HFA-305

Date of Approval AUG 26 2002

FREEDOM OF INFORMATION SUMMARY

Original ANADA 200-291

Clindamycin Hydrochloride Liquid

(Dogs and cats)

Sponsored by:

Delmarva Laboratories, Inc.
Suite 106
1500 Huguenot Road
Midlothian, VA 23113

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

ANADA:	200-291
Sponsor:	Delmarva Laboratories, Inc. Suite 106 1500 Huguenot Road Midlothian, VA 23113
Generic Name:	Clindamycin Hydrochloride Liquid
Trade Name:	Clinsol®
Dosage Form:	Liquid
How Supplied:	20 mL bottles
How Dispensed:	Rx
Amount of Active Ingredients:	25 mg/mL clindamycin HCL
Route of Administration:	Oral
Species:	Dogs and cats
Pharmacological Category:	Antibacterial
Labeled Dosage & Indications for Use:	**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.*

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), dental infections caused by or associated with susceptible strains of *Clostridium perfringens* and *Bacteroides fragilis.*

Dosage Schedule:

Dogs: 2.5 mg/lb body weight every 12 hours for a maximum of 28 days for the treatment of canine infected wounds, abscesses and dental infections.
5.0 mg/lb body weight every 12 hours for a maxmum of 28 days for the treatment of osteomyelitis.

Cats: 5.0 to 10.0 mg/lb body weight once every 24 hours for a maximum of 14 days depending on severity of the condition.

Pioneer Product/ Listed Product:	Antirobe® Liquid NADA 135-940 (Pharmacia & Upjohn)

2. TARGET ANIMAL SAFETY and DRUG EFFECTIVENESS

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act, (53 FR 50460, December 15, 1988, First GADPTRA Policy Letter) an abbreviated new animal drug application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety data, drug effectiveness data, and human food safety data (other than tissue residue data) are not required for approval of an ANADA. An ANADA relies on the target animal safety, drug effectiveness, and human food safety data in the pioneer's new animal drug application. Ordinarily the ANADA sponsor is required to show that the generic product is bioequivalent to the pioneer. ANADAs for drug products for food-producing animals will generally be

required to include bioequivalence and tissue residue studies.

A tissue residue study will generally be required to accompany clinical end-point and pharmacologic end-point bioequivalence studies, and blood level bioequivalence studies that can not quantify the concentration of the drug in blood throughout the established withdrawal period. For certain dosage forms, the agency will grant a waiver from conducting an *in vivo* bioequivalence study (55 FR 24645 June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October, 2000).

Based upon the formulation characteristics of the generic product, Delmarva Laboratories, Inc. was granted a waiver on May 16, 1997, from conducting an *in vivo* bioequivalence study for Clinsol®. The generic and pioneer products are solutions that contain the same active and inactive ingredients in the same concentrations .

3. HUMAN SAFETY:

Clinsol® is intended for use only in dogs and cats, which are non-food animals. Because this new animal drug is not intended for use in food-producing animals, data on human safety pertaining to drug residues in food were not required for approval of this ANADA.

Human Warnings are provided on the product label as follows:

"For Animal use only."

"Keep Out of Reach of Children."

Human Safety Relative to Possession, Handling, and Administration: Labeling contains adequate caution/warning statements.

4. AGENCY CONCLUSIONS:

This Abbreviated New Animal Drug Application filed under section 512(b) of the Federal Food, Drug, and Cosmetic (FFD&C) Act satisfies the requirements of section 512(n) of the Act and demonstrates that Clinsol®, when used under the proposed conditions of use, is safe and effective for the labeled indications.

The Three-year Exclusivity period for the feline claims granted to the pioneer ended on October 7, 1999. No new data was required for addition of the feline claims.

5. LABELING:

Attachments: **Pioneer Labeling:**

1 common package Insert for Clindamycin HCl capsules & drops
25 mg, 75 mg and 150 mg bottle labels

Generic Labeling:

20 mL bottle label, carton, and package insert

Copies of applicable labels may be obtained by writing to the:

Food and Drug Administration
Freedom of Information Staff (HFI-35)
5600 Fishers Lane
Rockville, MD 20857

Or requests may be sent via fax to: (301) 443-1726. If there are problems sending a fax, call (301) 827-6567.

Pharmacia
&Upjohn

in
ules

Aquadrops®
in hydrochloride liquid

0813805708

0813805708

Antirobe

brand of clindamycin hydrochloride capsules

Antirobe Aquadrops

brand of clindamycin hydrochloride liquid

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:

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

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

150 mg Capsule, each blue and white capsule (in bottles) or blue and green capsule (in blister packages) contains clindamycin hydrochloride equivalent to 150 mg of clindamycin.

ANTIROBE AQUADROPS Liquid is a palatable formulation intended for oral administration to dogs and cats. Each mL of ANTIROBE AQUADROPS 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.

Antirobe

brand of clindamycin hydrochloride capsules

Antirobe Aquadrops

brand of clindamycin hydrochloride liquid

OVERALL SUSCEPTIBILITY TO CLINDAMYCIN OF ANAEROBES ISOLATED FROM CANINE LESIONS. DATA OBTAINED FROM THREE VETERINARY DIAGNOSTIC LABORATORIES.

	Susceptible ≤3.2 µg/mL	Resistant ≥4.0 µg/mL
All Isolates	122/137 (89%)	15/137 (11%)
Clostridium spp.	41/49 (84%)	8/49 (16%)
Bacteroides spp.	42/46 (91%)	4/46 (9%)
Fusobacterium spp.	16/16 (100%)	0/16 (0%)
Peptostreptococcus spp.	15/16 (94%)	1/16 (6%)
Actinomyces spp.	5/6 (83%)	1/6 (17%)
Propionibacterium 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 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.[3]

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

Antirobe

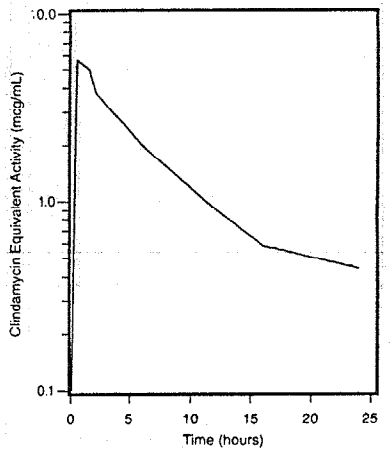
brand of clindamycin hydrochloride capsules

Antirobe Aquadrops

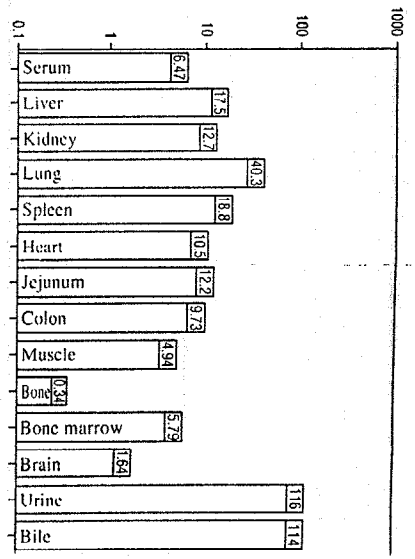
brand of clindamycin hydrochloride liquid

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



Feline Tissue Levels: Tissue concentrations measured at 10 days (µg/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.



Antirobe

brand of clindamycin hydrochloride capsule

Antirobe Aquadrops

brand of clindamycin hydrochloride liquid

METABOLISM AND EXCRETION

Extensive studies of the metabolism an excretion of clindamycin hydrochloride adminis tered orally in animals and humans have show that unchanged drug and bioactive and bioinac tive metabolites are excreted in urine and feces Almost all of the bioactivity detected in serur after ANTIROBE product administration is du to the parent molecule (clindamycin). Urin bioactivity, however, reflects a mixture of clir damycin and active metabolites, especiall N-dimethyl clindamycin and clindamycin sulfoxide

TOXICOLOGY AND SAFETY

Rat and Dog Data: One year oral toxicit studies in rats and dogs at doses of 30, 100 an 300 mg/kg/day (13.6, 45.5 and 136.4 mg/lb/day have shown clindamycin hydrochloride to b well tolerated. Differences did not occur in th parameters evaluated to assess toxicity whe comparing groups of treated animals with cor temporary controls. Rats administered clin damycin hydrochloride at 600 mg/kg/day (272. mg/lb/day) for six months tolerated the dru well; however, dogs orally dosed at 60 mg/kg/day (272.7 mg/lb/day) vomited, ha anorexia, and subsequently lost weight.

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

Cat Data: The recommended daily therapeut dose range for clindamycin hydrochloric (ANTIROBE AQUADROPS Liquid) is 11 to 2 mg/kg/day (5 to 10 mg/lb/day) depending on th severity of the condition. Clindamyc hydrochloride (ANTIROBE AQUADROP Liquid) was tolerated with little evidence of tox city in domestic shorthair cats when admini tered orally at 10x the minimum recommende therapeutic daily dose (11 mg/kg; 5 mg/lb) f 15 days, and at doses up to 5x the minimu recommended therapeutic dose for 42 day Gastrointestinal tract upset (soft feces to dia rhea) occurred in control and treated cats wi emesis occurring at doses 3x or greater tha the minimum recommended therapeutic dos (11 mg/kg/day; 5 mg/lb/day). Lymphocyt inflammation of the gallbladder was noted in greater number of treated cats at the 11 mg/kg/day (50 mg/lb/day) dose level than f control cats. No other effects were noted. Safe in gestating queens or breeding male cats h not been established.

INDICATIONS

Dogs

Aerobic bacteria: ANTIROBE Capsules ar ANTIROBE AQUADROPS Liquid are indicate for the treatment of soft tissue infectior (wounds and abscesses), dental infections ar osteomyelitis caused by susceptible strains *Staphylococcus aureus.*

Anaerobic bacteria: ANTIROBE Capsules ar ANTIROBE AQUADROPS Liquid are indicate for the treatment of soft tissue infections (dee

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: ANTIROBE AQUADROPS 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: ANTIROBE AQUADROPS 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 ANTIROBE Capsules and ANTIROBE AQUADROPS 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.

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

Not for human use.

*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.

Antirobe
brand of clindamycin hydrochloride capsules
Antirobe Aquadrops
brand of clindamycin hydrochloride liquid

PRECAUTIONS

ANTIROBE Capsules and ANTIROBE AQUADROPS 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 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.

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 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 capsule every 12 hours for each 10 pounds of body weight.
ANTIROBE 75 mg, administer 1 capsule every 12 hours for each 30 pounds of body weight.
ANTIROBE 150 mg, administer 1 capsule every 12 hours for each 60 pounds of body weight.

Liquid

ANTIROBE AQUADROPS, 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 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.

Antirobe
brand of clindamycin hydrochloride capsules
Antirobe Aquadrops
brand of clindamycin hydrochloride liquid

Dosage Schedule:

Capsules

ANTIROBE 25 mg, administer 1 capsule every 12 hours for each 5 pounds of body weight.
ANTIROBE 75 mg, administer 1 capsule every 12 hours for each 15 pounds of body weight.
ANTIROBE 150 mg, administer 1 capsule every 12 hours for each 30 pounds of body weight.
NADA #120-161, Approved by FDA

Liquid

ANTIROBE AQUADROPS, 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 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:

Liquid

ANTIROBE AQUADROPS, 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.
NADA #135-940, Approved by FDA

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

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.

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.

ANTIROBE AQUADROPS
Made by
Pharmacia & Upjohn Company
Kalamazoo, MI 49001, USA

ANTIROBE Capsules
Made in Canada for
Pharmacia & Upjohn Company
Kalamazoo, MI 49001, USA
By **Global Pharm Inc.**
Don Mills, Ontario, M3B 1Y5, CANADA

Revised March 1999

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692074

Directions _____

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Approved for use in canines and felines.
Recommended canine dosage:
For therapy of wounds, abscesses and dental infections, orally administer 2.5 mg/lb (1 mL/10 lbs) body weight every 12 hours.
For therapy of osteomyelitis orally administer 5.0 mg/lb (2 mL/10 lbs) body weight every 12 hours.
Recommended feline dosage:
For therapy of wounds, abscesses and dental infections, orally administer 1-2 mL/5 lb body weight once every 24 hours depending on the severity of the condition. See package insert for complete product information.
Warning—Not for human use.
Store at controlled room temperature 20° to 25° C (68° to 77° F) [see USP].
Each mL contains: Clindamycin hydrochloride equivalent to 25 mg clindamycin; and ethyl alcohol, 8.64%.

812 678 205

This carton contains 20 mL of ANTIROBE AQUADROPS Liquid in a 30 mL bottle.

CARTON MADE FROM 100% RECYCLED PAPERBOARD MINIMUM 35% POST CONSUMER CONTENT

Upjohn

773454

NDC 0009-3179-01 20 mL

Antirobe Aquadrops®

Liquid

clindamycin hydrochloride liquid

Equivalent to

25 mg per mL

clindamycin

For Use in Animals Only

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian. NADA #135-940, Approved by FDA

Upjohn

R-PC

NDC 0009-3179-01 20 mL

Antirobe Aquadrops®
Liquid
clindamycin hydrochloride liquid
Equivalent to
25 mg per mL
clindamycin

For Use in Animals Only
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Upjohn

NDC 0009-3179-01
Liquid
Antirobe Aquadrops®
Equivalent to
25 mg per mL
clindamycin

20 mL

Approved for use in canines and felines.
Recommended canine dosage: For therapy of wounds, abscesses and dental infections, orally administer 2.5 mg/lb (1 mL/10 lbs) body weight every 12 hours. For therapy of osteomyelitis orally administer 5.0 mg/lb (2 mL/10 lbs) body weight every 12 hours.
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Each mL contains: Clindamycin hydrochloride equivalent to clindamycin 25 mg; and ethyl alcohol, 8.64%.
812 682 104

005

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)-chloro-substitution 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.

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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.

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Fusobacterium spp.	16/16 (100%)	0/16 (0%)
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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

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 judgement 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 (clindamycin hydrochloride) Liquid, administer 5.0 mg/lb, administer 1 mL/5 lb body weight 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.

ANADA#200-291, Approved by FDA

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: Delmarva Laboratories, Inc.
Midlothian, VA 23113

By: Diamond Animal Health, Inc.
Des Moines, IA 50317

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. 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.

Propionibacterium 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.

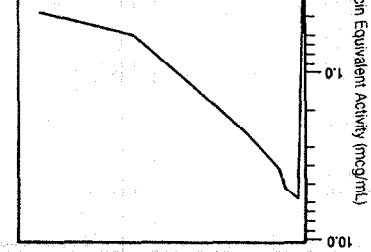
PHARMACOLOGY

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.

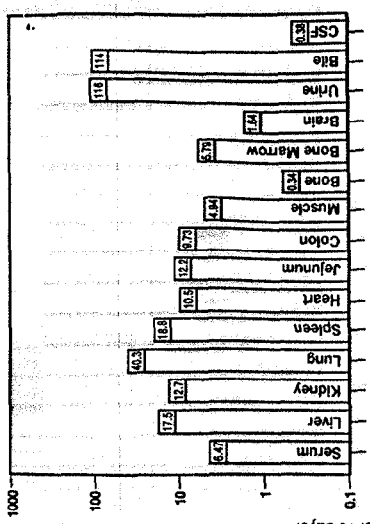
Canine Serum Levels: Therapeutically effective serum levels of clindamycin hydrochloride can be maintained by oral dosing at the rate of 2.5 mg/lb every 12 hours. Dogs orally dosed with clindamycin hydrochloride at 2.5 mg/lb every 12 hours during a 72 hours dosing regimen continuously maintained antibacterial 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.

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 (µg/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.



Approved for use in canines and felines.

Recommended canine dosage:

For therapy of wounds, abscesses and dental infections, orally administer 2.5 mg/lb (1 mL/10 lbs) body weight every 12 hours.

For therapy of osteomyelitis orally administer 5.0 mg/lb (2 mL/10 lbs) body weight every 12 hours.

Recommended feline dosage:

For therapy of wounds, abscesses and dental infections, orally administer 1-2 mL/5 lb body weight once every 24 hours depending on the severity of the condition.

See package insert for complete product information.

Warning—Not for human use.

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

Each mL contains: Clindamycin hydrochloride equivalent to 25 mg clindamycin; and ethyl alcohol, 8.64%.

DELMARVA LABORATORIES, INC.

Directions:

Manufactured for:
DELMARVA LABORATORIES, INC.
Midlothian, VA 23113
By: Diamond Animal Health
Des Moines, IA 50317

NDC-59079-501-20 20mL

CLINSOL™

Liquid
clindamycin hydrochloride liquid
Equivalent to
25 mg per mL
clindamycin

For Use In Animals Only

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

ANADA# 200-291, Approved by FDA

DELMARVA LABORATORIES, INC.

This carton contains 20mL of **Clinsol™** (clindamycin hydrochloride liquid) in a 30 mL bottle.

03265

Manufactured for:
DELMARVA LABORATORIES, INC.
Midlothian, VA 23113
By: Diamond Animal Health
Des Moines, IA 50317

:YSTONE#76187 PMS 235 BLACK DIE

G00022

102

Clinsol® 25 mg per mL Liquid
PMS 235 and Black
3" x 1.5" inches

Approved for use in canines and felines.
Recommended canine dosage: For therapy of wounds, abscesses and dental infections, orally administer 2.5 mg/lb (1 mL/10 lbs) body weight every 12 hours.
For therapy of osteomyelitis orally administer 5.0 mg/lb (2 mL/10 lbs) body weight every 12 hours.
Recommended feline dosage: For therapy of wounds, abscesses and dental infections, orally administer 1-2 mL/5 lb body weight once every 24 hours depending on the severity of the condition.
See package insert for complete product information.
Warning—Not for human use.
Store at controlled room temperature 15° to 30°C (59° to 86°F)
Each mL contains: Clindamycin hydrochloride equivalent to clindamycin 25 mg and ethyl alcohol, 8.64%.
Manufactured for: Delmarva Laboratories, Inc.
Midlothian, VA 23113
By: Diamond Animal Health, Inc.,
Des Moines, IA 50317 01694

NDC 59079-501-20 20mL

CLINSOL®

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