LINCOMYCIN HCL

(lin-koe-*mye*-sin) Lincocin®, Lincomix®

LINCOSAMIDE ANTIBIOTIC

Prescriber Highlights

- Lincosamide antibiotic similar to clindamycin; broad spectrum against many anaerobes, gram-positive aerobic cocci, Toxoplasma, etc.
- Contraindications: Horses, Rodents, Ruminants, Lagomorphs; Hypersensitivity to lincosamides
- Caution: Liver or renal dysfunction; consider reducing dosage if severe
- Adverse Effects: Gastroenteritis, pain at injection site if given IM; rapid IV administration can cause hypotension & cardiopulmonary arrest
- Distributed into milk; may cause diarrhea in nursing animals
- Drug interactions

Uses/Indications

Lincomycin has dosage forms approved for use in dogs, cats, swine, and in combination with other agents for chickens. Because clindamycin is generally better absorbed, more active, and probably less toxic, it has largely supplanted the use of lincomycin for oral and injectable therapy in small animals, but some clinicians believe that clindamycin does not offer enough clinically significant improvements over lincomycin to justify its higher cost. For further information, refer to the Pharmacology or Doses sections.

Pharmacology/Actions

The lincosamide antibiotics lincomycin and clindamycin, share mechanisms of action and have similar spectrums of activity although lincomycin is usually less active against susceptible organisms. Complete cross-resistance occurs between the two drugs; at least partial cross-resistance occurs between the lincosamides and erythromycin. They may act as bacteriostatic or bactericidal agents, depending on the concentration of the drug at the infection site and the susceptibility of the organism. The lincosamides are believed to act by binding to the 50S ribosomal subunit of susceptible bacteria, thereby inhibiting peptide bond formation.

Most aerobic gram-positive cocci are susceptible to the lincosamides (*Strep. faecalis* is not), including staphylococcus and streptococci. Other organisms that are generally susceptible include: *Corynebacterium diphtheriae, Nocardia asteroides,* Erysepelothrix*, and Mycoplasma* spp. Anaerobic bacteria that may be susceptible to the lincomycin include: *Clostridium perfringens. C. tetani* (not *C. difficile*), Bacteroides (including many strains of *B. fragilis*), Fusobacterium, Peptostreptococcus, Actinomyces, and Peptococcus.

Pharmacokinetics

The pharmacokinetics of lincomycin have not apparently been extensively studied in veterinary species. Unless otherwise noted, the following information applies to humans. The drug is rapidly absorbed from the gut, but only about 30–40% of the total dose is absorbed. Food both decreases the extent and the rate of absorption. Peak serum levels are attained about 2–4 hour after oral dosing. IM administration gives peak levels about double those reached after oral dosing, and peak at about 30 minutes post injection.

Lincomycin is distributed into most tissues. Therapeutic levels are achieved in bone, synovial fluid, bile, pleural fluid, peritoneal fluid, skin, and heart muscle. CNS levels may reach 40% of those in the serum if meninges are inflamed. Lincomycin is bound from 57–72% to plasma proteins, depending on the drug's concentration. The drug crosses the placenta and can be distributed into milk at concentrations equal to those found in plasma.

Lincomycin is partially metabolized in the liver. Unchanged drug and metabolites are excreted in the urine, feces and bile. Half-lives can be prolonged in patients with renal or hepatic dysfunction. The elimination half-life of lincomycin is reportedly 3–4 hours in small animals.

Contraindications/Precautions/Warnings

Although there have been case reports of parenteral administration of lincosamides to horses, cattle and sheep, the lincosamides are considered *contraindicated* for use in **rabbits**, **hamsters**, **guinea pigs**, **horses**, and **ruminants** because of serious gastrointestinal effects that may occur, including death.

Lincomycin is contraindicated in patients with known hypersensitivity to it or having a preexisting monilial infection.

Adverse Effects

Adverse effects reported in dogs and cats include gastroenteritis (emesis, loose stools, and infrequently bloody diarrhea in dogs). IM injections reportedly cause pain at the injection site. Rapid intravenous administration can cause hypotension and cardiopulmonary arrest.

Swine may develop gastrointestinal disturbances while receiving the medication.

Reproductive/Nursing Safety

Lincomycin crosses the placenta and cord blood concentrations are approximately 25% of those found in maternal serum. Safe use during pregnancy has not been established, but neither has the drug been implicated in causing teratogenic effects.

In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as in class: ***A*** (*Probably safe. Although specific studies may not have proved the safety of all drugs in dogs and cats, there are no reports of adverse effects in laboratory animals or women.*)

Because lincomycin is distributed into milk, nursing animals of mothers given lincomycin may develop diarrhea.

Overdosage/Acute Toxicity

There is little information available regarding overdoses of this drug. In dogs, oral doses of up to 300 mg/kg/day for up to one year or parenterally at 60 mg/kg/day apparently did not result in toxicity.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving lincomycin and may be of significance in veterinary patients:

- **CYCLOSPORINE**: Lincomycin may reduce levels
- **ERYTHROMYCIN**: *In vitro* antagonism when used with lincomycin; concomitant use should probably be avoided
- **KAOLIN**: Kaolin (found in several over-the-counter antidiarrheal preparations) has been shown to reduce the absorption of linco-

mycin by up to 90% if both are given concurrently; if both drugs are necessary, separate doses by at least 2 hours

- **NEUROMUSCULAR BLOCKING AGENTS** (*e.g.*, **pancuronium**): Lincomycin possesses intrinsic neuromuscular blocking activity and should be used cautiously with other neuromuscular blocking agents

Laboratory Considerations

- Slight increases in **liver function tests** (AST, ALT, Alk. Phosph.) may occur. There is apparently not any clinical significance associated with these increases.

Doses

- **DOGS:**

For susceptible infections:

a) For skin and soft tissue infections: 15.4 mg/kg PO q8h or 22 mg/kg PO q12h. Treatment for superficial pyoderma 21–42 days; for deep, resistant pyoderma 56 days;

For systemic infections: 22 mg/kg IM, SC, or IV (must be diluted and given as a slow drip infusion) q24h or 11 mg/kg IM or SC q12h for 12 days or less.

For bacteremia, sepsis: 11–22 mg/kg IV q8h for 12 days or less. (Greene, Hartmannn et al. 2006)

b) For pyoderma: 20 mg/kg twice daily (Halliwell 2002)

c) For superficial pyodermas: 20 mg/kg PO q12h (White 2007)

d) For pyoderma: 22 mg/kg PO twice daily; good for first time pyodermas. (Logas 2005b)

- **CATS:**

For susceptible infections:

a) For skin and soft tissue infections: 11 mg/kg IM q12h or 22 mg/kg IM q24h. Treatment for 12 days or less;

For systemic infections: 15 mg/kg PO q8h or 22 mg/kg PO q12h. Treatment for 12 days or less. (Greene, Hartmannn et al. 2006)

- **FERRETS:**

For susceptible infections:

a) 10–15 mg/kg PO three times daily; 10 mg/kg IM twice daily (Williams 2000)

- **SWINE:**

For susceptible infections:

a) For mycoplasmal (*M. hyopneumoniae*) pneumonia: Fed at 200 grams per ton of feed for 21 days or 11 mg/kg IM once daily (Amass 1999)

b) 11 mg/kg IM once daily for 3–7 days; or added to drinking water at a rate of 250 mg/gallon (average of 8.36 mg/kg/day) (Label directions; *Lincocin*®—Upjohn)

Monitoring

- Clinical efficacy
- Adverse effects; particularly severe diarrheas

Client Information

- Clients should be instructed to report the incidence of severe, protracted, or bloody diarrhea to the veterinarian.

Chemistry/Synonyms

An antibiotic obtained from cultures of *Streptomyces lincolnensis*, lincomycin is available commercially as the monohydrate hydrochloride. It occurs as a white to off-white, crystalline powder that is freely soluble in water. The powder may have a faint odor and has a pK_a of 7.6. The commercially available injection has a pH of 3–5.5 and occurs as a clear to slightly yellow solution.

Lincomycin may also be as: U-10149, NSC-70731, *Anbycin*®, *Frademicina*®, *Fredcina*®, *Linco*®, *Lincocin*®, *LincoMed*®, *Lincomix*®, *Linco-Ped*®, *Lincono*®, and *Macrolin*®.

Storage/Stability/Compatibility

Lincomycin capsules, tablets and soluble powder should be stored at room temperature (15–30°C) in tight containers. Lincomycin injectable products should be stored at room temperature; avoid freezing.

Lincomycin HCl for injection is reportedly physically **compatible** for at least 24 hours in the following IV infusion solutions and drugs: D_5W, D_5W in sodium chloride 0.9%, $D_{10}W$, sodium chloride 0.9%, Ringer's injection, amikacin sulfate, cephalothin sodium, chloramphenicol sodium succinate, cimetidine HCl, cytarabine, heparin sodium, penicillin G potassium/sodium (4 hours only), polymyxin B sulfate, tetracycline HCl, and vitamin B-complex with C.

Drugs that are reportedly physically **incompatible** when mixed with lincomycin, data conflicts, or compatibility is concentration and/or time dependent include: ampicillin sodium, carbenicillin disodium, methicillin sodium, and phenytoin sodium. Compatibility is dependent upon factors such as pH, concentration, temperature and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Lincomycin Oral Tablets: 100 mg, 200 mg, 500 mg; *Lincocin*® (Pharmacia); (Rx). Approved for use in dogs and cats.

Lincomycin Oral Solution: 50 mg/mL in 20 mL dropper bottles; *Lincocin*® *Aquadrops* (Pharmacia); (Rx). Approved for use in dogs and cats.

Lincomycin Sterile Injection: 100 mg/mL in 20 mL vials; *Lincocin*® (Pharmacia); (Rx). Approved for use in dogs and cats.

Lincomycin Sterile Injection: 25 mg/mL, 100 mg/mL & 300 mg/mL in 100 mL vials; approved for use in swine. Slaughter withdrawal (when used as labeled) = 48 hours. *Lincocin*® *Sterile Solution* (Pharmacia and Upjohn); *Lincomix*® *Injectable* (Pharmacia); *LincoMed*® (Bimeda); generic; (OTC)

There are also several lincomycin combination feed/water additive products for use in swine and/or poultry.

HUMAN-LABELED PRODUCTS:

Lincomycin Capsules: 500 mg (as hydrochloride); *Lincocin*® (Upjohn); (Rx)

Lincomycin Injection: 300 mg (as hydrochloride)/mL in 2 mL and 10 mL vials; *Lincocin*® (Upjohn), (Rx)

LIOTHYRONINE SODIUM

(lye-oh-*thye*-roe-neen) Cytomel®, Triostat®

THYROID HORMONE

Prescriber Highlights

- Form of T3 (active thyroid hormone) used for hypothyroidism particularly in animals unresponsive to T4
- Shorter duration of effect than levothyroxine
- Contraindications: Acute myocardial infarction, thyrotoxicosis, or untreated adrenal insufficiency
- Caution: Concurrent hypoadrenocorticism (treated), cardiac disease, diabetes, or elderly
- Adverse Effects: Only associated with OD's (tachycardia, polyphagia, PU/PD, excitability, nervousness, & excessive panting); some cats may appear apathetic
- Drug-drug; drug-lab interactions

Uses/Indications

Because of its shorter duration of action, liothyronine is generally not considered the drug of first choice in treating hypothyroidism. Infrequently, animals not responding to levothyroxine may respond to liothyronine.

Pharmacology/Actions

Thyroid hormones affect the rate of many physiologic processes including: fat, protein, and carbohydrate metabolism, increasing protein synthesis, increasing gluconeogenesis, and promoting mobilization and utilization of glycogen stores. Thyroid hormones also increase oxygen consumption, body temperature, heart rate and cardiac output, blood volume, enzyme system activity, and growth and maturity. Thyroid hormone is particularly important for adequate development of the central nervous system. While the exact mechanisms how thyroid hormones exert their effects are not well understood, it is known that thyroid hormones (primarily triiodothyronine) act at the cellular level.

In humans, triiodothyronine (T_3) is the primary hormone responsible for activity. Approximately 80% of T_3 found in the peripheral tissues is derived from thyroxine (T_4) which is the principle hormone released by the thyroid.

Pharmacokinetics

In dogs, peak plasma levels of liothyronine occur 2–5 hours after oral dosing. The plasma half-life is approximately 5–6 hours. In contrast to levothyroxine, it is believed that liothyronine is nearly completely absorbed by dogs and absorption is not as affected by stomach contents, intestinal flora changes, etc.

Contraindications/Precautions/Warnings

Liothyronine (and other replacement thyroid hormones) are contraindicated in patients with acute myocardial infarction, thyrotoxicosis, or untreated adrenal insufficiency. It should be used with caution, and at a lower initial dosage, in patients with concurrent hypoadrenocorticism (treated), cardiac disease, diabetes, or in elderly patients.

Adverse Effects

When administered at an appropriate dose to patients requiring thyroid hormone replacement, there should not be any adverse effects associated with therapy. For adverse effects associated with overdosage, see below.

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***A*** for use during pregnancy (*Adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.*)

Minimal amounts of thyroid hormones are excreted in milk and should not adversely affect nursing offspring.

Overdosage/Acute Toxicity

Chronic overdosage will produce signs of hyperthyroidism, including tachycardia, polyphagia, PU/PD, excitability, nervousness, and excessive panting. Dosage should be reduced and/or temporarily withheld until signs subside. Some (10%?) cats may exhibit signs of "apathetic" (listlessness, anorexia, etc.) hyperthyroidism.

Acute massive overdosage can produce signs resembling thyroid storm. After oral ingestion, treatment to reduce absorption of drug should be accomplished using standard protocols (emetics or gastric lavage, cathartics, charcoal) unless contraindicated by the patient's condition. Treatment is supportive and symptomatic. Oxygen, artificial ventilation, cardiac glycosides, beta-blockers (*e.g.*, propranolol), fluids, dextrose, and antipyretic agents have all been suggested for use if necessary.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving liothyronine and may be of significance in veterinary patients:

- **ANTIDEPRESSANTS, TRICYCLIC/TETRACYCLIC**: Increased risk for CNS stimulation and cardiac arrhythmias
- **ANTIDIABETIC AGENTS** (**insulin, oral agents**): Levothyroxine may increase requirements for insulin or oral agents
- **CHOLESTYRAMINE**: May reduce liothyronine absorption; separate doses by 4 hours
- **DIGOXIN**: Potential for reduced digoxin levels
- **KETAMINE**: May cause tachycardia and hypertension
- **SYMPATHOMIMETIC AGENTS** (**epinephrine**, **norepinephrine**, etc.): Levothyroxine can potentiate effects
- **WARFARIN**: Thyroid hormones increase the catabolism of vitamin K-dependent clotting factors that may increase the anticoagulation effects in patients on warfarin

Laboratory Considerations

The following drugs may have effects on thyroid function tests; evaluate results accordingly:

- **EFFECTS ON SERUM T_4**: aminoglutethimide↓, anabolic steroids/androgens↓, antithyroid drugs (PTU, methimazole)↓, asparaginase↓, barbiturates↓, corticosteroids↓, danazol↓, diazepam↓, estrogens↑ (**Note**: estrogens may have no effect on canine T_3 or T_4 concentrations), fluorouracil↑, heparin↓, insulin↑, lithium carbonate↓, mitotane (o,p-DDD)↓, nitroprusside↓, phenylbutazone↓, phenytoin↓, propranolol↑, salicylates (large doses)↓, and sulfonylureas↓.
- **EFFECTS ON SERUM T_3**: antithyroid drugs (PTU, methimazole)↓, barbiturates↓, corticosteroids↓, estrogens↑, fluorouracil↑, heparin↓, lithium carbonate↓, phenytoin↓, propranolol↓, salicylates (large doses)↓, and thiazides↑.
- **EFFECTS ON T_3 UPTAKE RESIN**: anabolic steroids/androgens↑, antithyroid drugs (PTU, methimazole)↓, asparaginase↑, corticosteroids↑, danazol↑, estrogens↓, fluorouracil↓, heparin↑, lithium carbonate↓, phenylbutazone↑, and salicylates (large doses)↑.
- **EFFECTS ON SERUM TSH**: aminoglutethimide↑, antithyroid drugs (PTU, methimazole)↑, corticosteroids↓, danazol↓, and lithium carbonate↑.