Extra-label clenbuterol use in food animals is prohibited by federal (USA) law.

The ARCI (Racing Commissioners International) has designated this drug as a class 3 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS: None

CLINDAMYCIN HCL
CLINDAMYCIN PALMITATE HCL
CLINDAMYCIN PHOSPHATE

(klin-da-*mye*-sin) Antirobe®, Cleocin®

LINCOSAMIDE ANTIBIOTIC

Prescriber Highlights

- **Lincosamide antibiotic, broad spectrum against many anaerobes, gram-positive aerobic cocci, Toxoplasma, etc.**
- **Contraindications: Horses, rodents, ruminants, lagomorphs; patients hypersensitive to lincosamides**
- **Caution: Liver or renal dysfunction; consider reducing dosage if severe**
- **Adverse Effects: gastroenteritis, esophageal injuries possible if "dry pilled", pain at injection site if given IM**

Uses/Indications

Clindamycin products are approved for use in dogs and cats. The labeled indications for dogs include wounds, abscesses and osteomyelitis caused by *Staphylococcus aureus*. Because clindamycin has excellent activity against most pathogenic anaerobic organisms, it is also used extensively for those infections. Clindamycin is used for a variety of protozoal infections, including toxoplasmosis. For further information, refer to the Dosage or Pharmacology 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, Toxoplasma, and *Mycoplasma* spp. Anaerobic bacteria that are generally susceptible to the lincosamides include: *Clostridium perfringens, C. tetani* (not *C. difficile*), Bacteroides (including many strains of *B. fragilis*), Fusobacterium, Peptostreptococcus, Actinomyces, and Peptococcus.

Pharmacokinetics

In dogs, oral bioavailability is about 73%, elimination half-life is reportedly 2–5 hours after oral administration and 10–13 hours after subcutaneous administration. Volume of distribution is about 0.9 L/kg.

In humans, the drug is rapidly absorbed from the gut and about 90% of the total dose is absorbed. Food decreases the rate of absorption, but not the extent. Peak serum levels are attained about 45–60 minutes after oral dosing. IM administration gives peak levels about 1–3 hours post injection.

Clindamycin is distributed into most tissues. Therapeutic levels are achieved in bone, synovial fluid, bile, pleural fluid, peritoneal fluid, skin, and heart muscle. Clindamycin also penetrates well into abscesses and white blood cells. CNS levels may reach 40% of those in the serum if meninges are inflamed. Clindamycin is about 93% bound to plasma proteins. The drug crosses the placenta and can be distributed into milk at concentrations equal to those in plasma.

Clindamycin is partially metabolized in the liver to both active and inactive metabolites. Unchanged drug and metabolites are excreted in the urine, feces, and bile. Half-lives can be prolonged in patients with severe renal or hepatic dysfunction.

Contraindications/Precautions/Warnings

Although there have been case reports of parenteral administration of lincosamides to horses, cattle, and sheep, the lincosamides are considered to be contraindicated for use in rabbits, hamsters, chinchillas, guinea pigs, horses, and ruminants because of serious gastrointestinal effects that may occur, including death. Clindamycin is contraindicated in patients with known hypersensitivity to it or lincomycin.

Patients with very severe renal and/or hepatic disease should receive the drug with caution and the manufacturer suggests monitoring serum clindamycin levels during high-dose therapy; consider dosage reduction.

Clindamycin use is generally avoided in neonatal small animals.

Adverse Effects

Adverse effects after oral administration reported in dogs and cats include gastroenteritis (emesis, loose stools, and infrequently bloody diarrhea in dogs). There have been case reports of esophageal injuries (esophagitis, strictures) occurring in cats when solid dosage forms were given without food or a water bolus. Cats may occasional show hypersalivation or lip smacking after oral administration. IM injections reportedly cause pain at the injection site.

C. difficile–associated pseudomembranous colitis has been reported in some species, but does not appear to be a significant risk when clindamycin is used in dogs or cats.

Reproductive/Nursing Safety

Clindamycin crosses the placenta, and cord blood concentrations are approximately 46% 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 clindamycin is distributed into milk, nursing puppies or kittens of mothers receiving clindamycin may develop diarrhea. However, in humans, the American Academy of Pediatrics considers clindamycin compatible with breastfeeding.

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 did not result in toxicity. Dogs receiving 600 mg/kg/day, developed anorexia, vomiting, and weight loss.

Drug Interactions

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

- **CYCLOSPORINE:** Clindamycin may reduce levels
- **ERYTHROMYCIN:** *in vitro* antagonism when used with clindamycin; concomitant use should probably be avoided
- **NEUROMUSCULAR BLOCKING AGENTS** (*e.g.*, **pancuronium**): Clindamycin 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 bacterial infections:

a) For infected wounds, abscesses and dental infections: 5.5–33 mg/kg PO q12h; for osteomyelitis: 11–33 mg/kg PO q12h. Treatment may continue for up to 28 days. If no response after 3–4 days, discontinue. (Package insert; *Antirobe*®—Pfizer)

b) For staphylococcal pyoderma: 11 mg/kg PO once daily for 7–28 days

For wounds, abscesses, dental infections, stomatitis: 5–11 mg/kg PO q12h for 7–28 days.

For osteomyelitis: 11 mg/kg PO q12h for 28 days

For systemic, bacteremia: 3–10 mg/kg IV, IM SC, PO q8h as long as needed (Greene and Watson 1998)

c) 5–11 mg/kg IM, SC or PO q12h avoid or reduce dose in patients with severe liver failure (Vaden and Papich 1995)

d) For sepsis: 11 mg/kg IV q12h (Hardie 2000)

e) For recurrent superficial pyodermas: 11 mg/kg PO once daily to twice a day; resistance can develop quickly (Logas 2005b)

f) For actinomycosis: 5 mg/kg SC q12h (Edwards 2006)

g) For susceptible hepatobiliary infections: 10–16 mg/kg SC once daily or 5–10 mg/kg PO q12h. In patients with liver function impairment: 5 mg/kg PO q12h or SC q24h (Center 2006b)

h) For anaerobic infections: 5–10 mg/kg PO, IV q12h (Greene and Jang 2006a)

i) For intra-abdominal sepsis 5–11 mg/kg IV, SC, PO q8–12h for 5–7 days combined with gentamicin or a parenteral 3rd generation cephalosporin (such as cefotaxime) or enrofloxacin.

For pancreatitis: 5–11 mg/kg IV, SC, PO q8–12h for 3–5 days. (Greene 2006)

j) For susceptible respiratory infections: 10 mg/kg PO, SC q12h (Greene and Reinero 2006)

k) For surgical prophylaxis for gram-positive aerobes and anaerobic coverage: 5–11 mg/kg PO 16–60 minutes preoperatively (Greene and Jang 2006b)

For susceptible protozoal infections:

a) For Toxoplasmosis: 12.5 mg/kg PO or IM q12h for 28 days

For Neospora: 10 mg/kg q12h for 4 weeks. Used concurrently with trimethoprim/sulfa (15 mg/kg PO q12h for 4 weeks)

For *Hepatozoon canis*: 10 mg/kg PO q8h for 2–4 weeks. Use concurrently with pyrimethamine (0.25 mg/kg PO once daily for 2–4 weeks) and trimethoprim/sulfa (15 mg/kg PO q12h for 2–4 weeks)

For *Babesia* spp.: 12.5 mg/kg q12h PO for 2 weeks (Lappin 2000)

c) For Babesia infections if specific antibabesial drugs (*e.g.*, diminazene, imidocarb, pentamidine) are not available: 25 mg/kg PO q12h for 7–21 days (Taboada and Lobetti 2006)

d) For *Hepatozoon americanum* infections: 10 mg/kg PO q8h for 14 days. Use concurrently with trimethoprim/sulfa (15 mg/kg PO q12h 14 days) and pyrimethamine (0.25 mg/kg PO once daily for 14 days) and then follow with decoquinate (for 2 years) once clinical signs have resolved. (Macintire, Vincent-Johnson et al. 2006)

- **CATS:**

For susceptible bacterial infections:

a) 5–10 mg/kg PO q12h (Jenkins 1987b); (Trepanier 1999)

b) For infected wounds, abscesses and dental infections: 11–33 mg/kg PO once a day (q24h). Do not treat acute infections for more than 3–4 days if no clinical response is seen. Maximum labeled treatment period = 14 days (Package insert; *Antirobe*®—Pfizer)

c) For sepsis: 11 mg/kg IV q12h (Hardie 2000)

d) For anaerobic infections: 5–10 mg/kg PO, IV q12h (Greene and Jang 2006a)

e) For intra-abdominal sepsis 5–11 mg/kg IV, SC, PO q8–12h for 5–7 days combined with gentamicin or a parenteral 3rd generation cephalosporin (such as cefotaxime) or enrofloxacin.

For pancreatitis: 5–11 mg/kg IV, SC, PO q8–12h for 3–5 days. (Greene 2006)

f) For susceptible respiratory infections: 10–15 mg/kg PO, SC q12h (Greene and Reinero 2006)

g) For surgical prophylaxis for gram-positive aerobes and anaerobic coverage: 5–11 mg/kg PO 16–60 minutes preoperatively (Greene and Jang 2006b)

For susceptible protozoal infections:

a) Toxoplasmosis:

To decrease zoonotic risk to susceptible humans by reducing shedding period in cats suspected of toxoplasmosis after fecal exam: 25–50 mg/kg PO daily; alternative medications include sulfonamides at 100 mg/kg PO daily, or pyrimethamine at 2 mg/kg daily PO.

For treatment of clinical toxoplasmosis: Clindamycin at 10 mg/kg PO q12h, trimethoprim-sulfonamide combination at 15 mg/kg PO q12h, and azithromycin at 10 mg/kg once daily for at least 28 days. Institute supportive care as needed. Patients with uveitis should receive topical, oral or parenteral glucocorticoids to reduce risk for secondary glaucoma and lens luxations. (Lappin 2004)

b) For enteroepithelial toxoplasmosis: 8–16 mg/kg PO or SC q8h for 14–28 days.

For systemic toxoplasmosis: 12.5–25 mg/kg PO or SC q12h for 14–28 days (Greene and Watson 1998)

- **FERRETS:**

  For susceptible infections:
  a) 5–10 mg/kg PO twice daily (Williams 2000)

- **BIRDS:**

  For susceptible infections:
  a) 25 mg/kg PO q8h (Tully 2002)
  b) For mild spore-forming enteric bacterial infections: 50 mg/kg PO q12h for 5–10 days (Flammer 2006)

- **REPTILES:**

  For susceptible infections (anaerobes):
  a) 5 mg/kg PO once daily (Lewbart 2001)
  b) For respiratory infections (anaerobes, mycoplasma): 5 mg/kg PO once daily for 14 days (Klaphake 2005b)

Monitoring

- Clinical efficacy
- Adverse effects; particularly severe diarrhea
- Manufacturer recommends doing periodic liver and kidney function tests and blood counts if therapy persists for more than 30 days

Client Information

- Clients should be instructed to report the incidence of severe, protracted, or bloody diarrhea to the veterinarian
- If using oral tablets or capsules, especially in cats, give medication followed by at least 6 mL (a little more than a teaspoonful) of liquid

Chemistry/Synonyms

A semisynthetic derivative of lincomycin, clindamycin is available as the hydrochloride hydrate, phosphate ester, and palmitate hydrochloride. Potency of all three salts is expressed as milligrams of clindamycin. The hydrochloride occurs as a white to practically white, crystalline powder. The phosphate occurs as a white to off-white, hygroscopic crystalline powder. The palmitate HCl occurs as a white to off-white amorphous powder. All may have a faint characteristic odor and are freely soluble in water. With the phosphate, about 400 mg are soluble in one mL of water. Clindamycin has a pK_a of 7.45. The commercially available injection has a pH of 5.5–7.

Clindamycin HCl may also be known as: chlorodeoxylincomycin hydrochloride, (7S)-chloro-7-deoxy-lincomycin hydrochloride, clindamycini hydrochloridum, U-28508, or U-25179E; many trade names are available.

Storage/Stability/Compatibility

Clindamycin capsules and the palmitate powder for oral solution should be stored at room temperature (15–30°C). After reconstitution, the palmitate oral solution (human-product) should not be refrigerated or thickening may occur. It is stable for 2 weeks at room temperature. The veterinary oral solution should be stored at room temperature and has an extended shelf life.

Clindamycin phosphate injection should be stored at room temperature. If refrigerated or frozen, crystals may form which resolubolize upon warming.

Clindamycin for injection is reportedly **compatible** for at least 24 hours in the following IV infusion solutions: D_5W, Dextrose combinations with Ringer's, lactated Ringer's, sodium chloride, $D_{10}W$, sodium chloride 0.9%, Ringer's injection, and lactated Ringer's injection. Clindamycin for injection is reportedly **compatible** with the following drugs: amikacin sulfate, ampicillin sodium, aztreonam, carbenicillin disodium, cefazolin sodium, cefonicid sodium, cefoperazone sodium, cefotaxime sodium, ceftazidime sodium, ceftizoxime sodium, cefuroxime sodium, cimetidine HCl, gentamicin sulfate, heparin sodium, hydrocortisone sodium succinate, kanamycin sulfate, methylprednisolone sodium succinate, magnesium sulfate, meperidine HCl, metoclopramide HCl, metronidazole, morphine sulfate, penicillin G potassium/sodium, piperacillin sodium, potassium chloride, sodium bicarbonate, tobramycin HCl (not in syringes), verapamil HCl, and vitamin B-complex with C.

Drugs that are reportedly **incompatible** with clindamycin include: aminophylline, ciprofloxacin, ranitidine HCl, and ceftriaxone 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:

Clindamycin (as the HCl) Oral Capsules: 25 mg, 75 mg, 150 mg, 300 mg; *Antirobe® Capsules* (Pfizer) Approved for use in dogs and cats). Also available in 25 mg, 75 mg, 150 mg, and 300 mg capsules as *Amtech® Clindamycin HCl Capsules* (IVX), *Clincaps®* (Butler), *Clindamycin Hydrochloride Capsules* (Phoenix), *Clindacure® Capsules* (no 300 mg caps—Vedco); (Rx). Approved for use in dogs.

Clindamycin (as the HCl) Oral Tablets: 25 mg, 75 mg, 150 mg; *Clintabs®* (Virbac). Approved for use in dogs.

Clindamycin (as the HCl) Oral Solution 25 mg/mL in 30 mL bottles. *Amtech® Clindamycin Hydrochloride Oral Liquid* (Butler, IVX), *Antirobe® Aquadrops* (Pfizer), *Clindacure®* (Vedco), *Clindrops®* (Butler), *Clindamycin Hydrochloride Drops* (Phoenix Pharmaceutical), *Clinda-Guard®* (RXV), *Clinsol®* (Virbac); (Rx). Approved for use in cats (not *Clinda-Guard®* or *Clindacure®*) and dogs.

HUMAN-LABELED PRODUCTS:

Clindamycin (as the HCl) Capsules: 75 mg, 150 mg, & 300 mg; *Cleocin®* (Upjohn); generic; (Rx)

Clindamycin (as the palmitate HCl) Granules for Oral Solution: 75 mg/5 mL (15 mg/mL) in 100 mL; *Cleocin® Pediatric* (Upjohn); (Rx)

Clindamycin (as the Phosphate) Injection: 150 mg/mL in 2 mL, 4 mL, 6 mL, 60 mL and 100 mL vials; 2 mL, 4 mL and 6 mL *ADD-Vantage* vials, 50 mL *Galaxy* containers and 60 mL bulk packages; *Cleocin® Phosphate* (Upjohn); (Rx); generic; (Rx)

Clindamycin Phosphate Suppositories: 100 mg (as base) *Cleocin®* (Pfizer); (Rx)

Also available in topical and vaginal preparations.

CLOFAZIMINE

(kloe-*fa*-zi-meen) Lamprene®

ANTIMYCOBACTERIAL ANTIBIOTIC

Prescriber Highlights

- May be difficult for veterinarians to obtain & accurately dose
- Antimycobacterial antibiotic that may be used as part of multi-drug therapy for leprosy-like or M. avium-related diseases in small animals
- Very limited clinical experience & documentation supporting its use in veterinary patients
- Skin, eye, excretion staining noted & dose limiting gastrointestinal adverse effects
- Treatment usually must continue for weeks to months

Uses/Indications

In small animals, clofazimine is sometimes used as part of multi-drug therapy against mycobacterial diseases, primarily leprosy-like or *M. avium*-related disease states.

In humans, clofazimine is used primarily as part of a multi-drug regimen in the treatment of all forms of leprosy (with rifampin and dapsone), or the treatment of Mycobacterium avium complex (MAC) (with at least two of the following agents: clarithromycin or azithromycin, rifampin or rifabutin, and ethambutol). It has also been used in some treatment regimens for Crohn's disease, pyoderma gangrenosum, etc.

Pharmacology/Actions

Clofazimine binds to mycobacterial DNA and inhibits growth. It is considered to be slowly bactericidal against susceptible organisms. Clofazimine has activity against a variety of mycobacteria including: *M. leprae, M. tuberculosis*, *M. avium* complex (MAC), *M. bovis*, and *M. chelonei*. Resistance is thought to occur only rarely; cross-resistance with dapsone or rifampin apparently does not occur. Clofazimine may have some antileishmanial activity. Clofazimine has antiinflammatory and immunosuppressive effects, but the mechanisms of action for these effects are not understood.

Pharmacokinetics

Clofazimine's pharmacokinetics have apparently not been determined in domestic animals. In humans, the microcrystalline form of the drug is variably absorbed after oral administration; bioavailability ranges from 45–70%. Food enhances absorption but increasing the dosage decreases the percentage absorbed. Clofazimine is highly lipid soluble and is distributed primarily to lipid tissue and the reticuloendothelial system. Throughout the body macrophages take up clofazimine. The drug crosses the placenta and is distributed into milk, but does not apparently cross into the CNS or CSF. Clofazimine is retained in the body for a long period; its elimination half-life is at least 70 days long. Bile excretion may be responsible for the majority of the drug's excretion, but excretion in sputum, sebum, and sweat may also contribute.

Contraindications/Precautions/Warnings

It is suggested that clofazimine be used with caution in patients with pre-existing gastrointestinal conditions such as diarrhea or abdominal pain.

Adverse Effects

There is very limited clinical experience with this medication in domestic animals and its adverse effect profile is not well documented. Apparently, the skin, eye, and excretion discoloration (described below) also occurs in animals. One case of a dog receiving clofazimine and rifampin to treat canine leproid granuloma resulted in hepatotoxicity.

In humans, clofazimine is usually well tolerated, particularly at dosages of 100 mg/day or less. The most troubling adverse effect in many patients is the dose-related skin, eye, and body fluid discoloration (pink to brownish-black) that occurs in most patients, as it may cause severe psychosocial effects; other drug regimens, not including clofazimine, are often chosen in patients with light skin color. This discoloration can persist for months to years after clofazimine has been discontinued. In dosages greater than 100 mg/day, gastrointestinal effects (pain, nausea, vomiting, diarrhea) become more likely and often limit the dosage that can be administered. Other adverse effects (CNS, increased liver enzymes, etc.) are reported in less than 1% of patients receiving the drug.

Reproductive/Nursing Safety

In humans, the FDA categorizes clofazimine as a category ***C*** drug for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans*). Very large doses (12–25X) demonstrated no teratogenic effects in rats or rabbits, but some effects were noted in mice. The World Health Organization (WHO) states that the drug is safe to use during pregnancy when used as part of one of their treatment protocols for leprosy.

Clofazimine does enter maternal milk and skin discoloration of nursing offspring can occur.

Overdosage/Acute Toxicity

Very limited data is available; the LD_{50} for rabbits is 3.3 g/kg and is greater than 5 g/kg in mice, rats, and guinea pigs. Treatment, if required, would include gut emptying and supportive care. Contact an animal poison control center for additional guidance.

Drug Interactions

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

- **ISONIAZID**: May reduce the clofazimine levels in the skin and increase the amounts in plasma and urine; clinical significance unclear
- **DAPSONE**: There is sketchy evidence that suggests dapsone may reduce the antiinflammatory effects of clofazimine; clinical significance unclear

Laboratory Considerations

- No clofazimine-related laboratory interactions noted

Doses

- **DOGS:**

  For *Mycobacterium avium* complex (MAC) as part of a multi-drug regimen:

  a) 4 mg/kg PO once daily. Other drugs that may be used in combination include doxycycline, clarithromycin, and/or enrofloxacin. (Greene and Gunn-Moore 1998)

  For *M. avium intracellularae* complex infections, leprosy, or opportunistic mycobacteriosis:

  a) 4–8 mg/kg PO once a day for 4 weeks usually as part of a multi-drug protocol. (Greene and Watson 1998)