Drug Interactions

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

- **NON-DEPOLARIZING MUSCLE RELAXANT DRUGS, OTHER**: May have a synergistic effect if used with vecuronium
- **SUCCINYLCHOLINE**: May speed the onset of action and enhance the neuromuscular blocking actions of vecuronium; do not give vecuronium until succinylcholine effects have subsided

The following agents may enhance or prolong the neuromuscular blocking activity of vecuronium:

- **AMINOGLYCOSIDES**
- **ANESTHETICS** (**halothane, isoflurane, sevoflurane**)
- **CLINDAMYCIN, LINCOMYCIN**
- **DANTROLENE**
- **MAGNESIUM SALTS**
- **PIPERACILLIN, MEZLOCILLIN**
- **QUINIDINE**
- **TETRACYCLINES**
- **VERAPAMIL**

Doses

- **DOGS:**
  a) 0.1 mg/kg IV initially (after meperidine and/or acepromazine pre-op 30 minutes before); may give subsequent incremental doses of 0.04 mg/kg IV. Duration of action after initial dose averages 25 minutes. (Jones and Seymour 1985)
  b) 10–20 mcg/kg IV (Morgan 2003)
  c) If using CRI propofol-fentanyl anesthesia: CRI maintenance infusion rate of vecuronium at 0.2 mg/kg/hr;
  If using CRI fentanyl-isoflurane or fentanyl-sevoflurane anesthesia: CRI maintenance infusion rate of vecuronium at 0.1 mg/kg/hr. (Nagahama, Nishimura et al. 2006)
- **CATS:**
  a) 20–40 mcg/kg (0.02–0.04 mg/kg) IV (Morgan 2003)

Monitoring

- Level of neuromuscular relaxation

Client Information

- This drug should only be used by professionals familiar with its use

Chemistry/Synonyms

Structurally similar to pancuronium, vecuronium bromide is a synthetic, nondepolarizing neuromuscular blocking agent. It contains the steroid (androstane) nucleus, but is devoid of steroid activity. It occurs as white to off-white, or slightly pink crystals or crystalline powder. In aqueous solution, it has a pK_a of 8.97, and the commercial injection has a pH of 4 after reconstitution. 9 mg are soluble in 1 mL of water; 23 mg are soluble in 1 mL of alcohol.

Vecuronium Bromide may also be known as: Org-NC-45, *Curlem®*, *Norcuron®*, *Rivecrum®*, *Vecural®*, or *Vecuron®*.

Storage/Stability/Compatibility

The commercially available powder for injection should be stored at room temperature and protected from light. After reconstitution with sterile water for injection, vecuronium bromide is stable for 24 hours at either 2–8°C or at room temperature (less than 30°C) if stored in the original container. As it contains no preservative, unused portions should be discarded after reconstitution. The drug is stable for 48 hours at room temperature or refrigerated when stored in plastic or glass syringes, but the manufacturer recommends that it be used within 24 hours.

Vecuronium bromide has been shown to be physically **compatible** with D_5W, normal saline, D_5 in normal saline, and lactated Ringer's.

It should not be mixed with alkaline solutions (*e.g.*, thiobarbiturates).

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Vecuronium Bromide Powder for Injection: 10 mg and 20 mg; in 10 mL and 20 mL vials, with and without diluent; *Norcuron®* (Organon); (Rx)

VERAPAMIL HCL

(ver-***ap***-a-mill) **Calan®, Isoptin®, Verelan®**

CALCIUM-CHANNEL BLOCKER

Prescriber Highlights

- **Calcium channel blocking agent used for supraventricular tachycardias in dogs & cats**
- **Contraindications: Cardiogenic shock or severe CHF (unless secondary to a supraventricular tachycardia), hypotension, sick sinus syndrome, 2nd or 3rd degree AV block, digoxin intoxication, or hypersensitive to verapamil. IV is contraindicated within a few hours of IV beta-adrenergic blockers.**
- **Caution: Heart failure, hypertrophic cardiomyopathy, & hepatic or renal impairment. Use very cautiously in patients with atrial fibrillation & Wolff-Parkinson-White (WPW) syndrome.**
- **Adverse Effects: Hypotension, bradycardia, tachycardia, exacerbation of CHF, peripheral edema, AV block, pulmonary edema, nausea, constipation, dizziness, headache, or fatigue**
- **Drug Interactions**

Uses/Indications

Veterinary experience with this agent is somewhat limited, but in dogs and cats verapamil may be useful for supraventricular tachycardias and, possibly, treatment of atrial flutter or fibrillation.

Pharmacology/Actions

A slow-channel calcium blocking agent, verapamil is classified as a class IV antiarrhythmic drug. Verapamil exerts its actions by blocking the transmembrane influx of extracellular calcium ions across membranes of vascular smooth muscle cells and myocardial cells. The result of this blocking is to inhibit the contractile mechanisms of vascular and cardiac smooth muscle. Verapamil has inhibitory effects on the cardiac conduction system and these effects produce its antiarrhythmic properties. Electrophysiologic effects include increased effective refractory period of the AV node, decreased automaticity and substantially decreased AV node conduction. On ECG, heart rate and RR intervals can be increased or decreased; PR and A-H intervals are increased. Verapamil has negative effects on myocardial contractility and decreases peripheral vascular resistance.

Pharmacokinetics

In humans, about 90% of a dose of verapamil is rapidly absorbed after oral administration, but because of a high first-pass effect, only about 20–30% is available to the systemic circulation. Patients with significant hepatic dysfunction may have considerably higher percentages of the drug systemically bioavailable. Food will decrease the rate and extent of absorption of the sustained-release tablets, but less so with the conventional tablets.

Verapamil's volume of distribution is between 4.5–7 L/kg in humans and has been reported to be approximately 4.5 L/kg in dogs. In humans, approximately 90% of the drug in the serum is bound to plasma proteins. Verapamil crosses the placenta and milk levels may approach those in the plasma.

Verapamil is metabolized in the liver to at least 12 separate metabolites, with norverapamil being the most predominant. The majority of the amounts of these metabolites are excreted into the urine. Only 3–4% is excreted unchanged in the urine. In humans, the half-life of the drug is 2–8 hours after a single IV dose, but it can increase after 1–2 days of oral therapy (presumably due to a saturable process of the hepatic enzymes). Serum half-lives of 0.8 hours and 2.5 hours have been reported in the dog.

Contraindications/Precautions/Warnings

Verapamil is contraindicated in patients with cardiogenic shock or severe CHF (unless secondary to a supraventricular tachycardia amenable to verapamil therapy), hypotension (<90 mmHg systolic), sick sinus syndrome, 2nd or 3rd degree AV block, digoxin intoxication, or hypersensitive to verapamil.

IV verapamil is contraindicated within a few hours of IV beta-adrenergic blocking agents (*e.g.*, propranolol) as they both can depress myocardial contractility and AV node conduction. Use of this combination in patients with wide complex ventricular tachycardia (QRS >0.11 seconds) can cause rapid hemodynamic deterioration and ventricular fibrillation.

Verapamil should be used with caution in patients with heart failure, hypertrophic cardiomyopathy, and hepatic or renal impairment. Toxicity may be potentiated in patients with hepatic dysfunction. It should be used very cautiously in patients with atrial fibrillation and Wolff-Parkinson-White (WPW) syndrome as fatal arrhythmias may result.

Because verapamil may increase blood glucose in dogs, it should be used with caution in diabetic animals.

Verapamil is potentially a neurotoxic substrate of P-glycoprotein; use with caution in those herding breeds (*e.g.*, Collies) that may have the gene mutation that causes a nonfunctional protein.

Adverse Effects

The following adverse reactions may occur: hypotension, bradycardia, tachycardia, exacerbation of CHF, peripheral edema, AV block, pulmonary edema, nausea, constipation, dizziness, headache or fatigue.

Reproductive/Nursing Safety

Oral verapamil in rats with doses 1.5–6 times the human dose was embryocidal and retarded fetal growth and development, probably due to reduced weight gains in dams. Verapamil crosses the placenta and can be detected in umbilical vein blood at delivery. In humans, the FDA categorizes this drug as category ***C*** 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.*)

Verapamil is excreted in milk. Consider discontinuing nursing if the dam requires verapamil therapy.

Overdosage/Acute Toxicity

Clinical signs of overdosage may include bradycardia, hypotension, hyperglycemia, junctional rhythms, and 2nd or 3rd degree AV block.

If overdose is secondary to a recent oral ingestion, emptying the gut and charcoal administration may be considered. Treatment is generally supportive in nature; vigorously monitor cardiac and respiratory function. Intravenous calcium salts (1 mL of 10% solution per 10 kgs of body weight) have been suggested to treat the negative inotropic clinical signs, but may not adequately treat clinical signs of heart block. Use of fluids and pressor agents (*e.g.*, dopamine, norepinephrine, etc.) may be utilized to treat hypotensive clinical signs. The AV block and/or bradycardia can be treated with isoproterenol, norepinephrine, atropine, or cardiac pacing. Patients that develop a rapid ventricular rate after verapamil due to antegrade conduction in flutter/fibrillation with WPW syndrome, have been treated with D.C. cardioversion, lidocaine, or procainamide.

Drug Interactions

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

- **ACE INHIBITORS:** May cause additive hypotensive effects
- **ALPHA-ADRENERGIC BLOCKERS** (*e.g.*, **prazosin**): May cause additive hypotensive effects
- **BETA-ADRENERGIC BLOCKERS** (*e.g.*, **propranolol**): May cause additive negative cardiac inotrope and chronotrope effects
- **DOXORUBICIN:** Verapamil may increase concentrations
- **COPP CHEMOTHERAPY** (**cyclophosphamide, vincristine, procarbazine, prednisone**): May decrease oral absorption of verapamil
- **CYCLOSPORINE:** Verapamil may increase levels
- **DANTROLENE:** Cardiovascular collapse reported in animals when used with verapamil
- **DIGOXIN:** Verapamil may increase the blood levels of digoxin; monitoring of digoxin levels recommended
- **DISOPYRAMIDE:** May cause additive effects; impair left ventricular function; use together within 24–48 hours not recommended
- **DIURETICS:** May cause additive hypotensive effects
- **ERYTHROMYCIN, CLARITHROMYCIN:** May increase verapamil levels
- **FLECAINIDE:** Possible additive effects; use is together with verapamil is to be avoided in humans
- **NEUROMUSCULAR BLOCKERS:** Neuromuscular blocking effects of nondepolarizing muscle relaxants may be enhanced by verapamil
- **PHENOBARBITAL:** May reduce verapamil levels
- **QUINIDINE:** Additive alpha-adrenergic blocking activity; increased hypotensive effect; verapamil can block quinidine's AV conductive effects and increase quinidine levels
- **RIFAMPIN:** May reduce verapamil levels
- **THEOPHYLLINE:** Verapamil may increase serum levels of theophylline and lead to toxicity
- **VINCRISTINE:** Calcium channel blockers may increase intracellular vincristine by inhibiting the drug's outflow from the cell

Laboratory Considerations

- Verapamil may elevate blood glucose in dogs and confuse **blood glucose** determinations

Doses

- **DOGS:**
  a) Initial dose of 0.05 mg/kg IV slowly, can repeat every 5 minutes up to a total dose of 0.15–0.2 mg/kg; Oral Dose: 0.5–2 mg/kg PO q8h (Ware 2000)
  b) For treatment of hypertension: 1–5 mg/kg PO q8h (Brovida 2002)
  c) 0.05–0.15 mg/kg slow IV to effect (Fox 2003a)
  d) 1–5 mg/kg PO three times daily; 0.05–0.25 mg/kg IV slowly (Kramer 2003c)
  e) For the acute termination of supraventricular tachycardia: Initial dose of 0.05 mg/kg should be administered over 1–2 minutes while ECG is monitored; if not effective, may repeat in 5–10 minutes. If arrhythmia still not terminated, may give one last dose of 0.05 mg/kg (total = 0.15 mg/kg). Effect may persist for 30 minutes or less. For longer control, may give as a CRI at 2–10 mcg/kg/minute. (Kittleson 2006c)
- **CATS:**
  a) Initial dose of 0.025 mg/kg IV slowly, can repeat every 5 minutes up to a total dose of 0.15–0.2 mg/kg; Oral Dose: 0.5–1 mg/kg PO q8h (Ware 2000)
- **HORSES:** (**Note:** ARCI UCGFS Class 4 Drug)
  a) To control ventricular rate in atrial fibrillation: 0.025–0.05 mg/kg IV q 30 minutes; give less than 0.2 mg/kg total dose (Reimer 2002)

Monitoring

- ECG
- Clinical signs of toxicity (see Adverse Effects);
- Blood pressure, during acute IV therapy
- Serum concentration, if efficacy or toxicity warrant (100–300 ng/mL is considered therapeutic)

Client Information

- To be effective, the animal must receive all doses as prescribed
- If animal becomes lethargic or becomes exercise intolerant, begins wheezing, has shortness of breath or cough, or develops a change in behavior or attitude, notify veterinarian.

Chemistry/Synonyms

A calcium channel blocking agent, verapamil HCl occurs as a bitter-tasting, nearly white, crystalline powder. It is soluble in water and the injectable product has a pH of 4–6.5.

Verapamil HCl tablets should be stored at room temperature (15–30°C); the injectable product should be stored at room temperature (15–30°C) and protected from light and freezing.

Verapamil HCl for injection is physically **compatible** when mixed with all commonly used intravenous solutions. However, a crystalline precipitate may form if verapamil is added to an infusion line with 0.45% sodium chloride with sodium bicarbonate running. Verapamil is reported to be physically **compatible** with the following drugs: amikacin sulfate, aminophylline, ampicillin sodium, ascorbic acid, atropine sulfate, bretylium tosylate, calcium chloride/gluconate, carbenicillin disodium, cefamandole naftate, cefazolin sodium, cefotaxime sodium, cefoxitin sodium, cephapirin sodium, chloramphenicol sodium succinate, cimetidine HCl, clindamycin phosphate, dexamethasone sodium phosphate, diazepam, digoxin, dobutamine HCl (slight discoloration due to dobutamine oxidation), dopamine HCl, epinephrine HCl, furosemide, gentamicin sulfate, heparin sodium, hydrocortisone sodium phosphate, hydromorphone HCl, insulin, isoproterenol, lidocaine HCl, magnesium sulfate, mannitol, meperidine HCl, metaraminol bitartrate, methicillin sodium, methylprednisolone sodium succinate, metoclopramide HCl, morphine sulfate, multivitamin infusion, nitroglycerin, norepinephrine bitartrate, oxytocin, pancuronium Br, penicillin G potassium/sodium, pentobarbital sodium, phenobarbital sodium, phentolamine mesylate, phenytoin sodium, potassium chloride/phosphate, procainamide HCl, propranolol HCl, protamine sulfate, quinidine gluconate, sodium bicarbonate, sodium nitroprusside, ticarcillin disodium, tobramycin sulfate, vasopressin, and vitamin B complex with C.

The following drugs have been reported to be physically **incompatible** with verapamil: albumin injection, amphotericin B, hydralazine HCl, nafcillin sodium, and trimethoprim/sulfamethoxazole. Compatibility is dependent upon factors such as pH, concentration, temperature, and diluent used; consult specialized references for more specific information.

Verapamil may also be known as: CP-16533-1, D-365, iproveratril hydrochloride, verapamili hydrochloridum; many trade names are available.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 4 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Verapamil HCl Tablets: 40 mg, 80 mg & 120 mg; *Calan*® (Searle); generic; (Rx)

Verapamil HCl Sustained/Extended-Release Tablets and Capsules: 100 mg, 120 mg, 180 mg, 200 mg, 240 mg, 300 mg and 360 mg; *Calan*® *SR* & *Covera-HS*® (Searle); *Isoptin*® *SR* (Abbott); *Verelan*® and *Verelan*® *PM* (Schwarz Pharma); generic; (Rx)

Verapamil HCl for Injection: 2.5 mg/mL in 2 mL, and 4 mL vials, amps and syringes, 2 mL fill in single-use *Carpuject* syringe; generic; (Rx)

VINBLASTINE SULFATE

(vin-***blas***-teen) Velban®

ANTINEOPLASTIC

Prescriber Highlights

- A Vinca alkaloid antineoplastic used for a variety of tumors in dogs (& sometimes cats)
- Contraindications: Preexisting leukopenia or granulocytopenia (unless a result of the disease being treated) or active bacterial infection; reduce dose if hepatic disease
- Adverse Effects: Gastroenterocolitis (nausea/vomiting), myelosuppression (more so than with vincristine); may also cause constipation, alopecia, stomatitis, ileus, inappropriate ADH secretion, jaw & muscle pain, & loss of deep tendon reflexes
- CATS can develop neurotoxicity causing constipation or paralytic ileus & aggravating anorexia; can also develop reversible axon swelling & paranodal demyelination
- Potentially teratogenic
- Avoid extravasation; wear gloves & protective clothing when preparing or administering
- Drug Interactions