For parenteral use: 4–8 mg/kg IM or SC; repeat in 10–14 days. May cause vomiting, ataxia, or death. Do not use in debilitated birds.

For immunostimulation: 0.3 mL/gallon of water for several weeks

As a parenteral immunostimulant: 2 mg/kg IM or SC. 3 doses at 14 day intervals (Clubb 1986)

b) As a nebulized immunostimulant: 1 mL (of 13.65% levamisole phosphate) in 15 mL saline (Spink 1986)

c) For Capillaria infections: 15–30 mg/kg orally as a single bolus or through a crop tube; or 2.25 mg/gallon of drinking water for 4–5 days. Repeat treatment in 10–14 days. (Flammer 1986)

d) Poultry: 18–36 mg/kg, PO (Brander, Pugh, and Bywater 1982)

e) Ratites: For *Libyastrongylus douglassi*: Give 30 mg/kg PO or IM at one month of age, then once a month for 7 treatments, then 4 times yearly (Jenson 1998)

Monitoring

- Clinical efficacy
- Adverse effects/toxicity observation

Client Information

- Levamisole is not approved for use in dairy animals of breeding age.
- Follow directions on the product label unless otherwise directed by veterinarian. Animals that are severely parasitized or in conditions with constant helminth exposure should be retreated 2–4 weeks after initial treatment.
- Do not administer injectable products IV.
- Report serious adverse effects to veterinarian.

Chemistry/Synonyms

The levo-isomer of dl-tetramisole, levamisole has a greater safety margin than does the racemic mixture. It is available commercially in two salts, a phosphate and a hydrochloride. Levamisole hydrochloride occurs as a white to pale cream colored, odorless or nearly odorless, crystalline powder. One gram is soluble in 2 mL of water.

Levamisole HCl may also be known as: cloridrato de levamizol, ICI-59623, levamisoli hydrochloridum, NSC-177023, R-12564, RP-20605, l-tetramisole hydrochloride, *Amtech®, Ascaridil®, Decaris®, Ergamisol®, Immunol®, Ketrax®, Levasole®, Meglum®, Prohibit®, Solaskil®, Vermisol®,* and *Vizole®*.

Storage/Stability/Compatibility

Levamisole hydrochloride products should be stored at room temperature (15–30°C), unless otherwise instructed by the manufacturer; avoid temperatures greater than 40°C. Levamisole phosphate injection should be stored at temperatures at or below 21°C (70°F); refrigeration is recommended and freezing should be avoided.

Levamisole tablets should not be crushed nor suspensions made from them.

Dosage Forms/Regulatory Status/Withdrawal Times

In cattle, sheep, and swine a level of 0.1 ppm has been established for negligible residues in edible tissues.

VETERINARY-LABELED PRODUCTS:

Levamisole Phosphate Injection: 136.5 mg/mL (13.65%) in 500 mL vials. Levamisole Injectable (AgriLabs), *Levasole® Injectable Solution 13.65%* (Schering Plough); Approved for use in cattle. Slaughter withdrawal (at labeled dosages) = 7 days. To prevent residues in milk, do not administer to dairy animals of breeding age.

Levamisole Hydrochloride Water Medication: 18.15 g in 0.71 oz bottle. *Levamisole Soluble Pig Wormer* (AgriLabs, Durvet, Aspen); (OTC); *Levasole® Soluble Pig Wormer* (Schering-Plough), *Amtech® Levamisole HCl Pig Wormer* (IVX); (OTC). Approved for use in swine. Slaughter withdrawal (at labeled dosages) = 72 hours

Levamisole Hydrochloride Antihelmintic Oral: *Levasole® Soluble Drench Powder* 46.8 grams/packet (Schering-Plough); (OTC). Approved for use in cattle (Not in dairy animals of breeding age), and sheep. Slaughter withdrawal (at labeled dosages) = 48 hours (cattle); 72 hours (sheep)

Levamisole Hydrochloride Soluble Drench Powder 46.8 grams/packet; 544.5 g/21.34 oz bottle. *Prohibit®* (AgriLabs) (OTC). Approved for use in cattle and sheep. Slaughter withdrawal (at labeled dosages) cattle = 48 hours, sheep = 72 hours. To prevent residues in milk, do not administer to dairy animals of breeding age.

Levamisole HCl Oral Tablets/Boluses: 184 mg bolus: *Levasole® Sheep Wormer Bolus* (Schering Plough); (OTC). Approved for use in sheep. Slaughter withdrawal (at labeled dosages) = 72 hours.

Levamisole 2.19 gram bolus: *Levasole® Cattle Wormer Boluses* (Schering-Plough); (OTC). Approved for use in beef (not for use in dairy animals of breeding age). Slaughter withdrawal (at labeled dosages) = 48 hours.

HUMAN-LABELED PRODUCTS:

Levamisole HCl Tablets: 50 mg levamisole base; *Ergamisol®* (Janssen); (Rx)

LEVETIRACETAM

(lee-ve-tye-***ra***-se-tam) Keppra®

ANTICONVULSANT

Prescriber Highlights

- **May be useful as a third drug adjunct for refractory canine epilepsy or when either phenobarbital or bromides are not tolerated; may also be useful in cats, but less is known**
- **Limited clinical experience; investigations ongoing regarding efficacy, adverse effects**
- **Appears to be well tolerated in dogs & cats**
- **Not substantially metabolized by liver; does not induce hepatic enzymes**
- **Dosage frequency (three times daily) problematic; cost may be prohibitive**

Uses/Indications

Levetiracetam may be useful as a third antiseizure medication in dogs that are not well controlled with phenobarbital and bromides or when either bromides or phenobarbital are not tolerated. Some evidence suggests that in dogs suffering from phenobarbital liver toxicity, the addition of levetiracetam will allow reduction of their phenobarbital dosage without increasing seizure frequency.

Levetiracetam may also be useful as add-on therapy in cats.

Pharmacology/Actions

The exact mechanism for levetiracetam's antiseizure activity is not well understood. It may selectively prevent hypersynchronization of epileptiform burst-firing and propagation of seizure activity. It does not affect normal neuronal excitability.

Pharmacokinetics

Little published pharmacokinetic data is available for dogs; elimination half-life is about 4 hours and volume of distribution is about 0.5 L/kg. In a very small sample size, levetiracetem half-life in cats was around 5 hours. In humans, levetiracetam is rapidly, and nearly completely, absorbed after oral administration. Peak levels occur about one hour after dosing. Presence of food in the gut delays the rate, but not the extent, of drug absorbed. Less than 10% of the drug is bound to plasma proteins. While not extensively metabolized, the drug's acetamide group is enzymatically hydrolyzed to the carboxylic acid metabolite that is apparently not active. Hepatic CYP P450 isoenzymes are not involved. Half-life in humans is about 7 hours; about 66% of a given dose is excreted unchanged via renal mechanisms, primarily glomerular filtration and active tubular secretion. Clearance can be significantly reduced in patients with impaired renal function.

Contraindications/Precautions/Warnings

Levetiracetam is contraindicated in patients who have previously exhibited hypersensitivity to it or any of its components. It should be used with caution in patients with renal impairment; dosage amounts or dosing frequency changes should be considered. In humans, renal elimination of levetiracetam correlates with creatinine clearance.

Adverse Effects

Levetiracetam appears to be very well tolerated in the limited number of dogs treated thus far. Changes in behavior, somnolence, and gastrointestinal effects could occur.

In cats, the drug appears to have a wide safety margin, but less clinical use has occurred in that species. Transient inappetance has been reported in some cats receiving the drug.

In humans, it is recommended to withdraw the drug slowly to prevent "withdrawal" seizures.

Reproductive/Nursing Safety

In pregnant dogs or cats, levetiracetam should be used with caution. In humans, the FDA categorizes levetiracetam 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*). At high dosages, levetiracetam has caused increased embryofetal mortality in rabbits and rats. At dosages equivalent to the maximum human therapeutic dose, levetiracetam caused minor skeletal abnormalities and retarded offspring growth in rats.

Levetiracetam is excreted into maternal milk and its safety in nursing offspring is unknown. Use with caution in nursing patients.

Overdosage/Acute Toxicity

Levetiracetam is a relatively safe agent. Dogs given 1200 mg/kg/day (approximately 20 times therapeutic dosage) developed only salivation and vomiting. Human patients given 6000 mg/kg during drug testing developed only drowsiness. Other effects noted in human overdoses (doses not specified) after the drug was released include depressed levels of consciousness, agitation, aggression and respiratory depression. Treatment is basically supportive; the drug can be removed with hemodialysis. In the circumstance of a significant overdose in animals, contact an animal poison control center for further recommendations.

Drug Interactions

No clinically significant adverse drug interactions were located.

Laboratory Considerations

No specific laboratory interactions or considerations noted.

Doses

- **DOGS:**
  a) As an add-on treatment for epilepsy in dogs refractory to phenobarbital and bromides: 20 mg/kg PO every 8 hours (Munana 2004b)
  b) As an add-on treatment for epilepsy in dogs refractory to phenobarbital and/or bromides: 7.1–23.8 mg/kg PO every 8 hours (Steinberg and Faissler 2004)
  c) 10–20 mg/kg PO q8h (Dickinson 2007)
  d) 10–20 mg/kg PO q8–12h (Podell 2006a)
  e) Initially, 20 mg/kg PO q8h. May increase dose in 20 mg/kg increments until efficacy achieved, side effects become apparent, or the drug becomes cost prohibitive. (Dewey 2005a)
- **CATS:**
  a) As an add-on to phenobarbital treatment for epilepsy: Initially, 20 mg/kg PO three times daily; slowly increase to effect (Pearce 2006b)

Monitoring

- At this point, in both humans and dogs, blood levels of levetiracetam are not monitored for either efficacy or toxicity.
- Veterinarians should have the owner keep a record of seizure activity to document efficacy and report any potential levetiracetam-associated adverse effects.

Client Information

- Clients should understand that limited experience has occurred with levetiracetam in dogs. Although it appears to be well tolerated, information on its safety and efficacy profile is still being generated.
- The current dosage frequency recommendation (q8h) may be difficult to adhere to, but the drug may not be effective if not followed.
- The cost of this medication can be very substantial; potentially several hundred dollars per month (depending on dog's size).

Chemistry/Synonyms

A pyrrolidone-derivative antiepileptic agent, levetiracetam occurs as an odorless, bitter-tasting, white to off-white crystalline powder. It is very soluble in water and soluble in ethanol. It is a chiral molecule with one asymmetric carbon atom. Levetiracetam is not related chemically to other antiseizure medications.

Levetiracetam may also be known as: S-Etriacetam, UCB-22059, UCB-L059, and *Keppra*®.

Storage/Stability

Levetiracetam tablets or oral solution should be stored at 25°C (77°F); excursions permitted to 15–30°C (59–86°F).

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Levetiracetam Tablets (film-coated, scored): 250 mg, 500 mg, 750 mg & 1000 mg; *Keppra*® (UCB); (Rx)

Levetiracetam Oral Solution: 100 mg/mL in 480 mL; *Keppra*® (UCB), (Rx)

Levetiracetam Solution for Injection: 100 mg/mL (45 mg sodium chloride & 8.2 mg sodium acetate trihydrate/5 mL) in 5 mL vials; *Keppra*® (UCB Pharma); (Rx)

LEVOTHYROXINE SODIUM

(lee-voe-thye-***rox***-een) Soloxine®, Synthroid®

THYROID HORMONE

Prescriber Highlights

- Thyroid hormone for hypothyroidism in all species
- Contraindications: Acute myocardial infarction, thyrotoxicosis, or untreated adrenal insufficiency
- Caution: Concurrent hypoadrenocorticism (treated), cardiac disease, diabetes, or elderly patients
- 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

Levothyroxine sodium is indicated for the treatment of hypothyroidism in all species.

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 fully 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 concentrations after oral dosing reportedly occur 4–12 hours after administration and the serum half-life is approximately 12–16 hours. There is wide variability from animal to animal, however.

Contraindications/Precautions/Warnings

Levothyroxine (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 those who are aged.

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 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.

A single acute overdose in small animals is less likely to cause severe thyrotoxicosis than with chronic overdosage. Vomiting, diarrhea, hyperactivity to lethargy, hypertension, tachycardia, tachypnea, dyspnea, and abnormal pupillary light reflexes may be noted in dogs and cats. In dogs, clinical signs may appear within 1–9 hours after ingestion. If ingestion occurred within 2 hours, treatment to reduce absorption of drug should be accomplished using standard protocols (emetics, 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; contact an animal poison control center for further guidance.

Drug Interactions

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

- **AMIODARONE:** May decrease the metabolism of T4 to T3
- **ANTACIDS, ORAL:** May reduce levothyroxine absorption; separate doses by 4 hours
- **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 levothyroxine absorption; separate doses by 4 hours
- **CORTICOSTEROIDS** (high dose): Decreased conversion of T4 to T3
- **DIGOXIN:** Potential for reduced digoxin levels
- **FERROUS SULFATE:** May reduce levothyroxine absorption; separate doses by 4 hours
- **HIGH FIBER DIET:** May reduce levothyroxine absorption
- **KETAMINE:** May cause tachycardia and hypertension
- **PHENOBARBITAL:** Possible increased metabolism of thyroxine; dosage adjustments may be needed
- **PROPYLTHIOURACIL:** Decreased conversion of T4 to T3
- **RIFAMPIN:** Possible increased metabolism of thyroxine; dosage adjustments may be needed
- **SERTRALINE:** May increase levothyroxine requirements
- **SUCRALFATE:** May reduce levothyroxine absorption; separate doses by 4 hours
- **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