# LINCOSAMIDES Veterinary—Systemic

This monograph includes information on the following: Clindamycin; Lincomycin.

Some commonly used brand names are:

For veterinary-labeled products—

AmTech Clindamycin Lincomix 50 Feed Medication Hydrochloride Capsules [Lincomycin]

[Clindamycin]

AmTech Clindamycin Lincomix Injectable Hydrochloride Oral [Lincomycin]

Liquid [Clindamycin]

Antirobe [Clindamycin] Lincomix Injectable Solution [Lincomycin]

Antirobe Aquadrops Lincomix 44 Premix
[Clindamycin] [Lincomycin]
Clincaps [Clindamycin] Lincomix 110 Premix
[Lincomycin]

ClindaCure [Clindamycin] Lincomix Soluble Powder

[Lincomycin]

Clinda-Guard
[Clindamycin]

Clindrops [Clindamycin]

Lincomycin 44 Premix
[Lincomycin 44G Premix
[Lincomycin]

Lincocin [Lincomycin] Lincomycin 110 Premix

[Lincomycin]

Lincocin Aquadrops | Lincomycin 110G Premix

[Lincomycin] | [Lincomycin]

Lincocin Injectable | Lincomycin Soluble

[Lincomycin] [Lincomycin]

Lincocin Sterile Solution
[Lincomycin] [Lincomycin]

Lincomix 20 Feed [Lincomycin]

Moorman's LN 10
[Lincomycin]

Lincomix 20 Feed [Lincomycin]

Note: For a listing of dosage forms and brand names by country availability, see the *Dosage Forms* section(s).

Category: Antibacterial (systemic).

#### Indications

Note: Bracketed information in the *Indications* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

#### General considerations

The lincosamides have activity against many gram-positive bacteria and many an aerobic bacteria, but are not effective against most gramnegative organisms.

Lincomycin has been shown to have efficacy against Staphylococcus species, Streptococcus species (except Streptococcus faecalis), Erysipelothrix insidiosa, Leptospira pomona, and Mycoplasma species. {R-3; 4} The activity of lincomycin against obligate anaerobes is seldom addressed in published literature. According to the National Committee for Clinical Laboratory Standards in the United States, clindamycin is the class antibiotic for the lincosamide family and the clindamycin disk is used in in vitro testing to assess susceptibility to both clindamycin and lincomycin {R-31}. Therefore, it is presumed that most anaerobes susceptible to clindamycin would likewise be susceptible to lincomycin, provided compensations for potency and kinetic disposition are made {R-39}.

Clindamycin has a spectrum of activity that includes Staphylococcus species, Streptococcus species (except Streptococcus faecalis), and Mycoplasma species, as well as anaerobic organisms, such as Bacteroides species, Fusobacterium species, Clostridium perfringens (but not necessarily other clostridia), Actinomyces species, Peptostreptococcus species, and many Propionibacterium species.

#### Accepted

- Dysentery, swine (treatment)—*Pigs:* Lincomycin hydrochloride for medicated feed and soluble powder are indicated in the treatment and control of swine dysentery caused by susceptible organisms. {**R-21**; **28**; **38**; **41**; **63**}
- Enteritis, necrotic (treatment)—Chickens: Lincomycin hydrochloride for medicated feed and soluble powder are indicated in the control of necrotic enteritis in chickens caused by susceptible organisms, such as Clostridium perfringens. {R-22; 28; 38; 41; 42; 56}
- Growth promotion and feed efficiency, increased—*Chickens* and *pigs*!: Lincomycin hydrochloride for medicated feed is indicated for increased weight gain in growing-finishing pigs and for increased weight gain and feed efficiency in broiler chickens. {R-38; 63}
- Joint infections (treatment)—*Pigs:* Lincomycin injection is indicated in the treatment of infectious arthritis caused by susceptible organisms, including susceptible *Staphylococcus* species, *Streptococcus* species, *Erysipelothrix rhusiopathiae*, and *Mycoplasma* species. {**R-4**; 5}
- Metritis (treatment) *Dogs:* Lin comycin injection, syrup, and tablets are indicated in the treatment of metritis caused by susceptible organisms. {R-3}
- Osteomyelitis (treatment)—*Dogs:* Clindamycin capsules and oral solution are indicated in the treatment of osteomyelitis caused by susceptible organisms, {R-1; 2} such as *Staphylococcus aureus*.{R-35; 36; 62} Periodontal infections (treatment)—
  - Cats: Clindamycin oral solution is indicated in the treatment of periodontal infections caused by susceptible bacteria {R-2; 30; 62}.
  - Dogs: Clindamycin capsules and oral solution are indicated in the treatment of periodontal infections caused by susceptible bacteria.
    {R-1; 2; 62}
- Porcine proliferative enteropathies (treatment) *Pigs:* Lincomycin hydrochloride for medicated feed is indicated in the control of porcine proliferative enteropathies (ileitis) caused by *Lawsonia intracellularis* **{R-38}**.
- Pneumonia, bacterial (treatment)—*Pigs:* Lincomycin injection<sup>1</sup> and lincomycin hydrochloride for medicated feed are indicated in the treatment of pneumonia caused by susceptible *Mycoplasma* species. {R-4: 5: 63}
- Respiratory tract infections (treatment)<sup>1</sup>—
  - Cats: Lincomycin injection, syrup, and tablets are indicated in the treatment of respiratory tract infections caused by susceptible organisms. {R-3}
  - Dogs: Lincomycin injection, syrup, and tablets are indicated in the treatment of respiratory tract infections caused by susceptible organisms. {R-3}
- Skin infections (treatment)<sup>1</sup>—*Dogs*: Lincomycin injection, syrup, and tablets are indicated and [clindamycin] {**R-20**} is effective in the treatment of skin infections, such as pustular dermatitis, caused by susceptible organisms. {**R-3**} To assure efficacy in the treatment of skin infections, underlying primary disorders, such as allergic inhalant dermatitis, should be identified and controlled {**R-1**; 30}.
- Soft tissue infections (treatment)—
  - Cats: Clindamycin oral solution and lincomycin injection<sup>1</sup>, syrup <sup>1</sup>, and tablets<sup>1</sup> are indicated in the treatment of soft tissue infections, including abscesses, caused by susceptible organisms. {R-2; 3; 30; 62}
  - Dogs: Clindamycin capsules and oral solution, and lincomycin injection<sup>1</sup>, syrup<sup>1</sup>, and tablets<sup>1</sup> are indicated in the treatment of soft tissue infections, including abscesses and infected wounds, caused by susceptible organisms. {R-1-3; 62}

#### Acceptance not established

- Metritis (treatment)—Dogs: There are insufficient data to confirm specifically the efficacy of [clindamycin]<sup>1</sup> in the treatment of metritis in dogs; however, because lincomycin is indicated for this use, clindamycin can be expected to be at least equally effective {R-15}.
- Osteomyelitis (treatment)—[Cats]<sup>1</sup>: There are insufficient data to confirm specifically the efficacy of clindamycin in the treatment of

- osteomyelitis in cats; however, the safety and predicted antimicrobial efficacy are supported by research. {R-24; 53; 54; 57}
- Respiratory tract infections (treatment)—Cats and dogs: There are insufficient data to confirm specifically the efficacy of [clindamycin]<sup>1</sup> in the treatment of respiratory infections in cats and dogs; however, because lincomycin is indicated for this use, clindamycin can be expected to be at least equally effective {R-15}.
- [Abscesses, laryngeal (treatment)]<sup>1</sup>—Cattle: There are insufficient data to confirm the efficacy and safety of lincomycin injection in the treatment of laryngeal abscesses in cattle. Reports of three cases showed a good response in laryngeal abscesses treated{R-44}.
- [Arthritis, septic (treatment)] Cattle and sheep: There are insufficient data to confirm the efficacy and safety of lincomycin inject ion in the treatment of septic arthritis in cattle and sheep. Case reports of a dozen cases show a resolution of clinical signs in approximately one-half of refractory joint infections treated (mixed infections of streptococci, staphylococci, and Corynebacterium pyogenes). [R-44]
- [Mastitis (treatment)]<sup>1</sup>—Cattle: There are insufficient data to confirm the efficacy and safety of parenteral lincomycin in the treatment of mastitis in cattle; however, there is evidence of distribution into milk in ruminants in concentrations sufficient to treat susceptible infections that are refractory to other antimicrobials. {R-14; 58} Although no studies have been performed to demonstrate the efficacy of lincomycin against gram-positive mastitis pathogens such as Staphylococcus or Corynebacterium, given lincomycin's distribution and the susceptibility patterns of these organisms, lincomycin therapy may be a legitimate choice when other conventional treatments are deemed unlikely to be effective.
- [Toxoplasmosis (treatment)]<sup>1</sup>—Cats: There are insufficient data to establish the efficacy of clindamycin in the treatment of Toxoplasma gondii infection in cats; however, it is considered to have fewer side effects and perhaps to be more effective in treating some aspects of the disease than is pyrimethamine {R-17-19; 34; 59}. Clindamycin may not effectively clear organisms from areas such as the central nervous system in chronically infected animals {R-18} and, in some cases, may be ineffective in resolving clinical signs involving the eye. {R-17}

# **Regulatory Considerations**

U.S.-

Withdrawal times have been established for the use of lincomycin in chickens and pigs (see the *Dosage Forms* section). Lincomycin is not labeled for use in chickens producing eggs for human consumption. {R-4; 38; 42}

#### Canada—

Withdrawal times have been established for the use of lincomycin in chickens and pigs (see the *Dosage Forms* section). Lincomycin is not labeled for use in chickens producing eggs for human consumption. {R-6; 41}

### Chemistry

#### Source:

Clindamycin hydrochloride—7(*S*)-Chloro derivative of lincomycin. {**R-27**}

Lincomycin hydrochloride—Produced by the growth of a member of the *lincolnensis* group of *Streptomyces lincolnensis* (family *Streptomycetaceae*). {R-3}

#### Chemical name:

Clindamycin hydrochloride—L-*threo*-alpha-D-*galacto*-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]amino]-1-thio-, (2*S*-*trans*)-, monohydrochloride. {**R-25**}

Lincomycin hydrochloride—D-*erythro*-alpha-D-*galacto* - Octopyranoside, methyl 6,8-dideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]amino]-1-thio-, monohydrochloride, monohydrate, (2*S-trans*)-. {**R-25**}

<sup>&</sup>lt;sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

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Molecular formula:
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Clindamycin hydrochloride—C<sub>18</sub>H<sub>33</sub>ClN<sub>2</sub>O<sub>5</sub>S·HCl. {R-25} Lincomycin hydrochloride— $C_{18}H_{34}N_{2}O_{6}S\cdot HCl\cdot H_{2}O.$  {R-25}

#### Molecular weight:

Clindamycin hydrochloride—461.44. {R-25} Lincomycin hydrochloride—461.01. {R-25}

#### Description:

Clindamycin Hydrochloride USP—White or practically white, crystalline powder. Is odorless or has a faint mercaptan-like odor. Is stable in the presence of air and light. Its solutions are acidic and are dextrorotatory. {R-26}

Lincomycin Hydrochloride USP—White or practically white, crystalline powder. Is odorless or has a faint odor. Is stable in the presence of air and light. Its solutions are acid and are dextrorotatory. {R-26}

Lincomycin Hydrochloride Injection USP—Clear, colorless to slightly yellow solution, having a slight odor. {R-26}

Clindamycin —7.7. {**R-14**} Lincomycin—7.6. {R-14}

# Solubility:

Clindamycin Hydrochloride USP —Freely soluble in water, in dimethylformamide, and in methanol; soluble in alcohol; practically insoluble in acetone. {R-26}

Lincomycin Hydrochloride USP—Freely soluble in water; soluble in dimethylformamide; very slightly soluble in acetone. {R-26}

# Pharmacology/Pharmacokinetics

Mechanism of action/Effect: The lincosamides inhibit protein synthesis in susceptible bacteria by binding to the 50 S ribosomal subunits of bacterial ribosomes and preventing peptide bond formation. {R-43} The lincosamides are usually considered bacteriostatic {R-43}; however, when clindamycin is present at sufficient concentrations, it may act as a bactericidal antibiotic against sensitive organisms. {R-43}

Other actions/effects: Clindamycin may interfere with the attachment and entry of *Toxoplasma gondii* tachyzoites into host cells. {R-33}

**Absorption:** Oral absorption of the lincosamides is rapid, but orally administered lincomycin is less well absorbed than clindamycin. Clindamycin —Oral absorption of clindamycin is high {R-1} and is unaffected by food.

Lincomycin—Oral absorption of lincomycin may be greatly reduced by the presence of food in the stomach. {R-48} Oral absorption:

Pigs-20 to 50%. {R-49} Rats-45 to 60%. {R-49}

Intramuscular absorption: Lincomycin hydrochloride is rapidly absorbed after intramuscular administration. {R-3}

**Distribution:** Clindamycin and lincomycin are widely distributed into most tissues, including respiratory tissue, soft tissue, bones, and joints {R-13; 23; 24}. The lincosamides are weak bases (commercial preparations are acidic) and are very lipid soluble at physiologic pH (7.4). Tissue concentrations may be higher than serum concentrations. **{R-48}** Small amounts are distributed into pancreatic and prostatic secretions. {R-48} There is evidence that clindamycin hydrochloride accumulates in polymorphonuclear granulocytes. {R-20} The lincosamides do not penetrate cerebrospinal fluid (CSF) well; {R-24} however, in healthy cats, concentrations of clindamycin in brain tissue after 10 days of therapy were 10 to 20% of serum concentration and were consistently higher than CSF concentrations. {R-24} Volume of distribution (area)—Intravenous administration:

Clindamycin phosphate—Dogs: 1.4 L per kg (L/kg). {R-16} Lincomycin—Calves:

6 weeks of age-1 to 1.2 L/kg (healthy calves or calves with induced Pasteurella haemolytica pneumonia). {R-46; 47} 9 months of age—1.3 L/kg. {**R-47**}

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Protein binding:
    Clindamycin—Sheep: Moderate (40 to 50%). {R-14; 51}
   Lincomycin-
        Cows—Low to moderate (26 to 46%). {R-52}
       Sheep—Low (30 to 40%). {R-14; 51}
        Note: Human protein binding of lincomycin decreases with
             increased plasma concentrations; the range of protein
             binding varies from low to high.
Biotransformation:
   Clindamycin—Active metabolites of clindamycin measured in urine
       along with parent compound include N-demethylclindamycin and
       clindamycin sulfoxide. {R-1}
   Lincomycin—The percentage of administered lincosamide
       metabolized by the liver is unknown. {R-49}
Half-life: Elimination—Intravenous administration:
   Clindamycin phosphate—Dogs: 3.2 hours. {R-16}
   Lincomycin:
        Calves, newborn to 2 weeks of age—3 hours. {R-47}
        Calves, 4 weeks to 9 months of age—2 to 2.5 hours. {R-46; 47}
Time to peak concentration:
   Clindamycin hydroc hloride-
       Dogs: Oral—1.3 hours (single dose of 5.5 to 11 mg per kg of
           body weight [mg/kg]). {R-1}
        Sheep: Intramuscular—1 hour (dose of 20 mg/kg). {R-14}
   Clindamycin phosphate—Dogs: Intramuscular—1 hour (dose of 11
       mg/kg). {R-16}
   Lincomycin hydrochloride—
       Dogs:
           Intramuscular—10 minutes to 2 hours (dose of 22 mg/kg).
            Oral—2 to 4 hours (dose of 22 mg/kg). {R-3}
       Sheep: Intramuscular—1 hour (dose of 20 mg/kg). {R-14}
Serum concentrations:
    Peak serum concentration—
       Clindamycin hydrochloride: Sheep—Intramuscular: 13.8 mcg/mL
            (single dose of 20 mg/kg). {R-14}
       Clindamycin phosphate: Dogs-Intramuscular: 5.3 mcg/mL (dose
           of 11 mg/kg) {R-16}.
       Lincomycin: Sheep—Intramuscular: 12.6 mcg/mL (dose of 20
           mg/kg). {R-14}
   Serum concentration after multiple dosing—Clindamycin
       hydrochloride (sample 12 hours after the last dose of an every-
       twelve-hour oral dose for 10 days): Cats—{R-53}
           3.5 mcg/mL (dose of 5.5 mg/kg).
            5.4 mcg/mL (dose of 11 mg/kg).
           6.5 mcg/mL (dose of 22 mg/kg).
Duration of action:
    Clindamycin—Cats and dogs: {R-15}
        12 hours, with an oral dose of 11 mg/kg.
        24 hours, with an oral dose of 22 mg/kg.
   Lincomycin—Dogs: Oral—For gram-positive organisms: 6 to 8 hours
       (22 mg/kg dose). {R-3}
   Note: Efficacy studies based on a 22 mg/kg dose every 12 hours for 3
         weeks in dogs show that duration of action for lincomycin is
         sufficient for it to be effective when administered every twelve
        hours {R-20}.
Elimination:
    Parent drug and metabolites are primarily excreted in the urine and
       the bile. {R-1; 3; 24; 48; 49} Small amounts are excreted in
       intestinal contents and pancreatic and prostatic fluids. {R-48}
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When lincomycin is administered orally to dogs, 77% of the dose is excreted in the feces and 14% of the dose is excreted in the urine. When administered intramuscularly, 38% of the dose is excreted

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in the feces and 49% is excreted in the urine. {R-3}
Less clindamycin than lincomycin is excreted in the urine. {R-50}
Clearance—Intravenous administration:
Clindamycin phosphate—Dogs: 5.3 mL per minute per kg (mL/min/kg). {R-16}
Lincomycin—Calves:
6 weeks of age—3.9 to 8.1 mL/min/kg. {R-46}
9 months of age—4.4 mL/min/kg. {R-46}
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#### **Precautions to Consider**

#### Cross-sensitivity and related problems

Animals sensitive to clindamycin may be sensitive to lincomycin and the reverse may also be true.

# Species sensitivity

Chinchillas, guinea pigs, hamsters, horses, ponies, and rabbits: {R-7-9; 11} The use of oral clindamycin or lincomycin is generally contraindicated in these species because of the risk of altering the gastrointestinal microflora and causing serious or fatal enterocolitis and diarrhea. Overgrowth of organisms such as Clostridium or Salmonella species has been suspected as the cause in many species. Cecal Escherichia coli, but not Clostridium species, have been cultured from rabbits showing adverse effects after lincomycin exposure. {R-9} Contamination of feed with lincomycin at or below feed additive concentrations used for pigs has caused severe or fatal diarrhea in rabbits, ponies, and horses. {R-7-9}

Ruminants: Ruminants exposed to oral lincomycin have also been reported to have side effects such as anorexia, ketosis, and sometimes severe diarrhea, {R-10; 12; 55} possibly caused by overgrowth of nonsusceptible bacteria; however, case reports and research studies using parenteral lincomycin have reported that only a small percentage of treated animals developed diarrhea and/or decreased milk production. {R-44-47}

Feeds contaminated with 3 to 24 parts per million (ppm) of lincomycin have caused ketosis and diarrhea in dairy cows {R-12}. After treatment with oral lincomycin for *Campylobacter*, two thirds of a range flock of sheep died; however, the flock had a history of *Salmonella* infections and grazed in an area with some oxalate-containing range plants, both of which were believed to play a role in the losses. {R-10}

# Pregnancy/Reproduction

The safety of clindamycin in pregnant or breeding animals has not been established. {R-1; 2; 13}

When lincomycin was given to pregnant dogs at 50 mg per kg of body weight (mg/kg) per day, no evidence of teratogenic effects on the embryos was seen. {R-3} Also, 75 mg of lincomycin per kg a day administered to breeding male and female rats during a breeding cycle had no observed effect on breeding or teratogenic effects on offspring. {R-3}

#### Lactation

Clindamycin and lincomycin are distributed into milk {R-14} in therapeutic concentrations. {R-40} With constant serum lincomycin concentrations, milk concentrations range from 2.5 to 6.2 times the serum concentration, depending on the pH of the milk. {R-14}

#### Pediatrics

No evidence of side effects was noted in newborn puppies and rats given lincomycin at doses of 30 to 90 mg/kg a day. {R-3}

# Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

» Anesthetics, hydrocarbon inhalation, such as:

Enflurane

Halothane

Isoflurane

Methoxyflurane, or

» Neuromuscular blocking agents

(concurrent use of these medications with clindamycin or lincomycin may enhance the neuromuscular blockade, resulting in respiratory depression or paralysis; {R-1; 48} caution is also recommended during surgery or the postoperative period; treatment with cholinesterase agents or calcium salts may help reverse the blockade {R-48})

#### **Human drug interactions**{R-61}

In addition to the above drug interactions reported in animals, the following drug interactions have been reported in humans, and are included in the human monographs *Clindamycin (Systemic)* and *Lincomycin (Systemic)* in *USP DI Volume I;* these drug interactions are intended for informational purposes only and may or may not be applicable to the use of clindamycin and lincomycin in the treatment of animals:

#### Antidiarrheals, adsorbent

(concurrent use of kaolin - or attapulgite-containing antidiarrheals with oral lincomycin may significantly decrease absorption of oral lincomycin; concurrent use with oral clindamycin may delay absorption; concurrent use should be avoided or patients should be advised to take adsorbent antidiarrheals not less than 2 hours before or 3 to 4 hours after oral lincosamides)

#### Antidiarrheals, antiperistaltic

(antiperistaltic agents, such as opiates, difenoxin, diphenoxylate, or loperamide, may prolong or worsen pseudomembranous colitis by delaying toxin elimination)

# Antimyasthenics

(concurrent use of medications with neuromuscular blocking action may antagonize the effect of antimyasthenics on skeletal muscle; temporary dosage adjustments of antimyasthenics may be necessary to control symptoms of myasthenia gravis during and following concurrent use)

# Chloramphenicol or

# Erythromycins

(may displace clindamycin or lincomycin from or prevent their binding to 50 S subunits of bacterial ribosomes, thus antagonizing the effects of the lincosamides; concurrent use is not recommended)

#### Opioid (narcotic) analgesics

(respiratory depressant effects of drugs with neuromuscular blocking activity may be additive to central respiratory depressant effects of opioid analgesics, possibly leading to increased or prolonged respiratory depression or paralysis [apnea]; caution and careful monitoring of the patient are recommended)

# Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: No significant laboratory value alterations have been reported in animals. Human laboratory value alterations have been reported and are included in this monograph.

# Human laboratory value alterations {R-61}

The following laboratory value alterations have been reported in humans, and are included in the human monographs *Clindamycin (Systemic)* and *Lincomycin (Systemic)* in *USP DI Volume I;* these laboratory value alterations are intended for informational purposes only and may or may not be applicable to the use of clindamycin and lincomycin in the treatment of animals:

With physiology/laboratory test values

Alanine aminotransferase (ALT [SGPT]), serum, and Alkaline phosphatase, serum, and

Aspartate aminotransferase (AST [SGOT]), serum

#### Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

# Risk-benefit should be considered when the following medical problems exist:

» Hepatic function impairment, severe

(because clindamycin and lincomycin are metabolized by the liver {R-1; 49}, it is possible that severe hepatic function impairment could prolong the half-lives of these medications; adjustments in dosage might be required {R-37})

» Hypersensitivity to clindamycin or lincomycin {R-1; 3}

(sensitivity or cross-sensitivity may occur)

» Renal function impairment, severe

(lincomycin is eliminated by the kidneys of dogs to a greater degree than is clindamycin {R-50}; very severe renal impairment may require dosage adjustments)

#### Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; » = major clinical significance):

Culture and susceptibility, in vitro, and

Minimum inhibitory concentration (MIC)

(*in vitro* cultures and MIC tests should be done on samples collected prior to lincosamide administration to determine pathogen susceptibility)

Note: The clindamycin disk is used for *in vitro* susceptibility testing to assess susceptibility to both clindamycin and lincomycin {**R**-31}.

# **Side/Adverse Effects**

Note: The pseudomembranous colitis reported in people as an adverse reaction to lincosamides as well as the colitis and diarrhea side effects reported in chinchillas, guinea pigs, horses, rabbits, and ruminants are considered to be caused by overgrowth of resistant organisms. Resistant *Clostridium* species are suspected, but other organisms or even other mechanisms may also be involved. {R-8-

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and, for humans, symptoms in parentheses where appropriate)—not necessarily inclusive:

#### Those indicating need for medical attention

Incidence more frequent

Chinchillas, guinea pigs, hamsters, horses, ponies, and rabbits {R-7-9;

11}

*Enterocolitis* (anorexia; collapse; dehydration; diarrhea, watery and sometimes hemorrhagic)

Incidence less frequent

Cats and dogs

# Anorexia; diarrhea; vomiting {R-1; 3; 54}

Note: Anorexia, diarrhea, and vomiting in cats and dogs are believed to result from local irritation because side effects have not been seen with parenteral treatment. Side effects are more likely with higher doses. {R-54}

Ruminants

With lincomycin-

# Anorexia; decreased milk production; diarrhea; ketosis

Note: Anorexia, decreased milk production, ketosis, and severe diarrhea have been reported to be most likely in ruminants administered lincomycin orally. {R-10; 12} However, some animals may develop adverse effect s with parenterally administered lincomycin. {R-45}

Incidence unknown

All species

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#### Hypersensitivity reactions {R-1; 3}

# Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Cats

*Lip smacking*—with clindamycin oral solution {**R-53**}; *salivation*—with clindamycin oral solution {**R-53**}

Incidence less frequent or rare

Pigs

Anal swelling {R-41; 42}; diarrhea {R-41; 42}—transient; irritable behavior {R-41; 42}; skin reddening {R-41; 42}

Note: Anal swelling, diarrh ea, irritable behavior, and skin reddening are generally self-limiting within 5 to 8 days.

#### Human side/adverse effects {R-61}

In addition to the above side/adverse effects reported in animals, the following side/adverse effects have been reported in humans, and are included in the human monographs *Clindamycin (Systemic)* and *Lincomycin (Systemic)* in *USP DI Volume I*; these side/adverse effects are intended for informational purposes only and may or may not be applicable to the use of clindamycin and lincomycin in the treatment of animals:

Incidence more frequent

Gastrointestinal disturbances; pseudomembranous colitis Incidence less frequent

Fungal overgrowth; hypersensitivity; neutropenia; thrombocytopenia

Indicating possible pseudomembranous colitis and the need for medical attention if they occur after medication is discontinued Abdominal or stomach cramps and pain, severe; abdominal tenderness; diarrhea, watery and severe, which may also be bloody; fever

#### Overdose

For information in cases of overdose or unintentional ingestion, contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center (888-426-4435 or 900-443-0000; a fee may be required for consultation) and/or the drug manufacturer.

#### **Client Consultation**

Medication should be administered for the full length of time prescribed.

Any signs of anorexia, diarrhea, or vomiting should be reported to the veterinarian

#### **CLINDAMYCIN**

# **Summary of Differences**

Indications: Has wider spectrum of activity than does lin comycin.

Indicated in the treatment of osteomyelitis, periodontal infections, and soft tissue infections. Used in the treatment of skin infections.

Pharmacology/pharmacokinetics: Highly absorbed after oral administration. Absorption is unaffected by the presence of food in the stomach.

#### **Oral Dosage Forms**

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

The dosing and strengths of the dosage forms available are expressed in terms of the clindamycin base (not the hydrochloride salt).

# CLINDAMYCIN HYDROCHLORIDE CAPSULES USP

**Usual dose:** 

Osteomyelitis—Dogs: Oral, 11 to 33 mg (base) per kg of body weight

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every twelve hours \{R-1\}.
    Periodontal infections and soft tissue infections—Dogs: Oral, 5.5 to
        33 mg (base) per kg of body weight every twelve hours{R-1}.
    [Skin infections] 1—Dogs: Oral, 11 mg (base) per kg of body weight
        every twenty-four hours. {R-20}
        Note: The above dose for the treatment of skin infections in dogs
             is based upon a clinical comparative efficacy study of
             clindamycin and lincomycin {R-20}.
Strength(s) usually available:
    U.S. {R-1; 6}-
        Veterinary-labeled product(s):
            25 mg (base) (Rx) [AmTech Clindamycin Hydrochloride
                Capsules; Antirobe; Clincaps; GENERIC].
            75 mg (base) (Rx) [AmTech Clindamycin Hydrochloride
                Capsules; Antirobe; Clincaps; GENERIC].
            150 mg (base) (Rx) [AmTech Clindamycin Hydrochloride
                Capsules; Antirobe; Clincaps; GENERIC].
            300 mg (base) (Rx) [Antirobe].
    Canada {R-2; 6}-
        Veterinary-labeled product(s):
            25 mg (base) (OTC) [Antirobe; nvClindamycin Capsules].
            75 mg (base) (OTC) [Antirobe; nvClindamycin Capsules].
            150 mg (base) (OTC) [Antirobe; nvClindamycin Capsules].
Packaging and storage: Store below 40 °C (104 °F), preferably between
    15 and 30 °C (59 and 86 °F), unless otherwise specified by
    manufacturer. Preserve in tight containers.
USP requirements: Preserve in tight containers. Contain an amount of
    clindamycin hydrochloride equivalent to the labeled amount of
    clindamycin, within –10% to +20%. Meet the requirements for
    Identification, Dissolution (80% in 30 minutes in phosphate buffer
    [pH 6.8] in Apparatus 1 at 100 rpm), Uniformity of dosage units, and
    Water (not more than 7.0%). {R-26}
CLINDAMYCIN HYDROCHLORIDE ORAL SOLUTION
    USP
Usual dose:
    Osteomyelitis; or
    [Skin infections] <sup>1</sup>—Dogs: See Clindamycin Hydrochloride Capsules
    Periodontal infections and soft tissue infections-
        Cats: Oral, 11 to 33 mg (base) per kg of body weight every
           twenty-four hours {R-1}.
        Dogs: Oral, 5.5 to 33 mg (base) per kg of body weight every
           twelve hours [R-1].
Note: Cats—Based on dosing studies, the following dosages have been
     used in cats for treatment of [osteomyelitis]<sup>1</sup> and [skin infections]<sup>1</sup>:
     Staphylococcal infections—Oral, 5.5 mg (base) per kg of body
     weight every twelve hours. {R-53}
     Anaerobic bacterial infections—Oral, 11 mg (base) per kg of body
     weight every twelve hours or 22 mg per kg of body weight every
     twenty-four hours. {R-53}
     Based on clinical efficacy and pharmacokinetic studies, the
     following dose has been used in cats for the treatment of
     [toxoplasmosis]<sup>1</sup>—Oral, 12.5 to 25 mg (base) per kg of body weight
     every twelve hours for two to four weeks. {R-17; 18; 53; 54; 57;
Strength(s) usually available:
    U.S. {R-6}-
        Veterinary-labeled product(s):
            25 mg (base) per mL (Rx) [AmTech Clindamycin
                Hydrochloride Oral Liquid; Antirobe Aquadrops;
                ClindaCure; Clinda-Guard; Clindrops; GENERIC.
```

Canada {R-6}-

Veterinary-labeled product(s):

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

**USP requirements:** Preserve in tight containers. Label oral solution to indicate that it is intended for veterinary use only. Contains the equivalent of the labeled amounts, within ±10%. Meets the requirements for Identification, Uniformity of dosage units, Deliverable volume, and pH (3.0–5.5){**R-26**}.

#### **LINCOMYCIN**

# **Summary of Differences**

Indications: Indicated in the treatment of swine dysentery; growth promotion and feed efficiency in chickens and pigs; joint infections in pigs; met ritis in dogs; pneumonia in pigs; respiratory tract infections in cats and dogs; skin infections in dogs; and soft tissue infections in cats and dogs. Indicated in the control of necrotic enteritis in chickens

Pharmacology/pharmacokinetics: Oral lincomycin is less well absorbed than intramuscular lincomycin; dosages are adjusted to compensate. Elimination of lincomycin is affected to a greater extent by severe renal function impairment than is clindamycin. Absorption is reduced by the presence of food in the stomach.

# **Oral Dosage Forms**

Note: The dosing and strengths of the dosage forms available are expressed in terms of lincomycin base (not the hydrochloride salt).

# LINCOMYCIN HYDROCHLORIDE FOR MEDICATED FEED

# Usual dose:

Growth promotion-

Chickens: Oral, 2 to 4 grams (base) per ton of feed, fed as the only ration. {R-38}

Pigs<sup>1</sup>: Oral, 20 grams (base) per ton of feed, fed as the only ration. {R-38}

Mycoplasma pneumonia—Pigs: Oral, 200 grams (base) per ton of feed, fed as the only ration for twenty-one days. {R-38}

Necrotic enteritis<sup>1</sup>—*Chickens:* Oral, 2 grams (base) per ton of feed, fed as the only ration. {**R-48**}

Porcine proliferative enteropathies (control)<sup>1</sup>—*Pigs:* Oral, 100 grams (base) per ton of feed, fed as the only ration for twenty-one days or until signsof disease disappear. A dose of 40 grams (base) per ton of feed, fed as the only ration, may follow the above dose or be used in place of the 100-gram dose in animals that have not yet had symptoms{**R-38**}.

Swine dysentery—Pigs:

Control—Oral, 40 grams (base) per ton of feed, fed as the only ration. {R-38: 42}

Treatment—Oral, 100 grams (base) per ton of feed (approximately 4.4 to 8.8 mg [base] per kg of body weight), fed as the only ration for twenty-one days or until signs of disease disappear. {R-38; 42}

#### Strength(s) usually available:

U.S. {**R-6**}—

Veterinary-labeled product(s):

10 grams (base) per pound of premix (OTC) [Moorman's LN

20 grams (base) per pound of premix (OTC) [*Lincomix 20 Feed Medication*].

<sup>&</sup>lt;sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

50 grams (base) per pound of premix (OTC) [Lincomix 50 Feed Medication].

#### Canada {R-6}-

Veterinary-labeled products:

44 grams (base) per kg of premix (OTC) [Lincomix 44 Premix; Lincomycin 44 Premix; Lincomycin 44G Premix].

110 grams (base) per kg of premix (OTC) [Lincomix 110 Premix; Lincomycin 110 Premix; Lincomycin 110G Premix].

#### Withdrawal times:

U.S. {R-38; 42}-

	Withdrawal time
	Meat
Species	(days)
Chickens	0
Pigs	0 or 6,
	depending on
	product

# Canada (R-63)-

When mixed at 2.2 grams of lincomycin (base) per metric ton (1000 kg) of feed for chickens and 44 grams (base) of lincomycin per metric ton of feed for pigs:

	Withdrawal time
	Meat
Species	(days)
Chickens	0
Pigs	0

When mixed at 110 or 220 grams (base) of lincomycin per metric ton of feed for pigs:

	Withdrawal time
	Meat
Species	(days)
Pigs	2

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a dry place. {R-42}

**Preparation of dosage form:** Premix should be mixed into the complete feed following manufacturer's directions to produce 2, 3, 4, 20, 40, 100, or 200 grams of lincomycin (base) per ton of feed.

# Additional information:

Not for use in breeding swine or laying chickens. {R-38; 42} In preparing feeds, appropriate cleanout procedures should be followed to prevent cross-contamination of other feeds. {R-42}

USP requirements: Not in USP {R-26}.

#### LINCOMYCIN HYDROCHLORIDE SOLUBLE POWDER USP

#### Usual dose:

Necrotic enteritis—*Chickens:* Oral, 64 mg (base) per gallon of water, administered as the only source of drinking water for seven days. {R-22; 28; 41; 56}

Swine dysentery—*Pigs:* Oral, 250 mg (base) per gallon of water (approximately 8.4 mg [base] per kg of body weight) a day, administered as the only source of drinking water for five to ten days {**R-28**; **41**}.

# Strength(s) usually available:

U.S.— {**R-6**}

Veterinary-labeled product(s):

400 mg (base) per gram of powder (OTC) [Lincomix Soluble Powder; Lincosol Soluble Powder; GENERIC].

Canada — {**R-6**}

Veterinary-labeled product(s):

400 mg (base) per gram of powder (OTC) [Lincomix Soluble Powder; GENERIC].

# Withdrawal times:

U.S.— {**R-41**}

	Withdrawal time
	Meat
Species	(days)
Chickens	0
Pigs	0 or 6,
	depending on
	product

#### Canada — {R-28}

When mixed at concentrations of 16 mg of lincomycin (base) per liter of water (61 mg per gallon) for chickens or 33 mg of lincomycin (base) per liter of water (125 mg per gallon) for pigs:

	Withdrawal time
	Meat
Species	(days)
Chickens	0
Pigs	1

Packaging and storage: Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer

Preparation of dosage form: Powder should be mixed into the drinking water following manufacturer's directions to produce 61, 64, 125, or 250 mg (base) per gallon. Fresh stock solutions should be prepared on the day of use and unused medicated water discarded after 2 days.

USP requirements: Preserve in tight containers. Label it to indicate that it is for veterinary use only. Contains an amount of Lincomycin Hydrochloride equivalent to the labeled amount of lincomycin, within ±10%. Meets the requirements for Identification, Water, and Minimum fill{R-26}.

### LINCOMYCIN HYDROCHLORIDE SYRUP USP

#### Usual dose:

Metritis<sup>1</sup>; or

Skin infections<sup>1</sup>—*Dogs:* Oral, 22 mg (base) per kg of body weight every t welve hours or 15.4 mg (base) per kg of body weight every eight hours. **{R-3}** 

Respiratory tract infections<sup>1</sup>—*Cats* and *dogs*: Oral, 22 mg (base) per kg of body weight every twelve hours or 15.4 mg (base) per kg of body weight every eight hours **{R-3}**.

Soft tissue infections — Cats and dogs: Oral, 22 mg (base) per kg of body weight every twelve hours or 15.4 mg (base) per kg of body weight every eight hours. {R-3}

#### Strength(s) usually available:

U.S. {**R-3**; 6}—

 $Veterinary-labeled\ product(s):$ 

50 mg (base) per mL (Rx) [Lincocin Aquadrops].

Canada { **R-6** }—

Veterinary-labeled product(s):

Not commercially available.

Packaging and storage: Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. {R-33} Store in a tight container.

**USP requirements:** Preserve in tight containers. Contains an amount of Lincomycin Hydrochloride equivalent to the labeled amount of lincomycin, within –10% to +20%, and one or more suitable colors, flavors, preservatives, and sweeteners in water. Meets the

requirements for Uniformity of dosage units (for syrup packaged in single-unit containers), Deliverable volume (for syrup packaged in multiple-unit containers), and pH (3–5.5). {R-26}

#### LINCOMYCIN HYDROCHLORIDE TABLETS

#### Usual dose:

```
Metritis<sup>1</sup>; or
```

Skin infections<sup>1</sup>—*Dogs:* Oral, 22 mg (base) per kg of body weight every twelve hours or 15.4 mg (base) per kg of body weight every eight hours. {**R-3**}

Respiratory tract infections —Cats and dogs: Oral, 22 mg (base) per kg of body weight every twelve hours or 15.4 mg (base) per kg of body weight every eight hours {R-3}.

Soft tissue infections<sup>1</sup>—Cats and dogs: Oral, 22 mg (base) per kg of body weight every twelve hours or 15.4 mg (base) per kg of body weight every eight hours. {R-3}

# $Strength(s)\ usually\ available:$

```
U.S.— {R-3; 6}

Veterinary-labeled product(s):

100 mg (base) (Rx) [Lincocin].

200 mg (base) (Rx) [Lincocin].

500 mg (base) (Rx) [Lincocin].
```

Canada—{R-6}
Veterinary-labeled product(s):

Not commercially available.

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

USP requirements: Not in USP {R-26}.

#### **Parenteral Dosage Forms**

Note: Bracketed information in the *Dosage Forms* section refers to uses that either are not included in U.S. product labeling or are for products not commercially available in the U.S.

The dosing and strengths of the dosage forms available are expressed in terms of lincomycin base (not the hydrochloride salt).

#### LINCOMYCIN INJECTION USP

#### Usual dose:

Joint infections; or

Mycoplasma pneumonia<sup>1</sup>—Pigs: Intramuscular, 11 mg (base) per kg of body weight every twenty-four hours for three to seven days. {R-4}

Metritis<sup>1</sup>; or

Skin infections<sup>1</sup>—*Dogs:* Intramuscular or intravenous, 22 mg (base) per kg of body weight every twenty-four hours or 11 mg (base) per kg of body weight every twelve hours. **{R-3**}

Respiratory tract infections<sup>1</sup>; or

Soft tissue infections<sup>1</sup>—Cats and dogs: Intramuscular or intravenous, 22 mg (base) per kg of body weight every twenty-four hours or 11 mg (base) per kg of body weight every twelve hours. {R-3}

Note: For intravenous administration, the injection should be diluted with 5% glucose or normal saline and administered as a drip infusion. {R-3}

Note: [Cattle]\(^1\)—Although the safety and efficacy have not been established for treatment of laryngeal abscesses, mastitis, or septic arthritis in cattle, a dose of 5 mg (base) lincomycin per kg of body weight every twenty-four hours, administered intramuscularly for five to seven days, has been used. {R-44; 45; 60} For deep-seated or severe infections, a dose of 10 mg (base) per kg of body weight every twelve hours has been recommended {R-46; 48}. [Sheep]\(^1\)—Although the safety and efficacy have not been established for treatment of septic arthritis in sheep, cases have been reported that responded to 5 mg (base) per kg of body weight, administered intramuscularly every twenty-four hours for three to five days. {R-44}

#### Strength(s) usually available:

U.S. {**R-6**}—

Veterinary-labeled product(s):

25 mg (base) per mL (OTC) [Lincocin Injectable; Lincocin Sterile Solution; Lincomix Injectable].

100 mg (base) per mL [Lincocin Sterile Solution [cats and dogs] (Rx); Lincocin Sterile Solution [pigs] (OTC); Lincomix Injectable (OTC)].

300 mg (base) per mL (OTC) [Lincocin Injectable; Lincocin Sterile Solution; Lincomix Injectable].

#### Canada {R-6}-

Veterinary-labeled product(s):

100 mg (base) per mL (OTC) [Lincomix Injectable Solution].

#### Withdrawal times:

Note: There are no established withdrawal times for cattle or sheep in the United States or Canada because lincomycin is not approved for use in these species.

If lincomycin is administered to cattle at the dose of 5 mg (base) per kg of body weight for four days, evidence has been compiled by the Food Animal Residue Avoidance Databank (FARAD) that suggests a milk withholding time of 96 hours {R-45; 60} and a meat withdrawal time of 7 days {R-60} would be sufficient to avoid residues. There is no available information to make recommendations for withdrawal times when lincomycin is administered to cattle concurrently with other medications or when doses greater than 5 mg (base) per kg of body weight every twentyfour hours are administered. Also, no recommendations can be made for withdrawal times when lincomycin is administered to sheep. If it is necessary to administer these doses, extended withdrawal times are recommended.

U.S.— {**R-4**}

Withdrawal time
Meat
(days)
2
Withdrawal time
Meat
(days)
2

**Packaging and storage:** Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer.

USP requirements: Preserve in single-dose or in multiple-dose containers, preferably of Type I glass. Contains benzyl alcohol as a preservative. Contains an amount of Lincomycin Hydrochloride in Water for Injection equivalent to the labeled amount of lincomycin, within –10% to +20%. Meets the requirements for Bacterial endotoxins, Sterility, pH (3.0–5.5), and Particulate matter, and for Injections. {R-26}

<sup>1</sup>Not included in Canadian product labeling or product not commercially available in Canada.

Developed: 07/17/96

Interim revision: 05/07/97; 10/15/99; 09/30/02; 04/04/03

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