Storage/Stability
Store refrigerated; do not freeze. Shake well before using.

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS:

Propionibacterium acnes (non-viable) IV: 0.4 mg/mL in 5 mL and 50 mL vials; *Immunoregulin*® (Neogen); (OTC-biologic; manufacturer states that use is restricted to use by, or under the supervision of a veterinarian). Labeled for use in dogs. *Eqstim*® (Neogen). For use in horses and restricted to use by or under to the supervision of a veterinarian.

HUMAN-LABELED PRODUCTS: None

PROPOFOL

(***proe***-po-fole) Rapinovet®, PropoFlo®, Diprivan®

INJECTABLE ANESTHETIC

Prescriber Highlights

- Short-acting injectable hypnotic agent
- Contraindications: Hypersensitivity to it or any component of the product
- Caution: Severe stress or having undergone trauma, hypoproteinemia, hyperlipidemia, seizures, or anaphylaxis history
- Adverse Effects: Transient respiratory depression is common but usually clinically tolerable. Apnea possible, especially if given too rapidly. May cause histamine release; anaphylactoid reactions possible. Hypotension, seizure-like clinical signs (paddling, opisthotonus, myoclonic twitching) during induction. Repeated doses in *Cats:* Increased Heinz body production, slowed recoveries, anorexia, lethargy, malaise, & diarrhea
- Little, if any, analgesia is provided
- Consider dose reduction if using other CNS depressant
- Sufficient monitoring & patient-support capabilities are mandatory
- Cats with preexisting liver disease may be susceptible to longer recovery times

Uses/Indications
In appropriate patients, propofol may be useful as an induction agent (especially before endotracheal intubation or an inhalant anesthetic), and as an anesthetic for outpatient diagnostic or minor procedures (*e.g.*, laceration repair, radiologic procedures, minor dentistry, minor biopsies, endoscopy, etc.).

Propofol is used as a treatment for refractory status epilepticus, as it tends to cause less cardiovascular depression and recoveries can be smoother than with pentobarbital. Propofol may be of particular usefulness for use in Greyhounds and in patients with preexisting cardiac dysrhythmias. At low dosages, propofol is being investigated as an appetite stimulant in dogs.

Propofol may be safely used in animals with liver or renal disease and mild to moderate cardiac disease.

In dogs, propofol's labeled indications are: **1)** for induction of anesthesia; **2)** for maintenance of anesthesia for up to 20 minutes; **3)** for induction of general anesthesia where maintenance is provided by inhalant anesthetics.

Pharmacology/Actions
Propofol is a short acting hypnotic unrelated to other general anesthetic agents. Its mechanism of action is not well understood.

In dogs, propofol produces rapid yet smooth and excitement-free anesthesia induction (in 30–60 seconds) when given slowly IV. Sub-anesthetic dosages will produce sedation, restraint and an unawareness of surroundings. Anesthetic dosages produce unconsciousness and good muscle relaxation.

Propofol's cardiovascular effects include arterial hypotension, bradycardia, (especially in combination with opiate premedicants) and negative inotropism. It causes significant respiratory depression, particularly with rapid administration or very high dosages. Propofol also decreases intraocular pressure, increases appetite and has antiemetic properties. It does not appear to precipitate malignant hyperthermia and has little or no analgesic properties.

Pharmacokinetics
After IV administration, propofol rapidly crosses the blood brain barrier and has an onset of action usually within one minute. Duration of action after a single bolus lasts about 2–5 minutes. It is highly bound to plasma proteins (95–99%), crosses the placenta, is highly lipophilic, and reportedly enters maternal milk.

Propofol's short duration of action is principally due to its rapid redistribution from the CNS to other tissues. It is rapidly biotransformed in the liver via glucuronide conjugation to inactive metabolites, which are then excreted primarily by the kidneys. Because cats do not glucuronidate as well as dogs or humans, this may help explain their problems with consecutive day administration (see Adverse Effects below).

There is limited data available on propofol's pharmacokinetic parameters in dogs. The steady state volume of distribution is >3L/kg, elimination half-life about 1.4 hours, and clearance about 50 mL/kg/min.

Contraindications/Precautions/Warnings
Propofol is contraindicated in patients hypersensitive to it or any component of the product. It should not be used in patients where general anesthesia or sedation is contraindicated. Propofol should only be used in facilities where sufficient monitoring and patient-support capabilities are available.

Because patients that are in shock, under severe stress, or have undergone trauma may be overly sensitive to the cardiovascular and respiratory depressant effects of propofol, it should be used with caution in these patients. Adequate perfusion should be maintained before and during propofol anesthesia; dosage adjustments may be necessary.

Because propofol is so highly bound to plasma proteins, patients with hypoproteinemia may be susceptible to untoward effects; general anesthetic agents may be a safer choice in these patients.

The benefits of propofol should be weighed against its risks in patients with a history of hyperlipidemia, seizures or anaphylactic reactions. Cats with preexisting liver disease may be susceptible to longer recovery times.

Adverse Effects
Transient respiratory depression is common but is usually clinically tolerable. However, there is a relatively high incidence of apnea with resultant cyanosis if propofol is given too rapidly; it should be given slowly (25% of the calculated dose every 30 seconds until desired effect). Treat with assisted ventilation until spontaneous ventilation resumes.

Propofol has been documented to cause histamine release in some patients and anaphylactoid reactions (rare) have been noted in humans. Propofol has direct myocardial depressant properties and resultant arterial hypotension has been reported.

Occasionally, dogs may exhibit seizure-like clinical signs (paddling, opisthotonus, myoclonic twitching) during induction, that, if persist, may be treated with intravenous diazepam. Propofol may have both anticonvulsant and seizure-causing properties. It should be used with caution in patients with a history of, or active seizure disorders, but some clinicians believe however, that propofol is actually more appropriate to use in seizure patients or in high seizure-risk procedures (*e.g.*, myelography) than is thiopental.

While propofol is not inexpensive, it should ideally be used in a single-use fashion, as it is a good growth medium (contains no preservative) for bacteria.

When used in combination with other CNS depressant premedicants (*e.g.,* acepromazine, narcotics, diazepam, etc.), a decrease in dosage of about 25% (from the single agent dose) should be considered. In very thin animals, consider dosage reduction as well.

When used repeatedly (once daily) in cats, increased Heinz body production, slowed recoveries, anorexia, lethargy, malaise, and diarrhea have been noted. Heinz body formation is due to oxidative injury to RBCs and has been documented in cats with other phenolic compounds as well. Consecutive use in dogs appears to be safe.

Pain upon injection has been reported in humans, but does not appear to be a clinically significant problem for dogs or cats. Extravasation of injection is not irritating nor does it cause tissue sloughing.

Propofol does not provide good analgesia, so appropriate analgesic agents should be used before and after painful procedures.

Reproductive/Nursing Safety

Propofol crosses the placenta and its safe use during pregnancy has not been established. High dosages (6X) in laboratory animals caused increased maternal death and decreased offspring survival rates after birth. 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 humans, propofol is not recommended for use in nursing mothers because propofol is excreted in maternal milk and the effects of oral absorption of small amounts of propofol are not known. Use with caution in nursing veterinary patients.

Overdosage/Acute Toxicity

Overdosages are likely to cause significant respiratory depression and, potentially, cardiovascular depression. Treatment should consist of propofol discontinuation, artificial ventilation with oxygen, and if necessary, symptomatic and supportive treatment for cardiovascular depression (*e.g.*, intravenous fluids, pressors, anticholinergics, etc.).

Drug Interactions

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

- **ANESTHETICS, INHALATION** (**halothane, isoflurane**): Propofol serum concentrations may be increased
- **ANESTHETICS, LOCAL**: Propofol dosage requirements for sedation or hypnosis reduced
- **ANTICHOLINERGICS**: Propofol-induced bradycardia may be exacerbated in animals, particularly when opiate premedicants are used
- **CLONIDINE**: When used as a premed, may reduce propofol dosage requirements
- **CNS DEPRESSANTS**: Increased sedative, anesthetic, and cardiorespiratory depression possible
- **DRUGS THAT INHIBIT THE HEPATIC P-450 ENZYME SYSTEM** (*e.g.*, **chloramphenicol, cimetidine, ketoconazole**, etc.): May potentially increase the recovery times associated with propofol; clinical significance is unclear, but it may be of significance in cats
- **FENTANYL**: In pediatric (human) patients increased risk for bradycardia
- **MEDETOMIDINE**: When propofol is used after medetomidine, hypoxemia may occur; dosage adjustments may be required along with adequate monitoring
- **MIDAZOLAM**: May have synergistic effects with propofol, midazolam plasma concentrations may be increased up to 20%
- **OPIATES**: May increase the serum concentrations of both the opiate and propofol if used together

Doses

- **DOGS & CATS:**

  Note: The *Rapinovet*® (Schering-Plough) package insert has very detailed dosing recommendations for both induction and maintenance of general anesthesia with propofol, including dosage adjustments when acepromazine, xylazine, butorphanol, oxymorphone or medetomidine premedication is used.

  As an anesthetic:

  a) As a single injection (25% of the calculated dose every 30 seconds until desired effect):

  For healthy, unpremedicated animal: 6 mg/kg IV;

  For healthy, premedicated animal: After tranquilizer (*e.g.*, acepromazine) = 4 mg/kg IV; after sedative (*e.g.*, xylazine, opioids) = 3 mg/kg IV.

  As a constant infusion:

  For sedation only: 0.1 mg/kg/minute;

  For minor surgery: 0.6 mg/kg/min, or 1 mL (10 mg) per minute per 12–25 kg of body weight (Robinson, Sanderson et al. 1993)

  b) Dogs: For induction without premedication: 5–6 mg/kg IV;

  With acepromazine (0.05 mg/kg IM, IV, or SC), propofol given at 3–4 mg/kg IV;

  With acepromazine and oxymorphone (0.09 mg/kg IM, IV or SC), propofol given at 2.3 mg/kg IV. Xylazine or medetomidine premeds may reduce propofol dose further.

  Cats: Premed with acepromazine (0.05–1 mg/kg IM) with or without an analgesic such as butorphanol (0.2–0.4 mg/kg IM) and induce with propofol at 4–6 mg/kg IV. Doses of propofol at 8–13 mg/kg IV will allow intubation without topical anesthesia, lower propofol dose if topical anesthesia is used. (Mathews 1999)

  c) 6 mg/kg IV; in healthy animals 25% of the calculated dose is administered every 30 seconds until intubation is possible. After induction, duration of anesthesia is only 2.5–9.4 minutes. Maintenance anesthesia obtained using either inhalational agents or a continuous infusion of propofol at approximately 0.4 mg/kg/minute. If anesthesia appears inadequate, a small bolus of 1 mg/kg followed by an increase in the infusion rate by 25%. If infusion is too deep, discontinue infusion until suitable anesthesia level is achieved. An infu-

sion dose of 0.1 mg/kg/min appears to be suitable dose for sedation in the dog. (Ilkiw 1992)

d) As an induction agent for halothane or isoflurane anesthesia: 6.6 mg/kg IV given over 60 seconds to unpremedicated dogs. Best achieved by early intubation and administration of the inhalant following propofol induction. (Bufalari, Miller et al. 1998)

For refractory status epilepticus:

a) Using IV bolus or constant rate IV infusion: 0.1–0.6 mg/kg/minute. Use only in settings where definitive airway control and hemodynamic support can occur. (Platt and McDonnell 2000)

b) If seizures persist after diazepam and phenobarbital therapy: 3–6 mg/kg IV followed by an infusion of 8–12 mg/kg/hour. Must closely monitor for hypoventilation and may require mechanical ventilatory support. (Munana 2004b)

c) If seizures persist after diazepam and phenobarbital therapy in dogs: Propofol IV bolus at 1–3.5 mg/kg up to 6 mg/kg followed by a CRI using a syringe pump of 0.1–0.25 mg/kg/minute (up to 0.6 mg/kg/minute) for 6–12 hours and then gradually decreased; maximum duration of propofol CRI is approximately 48 hours. If used in cats, carefully monitor PVC and CBC (Heinz body anemia, hemolytic anemia) and propofol dose should be kept as low, and duration of treatment as short, as possible. (Knipe 2006b)

RABBITS, RODENTS, SMALL MAMMALS:

a) Rabbits: 5–14 mg/kg slow IV (20 mg/kg/minute) to effect; not recommended as the sole agent for maintenance (Ivey and Morrisey 2000)

b) Mice: 26 mg/kg IV. Rats: 10 mg/kg IV (Adamcak and Otten 2000)

REPTILES:

a) Iguanas: 3 mg/kg IV via either intraosseous catheter or into the coccygeal or ventral abdominal vein. Wait 3–5 minutes before giving additional increments. May also be used in tortoises. (Heard 1999)

b) 5–15 mg/kg IV or IO; in snakes intracardiac route is usually used (Innis 2003)

Monitoring

- Level of anesthesia/CNS effects
- Respiratory depression
- Cardiovascular status (cardiac rate/rhythm; blood pressure)

Chemistry/Synonyms

Propofol is an alkylphenol derivative (2,6-diisopropylphenol). The commercially available injection is an emulsion containing 100 mg/mL of soybean oil, 22.5 mg/mL of glycerol, and 12 mg/mL of egg lecithin. The emulsion has a pH of 7–8.5. Propofol may also be known as disoprofol.

Propofol may also be known as: disoprofol, ICI-35868, propofolum, *Ansiven®*, *Bioprofol®*, *Cryotol®*, *Diprofol®*, *Diprivan®*, *Disoprivan®*, *Fresofol®*, *Ivofol®*, *Klimofol®*, *Oleo-Lax®*, *Pofol®*, *Profolen®*, *Pronest®*, *Propoabbott®*, *Propocam®*, *PropoFlo®*, *Propovan®*, *Provive®*, *Rapinovet®*, *Recofol®*, or *Recofol®*.

Storage/Stability/Compatibility

Store propofol injection below 22°C (72°F), but not below 4°C (40°F.); do not refrigerate or freeze. Protect from light. Shake well before using. Do not use if the emulsion has separated. The manufacturer recommends discarding any unused portion at the end of the anesthetic procedure or after 6 hours, whichever occurs sooner.

Propofol is physically **compatible** with the commonly used IV solutions (*e.g.*, LRS, D5W) when injected into a running IV line. Drugs that are reported to be **compatible** with Y-site administration include (partial listing): ampicillin, butorphanol, calcium gluconate, cefazolin, cefoxitin, clindamycin, dexamethasone sodium phosphate, dexmetomidine, diphenhydramine, dobutamine, dopamine, epinephrine, fentanyl, furosemide, heparin sodium, insulin, ketamine, lorazepam, magnesium sulfate, mannitol, naloxone, pentobarbital, phenobarbital, potassium chloride, propranolol, sodium bicarbonate, succinylcholine, thiopental, and vecuronium. It is **incompatible** with atracurium and vecuronium. Refer to specialized references or a hospital pharmacist for more information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Propofol Injectable: 10 mg/mL in 5 mL and 20 mL (single use) vials; *Rapinovet®* (Schering Plough); *PropoFlo®* (Abbott); (Rx). Approved for use in dogs and cats.

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

HUMAN-LABELED PRODUCTS:

Propofol Injection, Emulsion: 10 mg/mL in 20 mL amps & vials, 50 mL and 100 mL infusion vials and 50 mL prefilled single-use syringes; *Diprivan®* (AstraZeneca); Propofol (Baxter); (Rx)

PROPRANOLOL HCL

(proe-*pran*-oh-lole) Inderal®

BETA-ADRENERGIC BLOCKER

Prescriber Highlights

- Non specific beta blocker primarily used in veterinary medicine as an antiarrhythmic agent
- Contraindications: Heart failure, hypersensitivity to this class of agents, greater than 1st degree heart block, or sinus bradycardia; generally contraindicated in patients with CHF unless secondary to a tachyarrhythmia responsive to beta-blockers or with bronchospastic lung disease
- Caution: Significant renal or hepatic insufficiency, sinus node dysfunction, labile diabetic patients, digitalized or digitalis intoxicated patients
- Adverse Effects: Bradycardia, lethargy, & depression, impaired AV conduction, CHF or worsening of heart failure, hypotension, syncope, diarrhea, hypoglycemia, & bronchoconstriction
- May mask (treat) clinical signs of thyrotoxicosis
- If discontinuing drug, consider gradual withdrawal
- Drug Interactions

Uses/Indications

While propranolol is used for hypertension, migraine headache prophylaxis, and angina in human patients, it is used primarily in veterinary medicine for its antiarrhythmic effects. Dysrhythmias treated with propranolol include: atrial premature complexes, ventricular premature complexes, supraventricular premature complexes and tachyarrhythmias, ventricular or atrial tachyarrhythmias secondary to digitalis, atrial tachycardia secondary to Wolff-Parkinson-White