100 micrograms of levothyroxine is approximately equivalent to 65 mg (1 grain) of desiccated thyroid.

Levothyroxine sodium may also be known as: T_4, T_4 thyroxine sodium, levothyroxin natrium, levothyroxinum natricum, 3,5,3',5'-tetra-iodo-L-thyronine sodium, thyroxine sodium, L-thyroxine sodium, thyroxinum natricum, tirossina, and tiroxina sodica; many trade names are available.

Storage/Stability/Compatibility

Levothyroxine sodium preparations should be stored at room temperature in tight, light-resistant containers. The injectable product should be reconstituted immediately before use; unused injection should be discarded after reconstituting. Do not mix levothyroxine sodium injection with other drugs or IV fluids.

Levothyroxine sodium is reportedly unstable in aqueous solutions. If using a commercial liquid preparation, it is suggested to obtain validated stability data for the product.

Dosage Forms/Regulatory Status

All levothyroxine products require a prescription, but are not necessarily FDA approved. There have been bioavailability differences between products reported. It is recommended to use a reputable product and not to change brands indiscriminately.

VETERINARY-LABELED PRODUCTS:

Levothyroxine Sodium Tablets: 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.8 mg, (1 mg *Soloxine®*); *Amtech® Levothyroxine Sodium Tablets* (IVX); *Levosyn®* (V.E.T.); *Soloxine®* (Virbac); *Thyro-Tabs®* (Vet-A-Mix); *Thyrosyn®* (Vedco); *Thyroxine-L Tablets®* (Butler); *Thyrozine®* (Phoenix Pharmaceutical); *Thyrokare® Tablets* (Neogen); (Rx). Labeled for use in dogs.

Levothyroxine Sodium Tablets Chewable (Veterinary) 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.8 mg; *Canine Thyroid Chewable Tablets®* (Pala-Tech); *Nutrived® T-4 Chewable Tablets* (Vedco); *Heska Thyromed® Chewable Tablets* (Heska); (Rx). Labeled for use in dogs.

Levothyroxine Oral Solution: 1 mg/mL in 30 mL bottles: *Leventa® Oral Solution* (Intervet); (Rx) Labeled for use in dogs.

Levothyroxine Sodium Powder (Veterinary): 0.22% (1 gram of T_4 in 454 grams of powder): One level teaspoonful contains 12 mg of T_4. Available in 1 lb. and 10 lb. containers; *Equine Thyroid Supplement®* (Pala-Tech); *Thyrozine Powder®* (Phoenix Pharmaceutical); *Levoxine® Powder* (First Priority); *Thyro-L®* (Vet-A-Mix); *Throxine-L® Powder* (Butler); *Equi-Phar Thyrosyn Powder®* (Vedco); *Thyrokare® Powder* (Neogen); (Rx). Labeled for use in horses.

HUMAN-LABELED PRODUCTS:

Levothyroxine Sodium Tablets: 0.025 mg, 0.05 mg, 0.075 mg, 0.088 mg, 0.1 mg, 0.112 mg, 0.125 mg, 0.137 mg, 0.15 mg, 0.175 mg, 0.2 mg & 0.3 mg; *Synthroid®* (Abbott); *Levothroid®* (Forest); *Levoxyl®* (Jones Pharma); *Thyro-Tabs®* (Lloyd); *Unithroid®* (Lannett); generic; (Rx)

Levothyroxine Powder for Injection lyophilized: 200 micrograms & 500 micrograms in 10 mL vials; generic; (Rx)

LIDOCAINE HCL (SYSTEMIC)

(*lye*-doe-kane) Xylocaine®

ANTIARRHYTHMIC/LOCAL ANESTHETIC

Prescriber Highlights

- Local anesthetic & antiarrhythmic agent; may be useful to prevent post-operative ileus, reperfusion injury in horses
- Contraindications: Known hypersensitivity to the amide-class local anesthetics, severe degree of SA, AV, or intraventricular heart block (if not being artificially paced), or Adams-Stokes syndrome
- Caution: Liver disease, congestive heart failure, shock, hypovolemia, severe respiratory depression, marked hypoxia, bradycardia, or incomplete heart block having VPC's, unless the heart rate is first accelerated
- Cats might be more sensitive to the CNS effects of lidocaine; use with caution
- Patients susceptible to malignant hyperthermia should receive intensified monitoring
- Adverse Effects: Most common adverse effects reported are dose related (serum level) & mild. CNS signs include drowsiness, depression, ataxia, muscle tremors, etc.; nausea & vomiting (usually transient). Adverse cardiac effects usually only at high plasma concentrations
- When an IV bolus is given too rapidly, hypotension may occur
- Do NOT use the product containing epinephrine intravenously
- Drug interactions

Uses/Indications

Besides its use as a local and topical anesthetic agent, lidocaine is used to treat ventricular arrhythmias, principally ventricular tachycardia and ventricular premature complexes in all species. Cats may be more sensitive to the drug and some clinicians feel that it should not be used in this species as an antiarrhythmic, but this remains controversial. In horses, lidocaine may be useful to prevent post-operative ileus and reperfusion injury.

Pharmacology/Actions

Lidocaine is considered to be a class IB (membrane-stabilizing) antidysrhythmic agent. It is thought that lidocaine acts by combining with fast sodium channels when inactive which inhibits recovery after repolarization. Class IB agents demonstrate rapid rates of attachment and dissociation to sodium channels. At therapeutic levels, lidocaine causes phase 4 diastolic depolarization attenuation, decreased automaticity, and either a decrease or no change in membrane responsiveness and excitability. These effects will occur at serum levels that will not inhibit the automaticity of the SA node, and will have little effect on AV node conduction or His-Purkinje conduction.

Lidocaine apparently has some enhancing effects on intestinal motility in patients with postoperative ileus. The mechanism for this effect is not well understood, but probably involves more than just blocking increased sympathetic tone.

Lidocaine has been shown to be a scavenger of reactive oxygen species (ROS) and lipid peroxidation

Pharmacokinetics

Lidocaine is not effective orally as it has a high first-pass effect. If very high oral doses are given, toxic signs occur (due to active metabolites?) before therapeutic levels can be reached. Following a therapeutic IV bolus dose, the onset of action is generally within 2 minutes and has duration of action of 10–20 minutes. If a constant infusion is begun without an initial IV bolus, it may take up to an hour for therapeutic levels to be reached. IM injections may be given every 1.5 hours in the dog, but because monitoring and adjusting dosages are difficult, it should be reserved for cases where IV infusions are not possible.

After injection, the drug is rapidly redistributed from the plasma into highly perfused organs (kidney, liver, lungs, heart) and distributed widely throughout body tissues. It has a high affinity for fat and adipose tissue and is bound to plasma proteins, primarily alpha$_1$-acid glycoprotein. It has been reported that lidocaine binding to this protein is highly variable and concentration dependent in the dog and may be higher in dogs with inflammatory disease. Lidocaine is distributed into milk. The apparent volume of distribution (V_d) has been reported to be 4.5 L/kg in the dog.

Lidocaine is rapidly metabolized in the liver to active metabolites (MEGX and GX). The terminal half-life of lidocaine in humans is 1.5–2 hours and has been reported to be 0.9 hours in the dog. The half-lives of lidocaine and MEGX may be prolonged in patients with cardiac failure or hepatic disease. Less than 10% of a parenteral dose is excreted unchanged in the urine.

Contraindications/Precautions/Warnings

Cats tend to be more sensitive to the CNS effects of lidocaine; use with caution. Lidocaine is contraindicated in patients with known hypersensitivity to the amide-class local anesthetics, a severe degree of SA, AV or intraventricular heart block (if not being artificially paced), or Adams-Stokes syndrome. The use of lidocaine in patients with Wolff-Parkinson-White (WPW) syndrome is controversial. Some manufacturers state its use is contraindicated, but several physicians have used the drug in people.

Lidocaine should be used with caution in patients with liver disease, congestive heart failure, shock, hypovolemia, severe respiratory depression, or marked hypoxia. It should also be used with caution in patients with bradycardia or incomplete heart block having VPC's, unless the heart rate is first accelerated. Patients susceptible to developing malignant hyperthermia should receive lidocaine with intensified monitoring.

When preparing lidocaine for intravenous injection, be certain of the concentration and do not use products containing epinephrine.

Adverse Effects

At usual doses and if the serum level remains within the proposed therapeutic range (1–5 micrograms/mL), serious adverse reactions are quite rare. The most common adverse effects reported are dose related (serum level) and mild. CNS signs include drowsiness, depression, ataxia, muscle tremors, etc. Nausea and vomiting may occur, but are usually transient. Adverse cardiac effects generally only occur at high plasma concentrations and are usually associated with PR and QRS interval prolongation and QT interval shortening. Lidocaine may increase ventricular rates if used in patients with atrial fibrillation. If an IV bolus is given too rapidly, hypotension may occur.

Be certain not to use the product that contains epinephrine intravenously.

Reproductive/Nursing Safety

In humans, the FDA categorizes systemic lidocaine 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), systemic lidocaine is categorized as in class: ***B*** (*Safe for use if used cautiously. Studies in laboratory animals may have uncovered some risk, but these drugs appear to be safe in dogs and cats or these drugs are safe if they are not administered when the animal is near term.*)

Lidocaine is excreted in concentrations of approximately 40% of that found in the serum and would unlikely to pose significant risk to nursing offspring.

Overdosage/Acute Toxicity

In dogs, if serum levels of >8 micrograms/mL are attained, toxicity may result. Signs may include ataxia, nystagmus, depression, seizures, bradycardia, hypotension and, at very high levels, circulatory collapse. Because lidocaine is rapidly metabolized, cessation of therapy or reduction in infusion rates with monitoring may be all that is required for minor signs. Seizures or excitement may be treated with diazepam, or a short or ultrashort acting barbiturate. Longer acting barbiturates (*e.g.*, pentobarbital) should be avoided. Should circulatory depression occur, treat with fluids, pressor agents and, if necessary, begin CPR.

Drug Interactions

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

- **ANTIARRHYTHMICS, OTHER** (*e.g.*, **procainamide, quinidine, propranolol, phenytoin**): When administered with lidocaine may cause additive or antagonistic cardiac effects and toxicity may be enhanced
- **CIMETIDINE**: Lidocaine levels or effects may be increased
- **PHENYTOIN**: May increase lidocaine metabolism; decrease levels
- **PROPRANOLOL**: Lidocaine levels or effects may be increased
- **SUCCINYLCHOLINE**: Large doses of lidocaine may prolong succinylcholine-induced apnea

Laboratory Considerations

- Lidocaine may cause increased **creatine kinase** levels (CK).

Doses

- **DOGS:**
  a) Initial bolus of 2 mg/kg slowly IV, up to 8 mg/kg; or rapid IV infusion of 0.8 mg/kg/minute, if effective, then give constant rate infusion of 25–80 mcg/kg/minute (0.025–0.08 mg/kg/minute) (Ware 2000)
  b) For rapid conversion of life-threatening, incessant, unstable ventricular tachycardia: Initial IV bolus of 1–2 mg/kg preferably over 30 seconds to judge response, higher doses may be required but rarely need to give 4 mg/kg. Once effectiveness determined, begin constant rate infusion at 25–80 mcg/kg/minute. Adjust dose to attain efficacy but without side effects. To prevent adverse effects total dose should not exceed 8 mg/kg over approximately one hour. Alternatively may give lidocaine at 4 mg/kg IM, but not if shock is present. Effects generally are seen in 10–15 minutes, and persist for about 90 minutes. (Moise 2000)
  c) For ventricular arrhythmias: Initial dosage of 2–8 mg/kg IV slowly is given to effect while monitoring ECG; then following by a CRI of 25–75 mcg/kg/minute starting at a high dose and tapering down when possible. (Macintire 2006a)

■ **CATS:**

CAUTION: Cats are reportedly very sensitive to the CNS effects of lidocaine, monitor carefully and treat seizures with diazepam.

a) Initially, IV bolus of 0.25–0.5 mg/kg given slowly; can repeat at 0.15–0.25 mg/kg in 5–20 minutes; if effective, 10–20 mcg/kg/minute (0.01–0.02 mg/kg/min) as a constant rate IV infusion (Ware 2000)

b) 0.25–0.5 mg/kg slow IV, with the possibility of repeating up to twice more if needed. If diluting for accurate dosing, use an insulin/tuberculin syringe. May be used as first-line therapy, or after propranolol, if it was ineffective. (Cote 2004)

■ **HORSES:** (**Note:** ARCI UCGFS Class 2 Drug)

For ventricular tachyarrhythmias:

a) Initially IV bolus of 1–1.5 mg/kg. Will generally distinguish between ventricular tachyarrhythmias (effective) and supraventricular tachyarrhythmias (no effect). To maintain effect, a constant IV infusion will be required. (Hilwig 1987)

b) 0.25–0.5 mg/kg IV (slowly) every 5–10 minutes up to a total dose of 1.5 mg/kg (Mogg 1999)

For postoperative ileus:

a) Initially, IV bolus of 1.3 mg/kg followed by a IV infusion of 0.05 mg/kg/minute for 24 hours (Malone, Turner et al. 1999)

Monitoring

■ ECG

■ Signs of toxicity (see Adverse Effects and Overdosage)

■ If available and indicated, serum levels may be monitored. Therapeutic levels are considered to range from 1–6 micrograms/mL.

Client Information

■ This drug should only be used systemically by professionals familiar with its use and in a setting where adequate patient monitoring can be performed.

Chemistry/Synonyms

A potent local anesthetic and antiarrhythmic agent, lidocaine HCl occurs as a white, odorless, slightly bitter tasting, crystalline powder with a melting point between 74°–79°C and a pK_a of 7.86. It is very soluble in water and alcohol. The pH of the commercial injection is adjusted to 5–7, and the pH of the commercially available infusion in dextrose 5% is adjusted to 3.5–6.

Lidocaine may also be known as: lidocaini hydrochloridum, and lignocaine hydrochloride; many trade names are available; a common trade name is *Xylocaine*® (Astra).

Storage/Stability/Compatibility/Preparation

Lidocaine for injection should be stored at temperatures less than 40°C and preferably between 15–30°C; avoid freezing.

Lidocaine is physically **compatible** with most commonly used IV infusion solutions, including D5W, lactated Ringer's, saline, and combinations of these. It is also reportedly physically **compatible** with: aminophylline, bretylium tosylate, calcium chloride/gluceptate/gluconate, carbenicillin disodium, chloramphenicol sodium succinate, chlorothiazide sodium, cimetidine HCl, dexamethasone sodium phosphate, digoxin, diphenhydramine HCl, dobutamine HCl, ephedrine sulfate, erythromycin lactobionate, glycopyrrolate, heparin sodium, hydrocortisone sodium succinate, hydroxyzine HCl, insulin (regular), mephentermine sulfate, metaraminol bitartrate, methicillin sodium, metoclopramide HCl, nitrofurantoin sodium, oxytetracycline HCl, penicillin G potassium, pentobarbital sodium, phenylephrine HCl, potassium chloride, procainamide HCl, prochlorperazine edisylate, promazine HCl, sodium bicarbonate, sodium lactate, tetracycline HCl, verapamil HCl, and Vitamin B-Complex with C.

Lidocaine **may not be compatible** with dopamine, epinephrine, isoproterenol, or norepinephrine as these require low pH's for stability. Lidocaine is reportedly physically **incompatible** when mixed with: ampicillin sodium, cefazolin sodium, methohexital sodium, or 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.

To prepare IV infusion solution using the veterinary 2% solution add 1 gram (50 mL of 2% solution to 1 liter of D_5W or other compatible solution, this will give an approximate concentration of 1 mg/mL (1000 micrograms/mL). When using a mini-drip (60 drops/mL) IV set, each drop will contain approximately 17 micrograms. In small dogs and cats, a less concentrated solution may be used for greater dosage accuracy. When preparing solution be certain that you are not using the lidocaine product that contains epinephrine.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

There are injectable lidocaine products labeled for use in veterinary medicine (dogs, cats, horses, and cattle) as an injectable anesthetic, but it is not approved for use as an antiarrhythmic agent. Information regarding its use in food-producing species is conflicting; when using a food animal it is suggested to contact FARAD (see appendix).

Lidocaine HCl for Injection: 2% (20 mg/mL) in 100 mL & 250 mL multi-use vials; (contains preservatives). Manufacturers include: Vedco, Phoenix Pharmaceutical, Aspen, AgriLabs, IVX, Butler, & RXV; (Rx)

The ARCI (Racing Commissioners International) has designated this drug as a class 2 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Lidocaine Hydrochloride Injection: 0.5%, 1%, 1.5%, 2% & 4% in 5 mL, 10 mL, 20 mL, 30 mL & 50 mL single- & multi-dose vials, 2 mL & 5 mL amps, 5 mL syringe with laryngotracheal cannula & 1.8 mL cartridges; *Xylocaine*® & *Xylocaine MPF*® (AstraZeneca); generic; (Rx)

Premixed with D5W for IV infusion in concentrations of 2 mg/mL, 4 mg/mL, and 5 mg/mg, injections with epinephrine, topical liquids, patches, ointment, cream, lotion, gel, spray, & jelly available.

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-