- **ANTIARRHYTHMICS (oral)**: Sevelamer may reduce oral absorption; give at least one hour before or three hours after sevalamer capsules
- **CIPROFLOXACIN**: Concurrent administration with sevelamer may decrease absorption by 50%; administer ciprofloxacin and other oral fluoroquinolones at least one hour before or 3 hours after, sevelamer
- **ORAL MEDICATIONS**: There are only a few medications having documented reductions in oral administration when administered with sevelamer; consider dosing other oral drugs separately, particularly for drugs with narrow therapeutic indexes
- **VITAMINS**: Sevelamer may reduce vitamin absorption from food; consider administering vitamin supplements separately from sevelamer dose

Doses

- **DOGS:**
  a) For medium to large sized dog: 400 mg PO with meals (Vaden 2007)
- **CATS:**
  a) Has been used at 200 mg 2–3 times daily. Anecdotally appears to be safe and effective. (Sparkes 2006a)

Monitoring

- Serum phosphorus (and other electrolytes calcium, bicarbonate, chloride)
- Consider a baseline coagulation screening test before and after sevalamer therapy implementation as vitamin K absorption may be impacted by the drug

Chemistry/Synonyms

A phosphorus binding agent, sevalamer HCl is a complex chemical that is hydrophilic, but insoluble in water.

Sevelamer may also be known as GT16-026A and *Renagel®*.

Storage/Stability

Sevelamer capsules should be stored at room temperature and protected from moisture.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Sevalamer HCl Tablets: 400 mg and 800 mg (on an anhydrous basis); *Renagel®* (Genzyme); (Rx)

SEVOFLURANE

(see-voe-*floo*-rane) SevoFlo®, Ultane®

INHALATIONAL ANESTHETIC

Prescriber Highlights

- Inhalational anesthetic similar to isoflurane, but with more rapid induction & recovery
- Currently more expensive than isoflurane

Uses/Indications

Sevoflurane may be useful in a variety of species when rapid induction and/or rapid recoveries are desired with an inhalational anesthetic.

Pharmacology/Actions

While the precise mechanism that inhalant anesthetics exert their general anesthetic effects is not precisely known, they may interfere with functioning of nerve cells in the brain by acting at the lipid matrix of the membrane. Sevoflurane has a very low blood:gas partition coefficient (0.6) allowing very rapid anesthesia induction and recovery. Rapid mask induction is possible.

Pharmacologic effects of sevoflurane are similar to isoflurane and include: CNS depression, depression of body temperature regulating centers, increased cerebral blood flow, respiratory depression, hypotension, vasodilatation, myocardial depression (less so than with halothane), and muscular relaxation.

Minimal Alveolar Concentration (MAC; %) in oxygen reported for sevoflurane in various species: Dog = 2.09–2.4; Cat = 2.58; Horse = 2.31; Sheep = 3.3; Swine = 1.97–2.66; Human (adult) = 1.71–2.05. Several factors may alter MAC (acid/base status, temperature, other CNS depressants on board, age, ongoing acute disease, etc.).

Pharmacokinetics

Because of its low solubility in blood, only small concentrations of sevoflurane in the blood are required to be dissolved in blood before alveolar partial pressures are in equilibrium with arterial partial pressures. This low solubility means that sevoflurane is rapidly removed from the lungs. It is unknown what percent sevoflurane is bound to plasma proteins. The majority of sevoflurane is excreted via the lungs, but about 3% is metabolized in the liver via the cytochrome P450 2E1 isoenzyme system.

Contraindications/Precautions/Warnings

Sevoflurane is contraindicated in patients with a history or predilection towards malignant hyperthermia. It should be used with caution (benefits vs. risks) in patients with increased CSF or head injury, or renal insufficiency.

Because of its rapid action, use caution not to overdose during the induction phase. Because of the rapid recovery associated with sevoflurane use caution (and appropriate sedation during the recovery phase), particularly with large animals.

Geriatric animals may require less inhalation anesthetic.

Sevoflurane does not appear to be a good inhalational anesthetic in rabbits (breath holding, struggling).

Adverse Effects

Sevoflurane seems to be well tolerated. Hypotension may occur and is considered dose related. Dose-dependent respiratory depression and GI effects (nausea, vomiting, ileus) have been reported. While cardiodepression generally is minimal at doses causing surgical planes of anesthesia, it may occur; bradycardia is possible.

Malignant hyperthermia may be triggered by this agent (like other inhalational anesthetics).

Sevoflurane can react with carbon dioxide absorbents to produce "compound A", a nephrotoxin. After extensive clinical use in humans however, nephrotoxicity has not been demonstrated to be of clinical concern.

Sevoflurane should be used in precision, agent-specific, out of circuit vaporizers.

Reproductive/Nursing Safety

No overt fetotoxicity or teratogenicity has been demonstrated in lab animal studies, but definite safety has not been established for use during pregnancy.

Overdosage/Acute Toxicity

In the event of an overdosage, discontinue sevoflurane; maintain airway and support respiratory and cardiac function as necessary.

Drug Interactions

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

- **AMINOGLYCOSIDES, LINCOSAMIDES**: May enhance neuromuscular blockade
- **BARBITURATES** (**phenobarbital, pentobarbital**, etc.): May increase concentrations of inorganic fluoride
- **ISONIAZID**: May increase concentrations of inorganic fluoride
- **MIDAZOLAM**: May potentiate sevoflurane effects; decrease MAC
- **NON-DEPOLARIZING NEUROMUSCULAR BLOCKING AGENTS** (**atracurium, pancuronium, vecuronium**): Additive neuromuscular blockade may occur
- **OPIATES**: May potentiate sevoflurane effects; decrease MAC
- **ST. JOHNS WORT**: Increased risk for anesthetic complications; recommend discontinuing St. John's Wort 5 days in advance of surgery
- **SUCCINYLCHOLINE**: Sevoflurane may enhance effects
- **SYMPATHOMIMETICS** (**dopamine, epinephrine, norepinephrine, ephedrine, metaraminol**, etc.): While sevoflurane sensitizes the myocardium to the effects of sympathomimetics less so than halothane, arrhythmias may still result; caution and monitoring is advised
- **VERAPAMIL**: May cause cardiodepression

Laboratory Considerations

- Inhalational anesthetics may cause transient increases in **liver function tests, WBCs,** and **glucose**

Doses

Minimal Alveolar Concentration (MAC; %) in oxygen reported for sevoflurane in various species: Dog = 2.09–2.4; Cat = 2.58; Horse = 2.31; Sheep = 3.3; Swine = 1.97–2.66; Human (adult) = 1.71–2.05. Several factors may alter MAC (acid/base status, temperature, other CNS depressants on board, age, ongoing acute disease, etc.)

- **DOGS:**

  Inspired Concentration: The delivered concentration of *SevoFlo*® (sevoflurane) should be known. Since the depth of anesthesia may be altered easily and rapidly, only vaporizers producing predictable percentage concentrations of sevoflurane should be used. Sevoflurane should be vaporized using a precision vaporizer specifically calibrated for sevoflurane. Sevoflurane contains no stabilizer. Nothing in the drug product alters calibration or operation of these vaporizers. The administration of general anesthesia must be individualized based on the patient's response. **When using sevoflurane, patients should be continuously monitored and facilities for maintenance of patient airway, artificial ventilation, and oxygen supplementation must be immediately available.**

  Replacement of Desiccated CO2 Absorbents: When a clinician suspects that the CO2 absorbent may be desiccated, it should be replaced. An exothermic reaction occurs when sevoflurane is exposed to CO2 absorbents. This reaction is increased when the CO2 absorbent becomes desiccated.

  Premedication: No specific premedication is either indicated or contraindicated with sevoflurane. The necessity for and choice of premedication is left to the discretion of the veterinarian. Preanesthetic doses for premedicants may be lower than the label directions for their use as a single medication.

  Induction: For mask induction using sevoflurane, inspired concentrations up to 7% sevoflurane with oxygen are employed to induce surgical anesthesia in the healthy dog. These concentrations can be expected to produce surgical anesthesia in 3 to 14 minutes. **Due to the rapid and dose dependent changes in anesthetic depth, care should be taken to prevent overdosing. Respiration must be monitored closely in the dog and supported when necessary with supplemental oxygen and/or assisted ventilation.**

  Maintenance: *SevoFlo*® may be used for maintenance anesthesia following mask induction using sevoflurane or following injectable induction agents. The concentration of vapor necessary to maintain anesthesia is much less than that required to induce it. Surgical levels of anesthesia in the healthy dog may be maintained with inhaled concentrations of 3.7–4% sevoflurane in oxygen in the absence of premedication and 3.3–3.6% in the presence of premedication. The use of injectable induction agents without premedication has little effect on the concentrations of sevoflurane required for maintenance. Anesthetic regimens that include opioid, alpha2-agonist benzodiazepine or phenothiazine premedication will allow the use of lower sevoflurane maintenance concentrations. (Label directions; *SevoFlo*®—Abbott Animal Health)

Monitoring

- Respiratory and ventilatory status
- Cardiac rate/rhythm; blood pressure (particularly with "at risk" patients
- Level of anesthesia

Chemistry/Synonyms

Sevoflurane is an isopropyl ether inhalational anesthetic with a molecular wt. of 200, saturate vapor pressure at 20°C of 160 mmHg and a boiling pt. of 58.5°C. It is reported to have a pleasant odor and is not irritating to airways. It is non-flammable and non-explosive. Sevoflurane is a clear, colorless liquid that is miscible with ethanol or ether and slightly soluble in water.

Sevoflurane may also be known as: BAX-3084, MR-654, *Sevocris*®, *SevoFlo*®, *Sevorane*®, or *Ultane*®.

Storage/Stability

Sevoflurane should be stored at room temperature. Sevoflurane does not react with metal.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Sevoflurane in 250 mL btls; *SevoFlo*® (Abbott); (Rx). Approved for use in dogs.

HUMAN-LABELED PRODUCTS:

Sevoflurane in 250 mL btls; *Ultane*® (Abbott); (Rx)

SILDENAFIL CITRATE

(sil-***den***-ah-fil) Viagra®, Revatio®

VASODILATOR; PHOSPHODIESTERASE TYPE 5 INHIBITOR

Prescriber Highlights

- Used in veterinary medicine for treating pulmonary hypertension
- Contraindicated if patients receiving organic nitrates
- Adverse effects not well-known; inguinal flushing, possible GI effects reported
- Treatment may be very expensive

Uses/Indications

Sildenafil may be of benefit in the adjunctive treatment of pulmonary hypertension in small animals.

In humans, sildenafil is indicated for erectile dysfunction or pulmonary hypertension.

Pharmacology/Actions

Sildenafil inhibits cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type-5 (PDE5) found in the smooth muscle of the pulmonary vasculature, corpus cavernosum and elsewhere, where PDE5 is responsible for degradation of cGMP. Sildenafil increases cGMP thereby resulting in nitric oxide mediated vasodilatation within pulmonary vascular smooth muscle cells.

Pharmacokinetics

The pharmacokinetics of sildenafil has been reported in dogs (Walker, Ackland et al. 1999). Oral bioavailability is approximately 50% (higher than humans); volume of distribution is about 5.2 L/kg (versus 1.2 L/kg in humans); elimination half-life approximately 6 hours (significant interpatient variability; average human half life is about 4 hours).

Contraindications/Precautions/Warnings

Sildenafil should not be used concurrently with nitrates (see drug interactions) or in patients documented hypersensitive to it.

Pulmonary vasodilators may significantly worsen the cardiovascular status of patients with pulmonary veno-occlusive disease (PVOD).

Use with extreme caution in patients with resting hypotension, fluid depletion, severe left ventricular outflow obstruction, or autonomic dysfunction.

Adverse Effects

Because of limited use in dogs, the adverse effect profile is not fully known. Cutaneous flushing of the inguinal region has been reported and GI effects are possible. In humans, headache, visual disturbances, dyspepsia, nasal congestion, myalgia, priapism, dizziness, and back pain have been reported.

Reproductive/Nursing Safety

No evidence of teratogenicity, embryotoxicity or fetotoxicity was observed in pregnant rats or rabbits, dosed at 200 mg/kg/day during organogenesis. In a rat pre- and postnatal development study, the no-observed-adverse-effect dose was 30 mg/kg/day. 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.*)

It is not known if sildenafil or its metabolites are excreted in milk.

Overdosage/Acute Toxicity

Little information is available. An adult women ingested 2000 mg and survived but developed tachycardia, nonspecific ST-T changes on ECG, headache, dizziness, and flushing.

It is expected that overdoses in animals would mirror the drugs adverse effect profile; treat supportively.

Drug Interactions

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

- **ALPHA-ADRENERGIC BLOCKERS** (*e.g.,* **phentolamine, phenothiazines, phenoxybenzamine**): May increase hypotensive effects
- **AMLODIPINE:** Potential to increase hypotensive effects
- **ANTIHYPERTENSIVE, HYPOTENSIVE DRUGS:** Potentially could increase hypotensive effects
- **AZOLE ANTIFUNGALS** (**ketoconazole, itraconazole**): May reduce sildenafil metabolism and increase AUC
- **CIMETIDINE:** May reduce sildenafil metabolism and increase AUC
- **ERYTHROMYCIN, CLARITHROMYCIN:** May reduce sildenafil metabolism and increase AUC
- **HEPARIN:** May increase bleeding risks
- **NITRATES** (*e.g.,* **NTG, Isosorbide**): Significant potentiation of vasodilatory effects; life-threatening hypotension possible
- **NITROPRUSSIDE SODIUM:** Significant potentiation of vasodilatory effects; life-threatening hypotension possible
- **PHENOBARBITAL:** May decrease sildenafil concentrations
- **RIFAMPIN:** May decrease sildenafil concentrations

Laboratory Considerations

None were noted.

Doses

- **DOGS/CATS:**

  Dogs: From a retrospective study: median dose was 1.9 mg/kg (range from 0.5–2.7 mg/kg) q8–24h. Dogs may have been also treated with oxygen, ACE inhibitors, furosemide, amlodipine, diltiazem, theophylline, phenobarbital and/or antibiotics. (Bach, Rozanski et al. 2006)

  For pulmonary hypertension documented by Doppler, chronic pulmonary disease, right-sided heart failure (HW disease; congenital): 0.5–1 mg/kg PO two times daily (higher dose of 2–3 mg/kg three times a day may be tolerated and needed) (Tilley 2007)

Monitoring

- Clinical efficacy (improved syncope, cough, respiratory effort)
- Pulmonary artery pressure, systemic blood pressure

Client Information

- Brief clients on the experimental nature of using this medication in small animals and the costs of therapy

Chemistry/Synonyms

Sildenafil citrate occurs as a white to off-white crystalline powder with a solubility of 3.5 mg/mL in water and a molecular weight of 666.7.