For epistaxis prevention:

a) 0.3–0.6 mg/kg 60–90 minutes prior to race (Robinson 1987)

b) 250 mg IV 4 hours prior to racing (Foreman 1999)

- **BIRDS:**

As a diuretic:

a) 0.05 mg/300 gm IM twice daily (**Note**: Lories are very sensitive to this agent and can be easily overdosed) (Clubb 1986)

- **REPTILES:**

For most species:

a) 5 mg/kg IV or IM as needed (Gauvin 1993)

Monitoring

- Serum electrolytes, BUN, creatinine, glucose
- Hydration status
- Blood pressure, if indicated
- Clinical signs of edema, patient weight, if indicated
- Evaluation of ototoxicity, particularly with prolonged therapy or in cats

Client Information

- Clients should contact veterinarian if clinical signs of water or electrolyte imbalance occur, such as excessive thirst, lethargy, lassitude, restlessness, reduced urination, GI distress or fast heart rate.

Chemistry/Synonyms

A loop diuretic related structurally to the sulfonamides, furosemide occurs as an odorless, practically tasteless, white to slightly yellow, fine, crystalline powder. Furosemide has a melting point between 203°–205°C with decomposition, and a pK_a of 3.9. It is practically insoluble in water, sparingly soluble in alcohol, and freely soluble in alkaline hydroxides. The injectable product has its pH adjusted to 8–9.3 with sodium hydroxide.

Furosemide may also be known as: frusemide, furosemidum, and LB-502; many trade names are available.

Storage/Stability/Compatibility

Furosemide tablets should be stored in light-resistant, well-closed containers. The oral solution should be stored at room temperature and protected from light and freezing. Furosemide injection should be stored at room temperature. A precipitate may form if the injection is refrigerated, but will resolubolize when warmed without alteration in potency. The human injection (10 mg/mL) should not be used if it has a yellow color. The veterinary injection (50 mg/mL) normally has a slight yellow color. Furosemide is unstable at an acid pH, but is very stable under alkaline conditions.

Furosemide injection (10 mg/mL) is reportedly physically **compatible** with all commonly used intravenous solutions and the following drugs: amikacin sulfate, cimetidine HCl, kanamycin sulfate, tobramycin sulfate, and verapamil.

It is reportedly physically **incompatible** with the following agents: ascorbic acid solutions, dobutamine HCl, epinephrine, gentamicin sulfate, netilmicin sulfate and tetracyclines. It should generally not be mixed with antihistamines, local anesthetics, alkaloids, hypnotics, or opiates.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Furosemide Tablets: 12.5 mg, 50 mg; *Salix*® (Intervet); *Disal*® *Tablets* (Boehringer Ingelheim), *Furotabs*® (Butler); generic (Phoenix Pharmaceutical); (Rx). Products may be approved for use in dogs and cats.

Furosemide Oral Solution (Syrup): 10 mg/mL in 60 mL; generic (IVX, First Priority); (Rx) Approved for use in dogs.

Furosemide for Injection: 50 mg/mL (5%) in 50 mL and 100 mL vials; *Disal*® *Injection* (Boehringer Ingelheim), *Salix*® *Injection* (Intervet), *Furoject*® (Butler), generic (AgriLabs, IVX, Vet Tek, Phoenix Pharmaceutical), (Rx). Products may be approved for use in dogs, cats and horses.

HUMAN-LABELED PRODUCTS:

Furosemide Tablets: 20 mg, 40 mg, & 80 mg; *Lasix*® (Aventis); generic; (Rx)

Furosemide Oral Solution: 10 mg/mL in 60 mL and 120 mL; 40 mg/5 mL in 500 mL and UD 5 mL and 10 mL; generic; (Rx)

Furosemide Injection: 10 mg/mL in 2 mL, 4 mL and 10 mL single-dose vials and 10 mL multi-dose vial; generic; (Rx)

GABAPENTIN

(gab-ah-***pen***-tin) Neurontin®

ANTICONVULSANT; NEUROPATHIC PAIN ANALGESIC

Prescriber Highlights

- **May be useful in dogs & cats as adjunctive therapy for refractory or complex partial seizures or the treatment of pain**
- **Caution in patients with diminished renal function, but dogs partially (30–40%) metabolize the drug (humans do not)**
- **Avoid use of xylitol-containing oral liquid in dogs**
- **Sedation most likely adverse effect, but adverse effect profile not well-defined for animals**
- **Expense may be a significant issue, but may decrease as generics are now available**

Uses/Indications

Gabapentin may be useful as adjunctive therapy for refractory or complex partial seizures, or in the treatment of chronic pain in dogs or cats.

Pharmacology/Actions

Gabapentin has analgesic effects and can prevent allodynia (sensation of pain resulting from a normally non-noxious stimulus) or hyperalgesia (exaggerated response to painful stimuli). It also has anticonvulsant activity. The mechanism of action of gabapentin, for either its anticonvulsant or analgesic actions is not understood. While gabapentin is structurally related to GABA, it does not appear to alter GABA binding, reuptake, or degradation, or serve as a GABA agonist *in vivo*.

Pharmacokinetics

In dogs, oral bioavailability is about 80% at a dose of 50 mg/kg. Peak plasma levels occur about 2 hours post dose. Elimination is primarily via renal routes, but gabapentin is partially metabolized to N-methyl-gabapentin. Elimination half-life is approximately 2–4 hours in dogs. No pharmacokinetic data for cats was located.

In humans, gabapentin bioavailability decreases as dosage increases. At doses of 900 mg/day, 60% of the dose is absorbed. Percentage absorbed is reduced as doses are increased to a minimum of 27%

of the dose being absorbed when 4800 mg/day is administered. Presence of food only marginally alters absorption rate and extent of absorption. Gabapentin is only minimally bound to plasma proteins; CSF levels are approximately 20% of those in plasma. The drug is not significantly metabolized and is almost exclusively excreted unchanged into the urine. Elimination half-lives in humans are approximately 5–7 hours.

Contraindications/Precautions/Warnings

Gabapentin is considered contraindicated in patients hypersensitive to it. Because gabapentin is eliminated via renal routes (practically 100% in humans), it should be used with caution in patients with renal insufficiency; if required, dosage adjustment should be considered. In dogs, the drug is also metabolized (30–40%) of a dose, so dosage adjustment may not be required in dogs with mild to moderate renal dysfunction.

In general, avoid the use of the commercially available human oral solution (*Neurontin®*) in dogs as it reportedly contains 300 mg/mL xylitol. As the threshold dose that can cause hypoglycemia in dogs is approximately 100 mg/kg, doses of up to 15 mg/kg in dogs using the solution should be safe, but further data is needed to confirm this. Additionally, xylitol may be hepatotoxic in dogs. Doses of 500 mg/kg of xylitol are currently thought to be the threshold for this toxicity, but there have been anecdotal reports of it occurring at much lower doses. In cats, at the dosages used presently, xylitol toxicity does not appear to be a problem with gabapentin oral solution, but use with caution.

Adverse Effects

Sedation is probably the most likely adverse effect seen in small animals. Starting the dose at the lower end of the range and increasing with time, may alleviate this effect. In humans, the most common adverse effects associated with gabapentin therapy are dizziness, somnolence, and peripheral edema.

Gabapentin was associated with an increased rate of pancreatic adenocarcinoma in male rats. It is unknown if this effect crosses into other species.

Abrupt discontinuation of the drug has lead to withdrawal-precipitated seizures. In humans, it is recommended to wean off the drug when it is used for epilepsy treatment.

Reproductive/Nursing Safety

In humans, the FDA categorizes gabapentin 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 (at or above human maximum dosages), gabapentin was associated with a variety of fetotoxic and teratogenic effects (*e.g.*, delayed ossification, hydronephrosis, fetal loss) in rats, mice and rabbits.

Gabapentin enters maternal milk. It has been calculated that a nursing human infant could be exposed to a maximum dosage of 1 mg/kg/day. This is 5–10% of the usual pediatric (>3 yrs old) therapeutic dose. In veterinary patients, this appears unlikely to be of significant clinical concern.

Overdosage/Acute Toxicity

In humans, doses of up to 49 grams have been reported without fatality. Most likely effects include ataxia, lethargy/somnolence, diarrhea, etc.

The commercially available oral solution contains 300 mg/mL; doses of 0.33 mL/kg may cause hypoglycemia or liver toxicity in dogs.

There were 256 exposures to gabapentin reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2005–2006. In these cases 211 were dogs with 13 showing clinical signs and the remaining 45 cases were cats with 11 showing clinical signs. Common findings in dogs recorded in decreasing frequency included lethargy, ataxia, sedate, vomiting and bulging eyes. Common findings in cats recorded in decreasing frequency included ataxia, lethargy, bradycardia, depression, and mydriasis. Treatment is basically supportive with general decontamination procedures including emesis, activated charcoal, and cathartics. The drug can be removed with hemodialysis.

Drug Interactions

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

- **ANTACIDS:** Oral antacids given concurrently with gabapentin may decrease oral bioavailability by 20%; if antacids are required, separate doses at least 2 hours from gabapentin
- **HYDROCODONE:** Co-administration of gabapentin and hydrocodone may increase the AUC (area under the curve) of gabapentin and increase the efficacy and/or adverse effects of the drug. Gabapentin can reduce the AUC of hydrocodone, potentially reducing the drug's effectiveness.
- **MORPHINE:** May increase gabapentin levels

Laboratory Considerations

- There are reports of gabapentin causing false-positive **urinary protein** readings on *Ames N-Multistix SG* dipstick tests. The use of a sulfosalicylic acid precipitation test to determine presence of urine protein is recommended for patients receiving gabapentin.

Doses

- **DOGS:**

  For ancillary therapy of refractory seizures:
  a) 10–30 mg/kg PO q8–12h (Podell 2006a)
  b) 25–60 mg/kg/day PO *divided* q6–8h, the author initially uses 10 mg/kg PO q8h. (Dewey 2005b)
  c) 10–30 mg/kg PO q8h. **Note:** expensive and of limited benefit (Berry 2003)

  As an analgesic:
  a) For adjunctive treatment of chronic or cancer pain: 3 mg/kg PO once a day (Lascelles 2003)
  b) 1.25–10 mg/kg PO q24h (once daily) (Hardie 2006)

- **CATS:**

  For ancillary therapy of refractory seizures:
  a) 5 mg/kg PO three times daily (Pearce 2006b)
  b) 5–10 mg/kg PO q8–12h (Podell 2006a)
  c) 10–30 mg/kg PO q8h (**Note:** expensive and of limited benefit) (Berry 2003)

  As an analgesic:
  a) 1.25–10 mg/kg PO q24h (once daily) (Hardie 2006)
  b) For adjunctive treatment of chronic or cancer pain: 3 mg/kg PO once a day (Lascelles 2003), (Hardie, Lascelles et al. 2003)
  c) For adjunctive analgesia associated with neuropathic pain: While suggested range in cats is 2.5–5 mg/kg PO q12h, this author starts at 5 mg/kg and increases (up to 10 mg/kg) if no effect seen in two hours. May be a higher requirement in cats for post-seizure or CPR vocalization and thrashing. Wean off slowly or patient may experience worse pain. Reduce in renal insufficiency. Usually the limit of dosing is reached when patient is sedated. (Mathews 2006)

Monitoring
- **Note:** Gabapentin serum levels are not monitored at present.
- Clinical efficacy and adverse effects should be monitored.

Client Information
- Clients should report any significant adverse effects such as ataxia or hypersomnolence

Chemistry/Synonyms
Gabapentin occurs as white to off-white crystalline solid that is freely soluble in water. It has a pK_{a1} of 3.7 and a pK_{a2} of 10.7. It is structurally related to GABA (gamma-aminobutyric acid).

Gabapentin may also be known as: CI-945, GOE-3450, *Aclonium®, Equipax®, Gantin®, Gabarone®, Neurontin®, Neurostil®* and *Progresse®*.

Storage/Stability/Compatibility
The commercially available capsules and tablets should be stored at room temperature (25°C, 77°F); excursions permitted to 15–30°C (59–86°F). The oral liquid should be stored in the refrigerator at 2–8°C (36–46°F).

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:

Gabapentin Capsules & Tablets: 100 mg, 300 mg, 400 mg; 600 mg, & 800 mg (film-coated); *Gabarone®* or Gabapentin (Ivax); *Neurontin®* (Pfizer); generic, (Rx)

Gabapentin Solution: 250 mg/5mL (50 mg/mL) in 470 mL; *Neurontin®* (Pfizer); (Rx) **Note:** Contains xylitol. Use with caution in dogs.

GEMCITABINE HCL

(jem-***site***-ah-ben) Gemzar®

ANTINEOPLASTIC

Prescriber Highlights
- Antineoplastic agent that may potentially be useful for treating several cancers in dogs or cats
- Very limited clinical use & research performed thus far
- Myelosuppression most likely adverse effect
- Very expensive

Uses/Indications
Very limited clinical use and research performed with this drug to date have demonstrated limited clinical efficacy. However, it potentially may be useful as a radiosensitizer for non-resectable tumors, as part of combination protocols, or as a single agent for tumors not amenable to more accepted therapies. Follow research reports for the most up-to-date information.

In humans, gemcitabine has shown some efficacy in treating pancreatic carcinoma, small-cell lung carcinoma, lymphoma, bladder and other soft tissue carcinomas.

Pharmacology/Actions
Gemcitabine exhibits cell phase specificity and acts primarily on the S phase. It also inhibits cell progression through the G1/S-phase boundary.

Gemcitabine is metabolized intracellularly to diflurodeoxycytidine monophosphate (dFdCMP) that is then converted into diphosphate (dFdCDP) and triphosphate (dFdCTP) forms, the metabolites that give the drug its activity. The diphosphate inhibits ribonucleotide reductase. The triphosphate competes with deoxycytidine triphosphate (dTCP; the "normal" nucleotide) for incorporation into DNA strands.

Pharmacokinetics
In dogs, gemcitabine exhibits first order elimination and has a terminal half-life of about 1.5–3.2 hours. Volume of distribution (steady-state) is around 1 L/kg.

In humans, gemcitabine levels achieve steady state in about 15 minutes during a 30 minute infusion. Protein binding is negligible. Volume of distribution is about 50 L/m^2. Less than 10% of the drug is excreted unchanged in the urine.

Contraindications/Precautions/Warnings
Gemcitabine is contraindicated in patients hypersensitive to it. It should be used with caution in patients with diminished renal or hepatic function.

Adverse Effects
Gemcitabine may cause myelosuppression and can affect red cell, white cell, and platelet cell lines, but neutrophils and platelets appear to be most affected. Neutrophil nadirs usually occur 3–7 days post treatment. GI effects have been reported in animals receiving the drug, but are usually mild. Retinal hemorrhage could occur in animals receiving gemcitabine.

In a pilot study (Kosarek, Kissabeth et al. 2005) in 19 dogs receiving up to 675 mg/m2 biweekly demonstrated "minimal and acceptable toxicity." Another study (Turner, Hahn et al. 2006) where dogs with lymphoma were given gemcitabine as single agent therapy at 400 mg/m2 weekly for 3 weeks and then off one week, showed significant decreases in neutrophils and platelets 7 days post treatment. 15 of the 21 dogs in the study required dosage reduction or delay in retreatment. Only 7 of the 21 dogs finished the initial 4 week cycle and a second cycle did not result in any objective therapeutic response.

Reproductive/Nursing Safety
In pregnant humans, gemcitabine is designated by the FDA as a category ***D*** drug (*There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.*)

It is unknown whether gemcitabine is excreted in maternal milk.

Overdosage/Acute Toxicity
There is no known antidote to gemcitabine in an overdose situation. Myelosuppression should be expected. Treatment is supportive.

Drug Interactions
No specific drug interactions were noted, but toxic effects (myelosuppression, GI) could be additive when used with other drugs that also cause those effects.