.015-4.0
Fusobacterium spp.	17	0.25	0.25	≤0.015-0.5
Peptostrepto-coccus spp.	18	0.13	0.5	≤0.015-8.0
Porphyromonas spp.	13	0.06	0.25	≤0.015-8.0

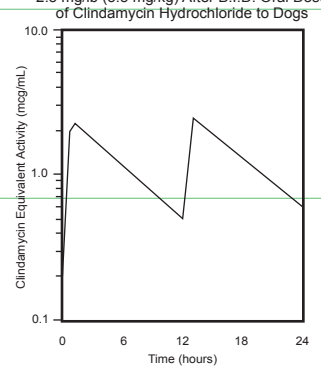
[1] The correlation between the *in vitro* susceptibility data and clinical response has not been determined.

PHARMACOLOGY

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

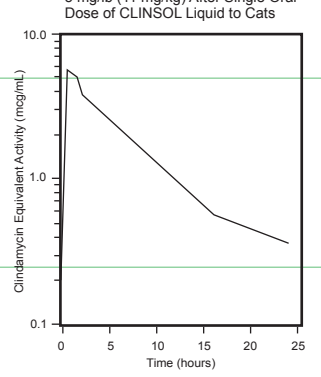
Dog Serum Levels: Serum levels at or above 0.5 µg/mL can be maintained by oral dosing at a rate of 2.5 mg/lb of clindamycin hydrochloride every 12 hours. This same study revealed that average peak serum concentrations of clindamycin occur 1 hour and 15 minutes after oral dosing. The elimination half-life 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 Clindamycin Hydrochloride 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 CLINSOL Liquid 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 clindamycin hydrochloride 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.

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 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 gall bladder.

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

Cat Data: The recommended daily therapeutic dose range for clindamycin hydrochloride (CLINSOL® Liquid) is 11 to 33 mg/kg/day (5 to 15 mg/lb/day) depending on the severity of the condition. Clindamycin hydrochloride (CLINSOL 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 (11mg/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 dose level than for control cats. No other effects were noted. Safety in gestating queens or breeding male cats has not been established.

INDICATIONS

CLINSOL Liquid (for use in dogs and cats) is 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 ecrophorum* and *Clostridium perfringens.*
Dental infections due to *Staphyloccus aureus, Bacteroides fragilis, Prevotella melaninogenicus, Fusobacterium necrophorum* and *Clostridium perfringens.*
Osteomyelitis due to *Staphylococcus aureus, Bacteroides fragilis, Prevotella*

melaninogenicus, Fusobacterium necrophorum and *Clostridium pefringens.*

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

CONTRAINDICATIONS

CLINSOL Liquid is 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 clindamycin hydrochloride occasionally results in overgrowth of non-susceptible organisms such as clostridia and yeasts. Therefore, the administration of CLINSOL Liquid 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, CLINSOL Liquid 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 adverse reactions or a suspected adverse reaction, call 1-800-338-3659.

DOSAGE AND ADMINISTRATION

Dogs:
Infected Wounds, Abscesses, and Dental Infections

Oral: 2.5-15.0 mg/lb (1-6 mL/10 lbs) body weight every 12 hours.

Duration: Treatment with clindamycin hydrochloride 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 Liquid, administer 1-6 mL/10 pounds body weight every 12 hours.

Dogs:
Osteomyelitis

Oral: 5.0-15.0 mg/lb (2-6 mL/10 lbs) body weight every 12 hours.

Duration: Treatment with clindamycin hydrochloride 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 Liquid, administer 2-6 mL/10 pounds body weight every 12 hours.

Cats:
Infected Wounds, Abscesses, and Dental Infections

5.0-15.0 mg/lb (1-3 mL/5 lbs) body weight once every 24 hours depending on the severity of the condition.

Duration: Treatment with clindamycin hydrochloride 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:
CLINSOL Liquid, 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.

HOW SUPPLIED

CLINSOL 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-051311-500-25.

ANADA #200-291, Approved by FDA

To report a suspected adverse reaction or to request a material safety data sheet (MSDS), call 1-800-338-3659.

Store at controlled room temperature 20˚ to 25˚ C (68˚ to 77˚ F) [see USP].

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

Mfd. by
Virbac AH, Inc.
Fort Worth, TX 76137-4611, USA

10/12

301615-03

CLINSOL is a registered trademark of Virbac AH, Inc.

SIGNOFF & FILE INFO

Virbac ANIMAL HEALTH

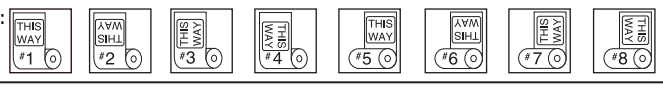
Colors: Black

Product Name:	Clinsol 25mg Liquid (U.S.)	File Name:	301615-03 Clinsol 20ml Insert.ai
Product Size:	20mL	Trim Size:	W: 9" x H: 5-7/8"
Component No.:	301615	Corner Radius:	N/A
Revision No.:	03	Material:	White Paper
Product No.:	902520	Material Specs:	
Product UPC:	N/A	Colors:	1 Flat Color
UPC 14:	N/A	Date:	10/11/12
Country:	USA		

Product Implementation Direction:
☐ Mandatory Change: Effective Date_____ ☐ Revision Update Only (Use up current inventory)
Destroy Inventory: ☐ Immediately ☐ On effective date ☐ Product Group/Brand Change

Notes:

Unwind Format for Labels: N/A



24

SIGN WITHIN 24 HOURS
OR PASS ON TO ANOTHER PERSON ON LIST

Product Manager:_____ Date:_____
Marketing Director:_____ Date:_____
Regulatory:_____ Date:_____
R&D:_____ Date:_____
Business Development:_____ Date:_____
Formulations:_____ Date:_____
Manufacturing:_____ Date:_____
Quality Assurance:_____ Date:_____
Translation:_____ Date:_____
Supply Chain:_____ Date:_____
Rev 5/12 Project Manager:_____ Date:_____