■ **DOGS:**

For neoplastic diseases (usually used in combination protocols with other drugs; see the appendix for sample protocols):

a) 0.5–0.75 mg/m2 IV every 7–14 days (O'Keefe and Harris 1990)
b) 0.5 mg/m2 every 7–14 days (Coppoc 1988)
c) 0.5 mg/m2 IV weekly (MacEwen and Rosenthal 1989)
d) For transmissible venereal tumor: 0.025 mg/kg (maximum dose 1 mg) IV once weekly. Generally requires 3–6 weeks of therapy. Usually tumor regression noted within 2 weeks of initial treatment. (Herron 1988)
e) For transmissible venereal tumor: 0.5 mg/m2 (maximum dose 1 mg) IV every 7 days until there is no evidence of disease. Generally requires 4–6 weeks of therapy. (Rosenthal 1985)

For immune-mediated thrombocytopenia:

a) Used only when other therapies are ineffective and bone marrow aspirate demonstrates adequate megakaryocytopoiesis: 0.02 mg/kg IV once weekly (Feldman 1989)
b) If refractory to prednisone (3–5 days), give vincristine at 0.5–0.7 mg/m2 IV bolus or as an infusion over 4–6 hours (Trepanier 1999)
c) 0.02 mg/kg IV once; generally single use (Cohn 2004)

■ **CATS:**

For neoplastic diseases (usually used in combination protocols with other drugs; see the appendix for additional sample protocols):

a) 0.5–0.75 mg/m2 IV once a week (Couto 1989b)
b) For feline lymphoma: A neutrophil count over 4,500 cells/UL is required. Cats should be well hydrated before treatment and fluid therapy should be continued for 24–36 hours. On day 1 give vincristine at 0.5 mg/m2 IV and cyclophosphamide at 250 mg/m2 IV or orally. These drugs may be administered by slow IV push. If no adverse reactions and neutrophil count is over 4,500, may repeat on day 21. On day 42, premedicate with diphenhydramine (2.2. mg/kg SC) and give doxorubicin at 1 mg/kg IV over 20 minutes into the injection port of an IV drip set. This regimen is repeated until a total of six cycles have been administered. If cat is in complete remission at the end of the of the 6 cycles, consider stopping therapy. Treatment is delayed if neutropenia of thrombocytopenia occur. If hemorrhagic cystitis occurs, discontinue cyclophosphamide. Monitor renal function throughout therapy. (Legendre 2003)

Monitoring

■ Efficacy (tumor burden reduction or platelet count)
■ Toxicity (peripheral neuropathic clinical signs; complete blood counts with platelets; liver function tests prior to therapy and repeated as necessary; serum uric acid)

Client Information

■ Clients must be briefed on the possibilities of severe toxicity developing from this drug, including drug-related mortality
■ Clients should contact the veterinarian if the patient exhibits any signs of profound depression, abnormal bleeding (including bloody diarrhea) and/or bruising, severe constipation, or severe peripheral neuropathic signs

Chemistry/Synonyms

Commonly referred to as a Vinca alkaloid, vincristine sulfate is isolated from the plant *Cantharanthus roseus* (*Vinca rosea Linn*) and occurs as a white or slightly yellow, hygroscopic, amorphous or crystalline powder that is freely soluble in water and slightly soluble in alcohol. The commercially available injection has a pH of 3–5.5. Vincristine sulfate has pK_as of 5 and 7.4

Vincristine Sulfate may also be known as: leurocristine sulfate, VCR, LCR compound 37231, leurocristine sulphate, NSC-67574, 22-oxovincaleukoblastine sulphate, sulfato de vincristina, vincristini sulfas and *Oncovin*®; many other trade names are available.

Storage/Stability/Compatibility

Vincristine sulfate injection should be protected from light and stored in the refrigerator (2–8°C).

Vincristine sulfate is reportedly physically **compatible** with the following intravenous solutions and drugs: D_5W, bleomycin sulfate, cytarabine, fluorouracil, and methotrexate sodium. In syringes or at Y-sites with: bleomycin sulfate, cisplatin, cyclophosphamide, doxorubicin HCl, droperidol, fluorouracil, heparin sodium, leucovorin calcium, methotrexate sodium, metoclopramide HCl, mitomycin, and vinblastine sulfate.

Vincristine sulfate is reportedly physically **incompatible** with furosemide. Compatibility is dependent upon factors such as pH, concentration, temperature, and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Vincristine Sulfate Injection: 1 mg/mL in 1 mL, 2 mL and 5 mL vials and flip-top vials; *Vincasar® PFS* (Genesia Sicor); generic; (Rx)

VITAMIN E/SELENIUM
VITAMIN E

(se-*lee*-nee-um)

NUTRITIONAL; FAT SOLUBLE VITAMIN

Prescriber Highlights

- **Lipid-soluble vitamin (E) with or without selenium used alone for discoid lupus erythematosus, canine demodicosis, acanthosis nigricans, hepatic fibrosis, or adjunctive therapy of exocrine pancreatic deficiency or hepatopathy in dogs & cats; used in combination for selenium-tocopherol deficiency (white muscle disease)**
- **Contraindications: Vitamin E/selenium products should only be used in the species for which they are approved**
- **Selenium overdoses can be extremely toxic**
- **Adverse Effects: Anaphylactoid reactions; IM injections may cause transient muscle soreness. Selenium OD's can cause depression, ataxia, dyspnea, blindness, diarrhea, muscle weakness, & a "garlic" odor on the breath**

Uses/Indications

Depending on the actual product and species, vitamin E/selenium is indicated for the treatment or prophylaxis of selenium-tocopherol deficiency (STD) syndromes in ewes and lambs (white muscle disease), sows, weanling and baby pigs (hepatic necrosis, mulberry heart disease, white muscle disease), calves and breeding cows (white muscle disease), and horses (myositis associated with STD).

Vitamin E may be useful as adjunctive treatment of discoid lupus erythematosus, canine demodicosis, and acanthosis nigricans

in dogs. It may also be of benefit in the adjunctive treatment of hepatic fibrosis or adjunctive therapy of copper-associated hepatopathy in dogs.

Pharmacology/Actions

Both vitamin E and selenium are involved with cellular metabolism of sulfur. Vitamin E has antioxidant properties and, with selenium, protects against red blood cell hemolysis and prevents the action of peroxidase on unsaturated bonds in cell membranes.

Pharmacokinetics

After absorption, vitamin E is transported in the circulatory system via beta-lipoproteins. It is distributed to all tissues and stored in adipose tissue. Vitamin E is only marginally transported across the placenta. Vitamin E is metabolized in the liver and excreted primarily into the bile.

Pharmacokinetic parameters for selenium were not located.

Contraindications/Precautions/Warnings

Vitamin E/selenium products should only be used in the species for which they are approved. Because selenium can be extremely toxic, the promiscuous use of these products cannot be condoned.

Give slowly when administering intravenously to horses.

Adverse Effects

Anaphylactoid reactions have been reported. Intramuscular injections may be associated with transient muscle soreness. Other adverse effects are generally associated with overdoses of selenium (see below).

Overdosage/Acute Toxicity

Selenium is quite toxic in overdose quantities, but has a fairly wide safety margin. Cattle have tolerated chronic doses of 0.6 mg/kg/day with no adverse effects (approximate therapeutic dose is 0.06 mg/kg). Clinical signs of selenium toxicity include depression, ataxia, dyspnea, blindness, diarrhea, muscle weakness, and a "garlic" odor on the breath. Horses suffering from selenium toxicity may become blind, paralyzed, slough their hooves, and lose hair from the tail and mane. Dogs may exhibit clinical signs of anorexia, vomiting, and diarrhea at high dosages.

Drug Interactions

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

- **IRON**: Large doses of vitamin E may delay the hematologic response to iron therapy in patients with iron deficiency anemia.
- **MINERAL OIL**: May reduce the absorption of orally administered vitamin E
- **VITAMIN A**: Absorption, utilization and storage may be enhanced by vitamin E

Doses (Vitamin E alone):

For doses of vitamin E/selenium products see the Dosage Form section

- **DOGS:**

  For adjunctive treatment of discoid lupus erythematosus, canine demodicosis or acanthosis nigricans:

  a) 200–400 IU PO three times daily; variable efficacy, but relatively innocuous at these dosages (White 2000)

  For adjunctive treatment of hepatic fibrosis:

  a) 100–400 IU q12h PO (Rutgers 2000)

  For adjunctive treatment of copper-associated hepatopathy:

  a) 400–600 IU PO per day (Johnson 2000)

  For treatment of tocopherol deficiency associated with exocrine pancreatic disease:

  a) 100–400 IU PO once daily for one month then every 1–2 weeks as needed (Williams 2000)

- **CATS:**

  For treatment of tocopherol deficiency associated with exocrine pancreatic disease:

  a) 30 IU PO once daily for one month then every 1–2 weeks as needed (Williams 2000)

  For adjunctive treatment of hepatic lipidosis:

  a) 10 IU/kg once PO once daily) (Scherk and Center 2005)

- **HORSES:**

  For adjunctive treatment of ionophore (monensin) toxicity:

  a) 4–12 Units/kg PO once daily (Mogg 1999)

  For adjunctive therapy for EPM:

  a) 8000–9000 IU PO per day (Dowling 1999)

  For adjunctive therapy for metabolic syndrome:

  a) 10,000 IU PO once daily (Johnson 2003b)

  For adjunctive treatment of perinatal asphyxia syndrome (hypoxic ischemic encephalopathy):

  a) Foals: 4,000 IU PO once daily; Mares: 10,000 IU PO once daily (Slovis 2003b)

Monitoring

- Clinical efficacy
- Blood selenium levels (when using the combination product). Normal values for selenium have been reported as: >1.14 micromol/L in calves, >0.63 micromol/L in cattle, >1.26 micromol/L in sheep, and >0.6 micromol/L in pigs. Values indicating deficiency are: <0.40 micromol/L in cattle, <0.60 micromol/L in sheep, and <0.20 micromol/L in pigs. Intermediate values may result in suboptimal production
- Optionally, glutathione peroxidase activity may be monitored

Chemistry/Synonyms

Vitamin E is a lipid soluble vitamin that can be found in either liquid or solid forms. The liquid forms occur as clear, yellow to brownish red, viscous oils that are insoluble in water, soluble in alcohol and miscible with vegetable oils. Solid forms occur as white to tan-white granular powders that disperse in water to form cloudy suspensions. Vitamin E may also be known as alpha tocopherol.

Selenium in commercially available veterinary injections is found as sodium selenite. Each mg of sodium selenite contains approximately 460 micrograms (46%) of selenium.

Storage/Stability

Vitamin E/Selenium for injection should be stored at temperatures less than 25°C (77°F).

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Vitamin E (Alone) Injection

Vitamin E Injection: 300 mg/mL in 250 mL vials; *Emulsivit® E-300* (Vedco); *Vital E®-300* (Schering-Plough); (OTC or Rx)

Vitamin E/Selenium Oral

Equ-SeE® (Vet-A-Mix) (one teaspoonful contains 1 mg selenium and 220 IU vitamin E) and *Equ-Se5E®* (one teaspoonful contains 1 mg selenium and approximately 1100 IU vitamin E); (Vet-a-Mix); (OTC) Approved for oral use in horses.

Other top dress equine products containing Vitamin E and Selenium include: Vitamin E and Selenium Powder (Farnam, Horse Health), *Vitamin E and Selenium Crumbles*® (Horse Health)

Vitamin E/Selenium Injection

Mu-Se® (Schering); (Rx): Each mL contains: selenium 5 mg (as sodium selenite); Vitamin E 68 IU; 100 mL vial for injection. Approved for use in non-lactating dairy cattle and beef cattle. Slaughter withdrawal (at labeled doses) = 30 days. Dose: For weanling calves: 1 mL per 200 lbs. body weight IM or SC. For breeding beef cows: 1 mL per 200 lbs. body weight during middle third of pregnancy and 30 days before calving IM or SC.

Bo-Se® (Schering); (Rx): Each mL contains selenium 1 mg (as sodium selenite) and Vitamin E 68 IU; 100 mL vial for injection. Approved for use in calves, swine and sheep. Slaughter withdrawal (at labeled doses) = 30 days (calves); 14 days (lambs, ewes, sows, and pigs). Dose: Calves: 2.5–3.75 mL/100 lbs body weight (depending on severity of condition and geographical area) IM or SC. Lambs (2 weeks of age or older): 1 mL per 40 lbs. body weight IM or SC (1 mL minimum). Ewes: 2.5 mL/100 lbs. body weight IM or SC. Sows and weanling pigs: 1 mL/40 lbs. body weight IM or SC (1 mL minimum). Do not use on newborn pigs.

L-Se® (Schering); (Rx): Each mL contains: selenium 0.25 mg (as sodium selenite) and Vitamin E 68 IU in 30 mL vials. Approved for use in lambs and baby pigs. Slaughter withdrawal (at labeled doses) = 14 days. Dose: Lambs: 1 mL SC or IM in newborns and 4 mL SC or IM in lambs 2 weeks of age or older; Baby Pigs: 1 mL SC or IM.

E-Se® (Schering); (Rx): Each mL contains selenium 2.5 mg (as sodium selenite) and Vitamin E 68 IU in 100 mL vials. Approved for use in horses. Dose: Equine: 1 mL/100 lbs. body weight slow IV or deep IM (in 2 or more sites; gluteal or cervical muscles). May be repeated at 5–10 day intervals.

Seletoc® (Schering); (Rx): Each mL contains selenium 1 mg (as sodium selenite) and Vitamin E 68 IU in 10 mL vials. Approved for use in dogs. Dose: Dogs: Initially, 1 mL per 20 pounds of body weight (minimum 0.25 mL; maximum 5 mL) SC, or IM in divided doses in 2 or more sites. Repeat dose at 3 day intervals until satisfactory results then switch to maintenance dose. If no response in 14 days reevaluate. Maintenance dose: 1 mL per 40 lbs body weight (minimum 0.25 mL) repeat at 3–7 day intervals (or longer) to maintain.

HUMAN-LABELED PRODUCTS:

Vitamin E Tablets: 100 IU, 200 IU, 400 IU, 500 IU & 800 IU; generic (various; OTC)

Vitamin E Capsules: 100 IU, 200 IU, 400 IU & 1000 IU; *Mixed E 400 Softgels*® & *d'ALPHA E 1000 Softgels*® (Naturally); *Vita-Plus E*® (Scot-Tussin); generic; (OTC)

Vitamin E Drops: 15 IU/0.3 mL in 12 mL & 30 mL; *Aquasol E*® (Mayne Pharma); *Aquavit-E*® (Cypress); (OTC)

Vitamin E Liquid: 15 IU/30 mL in 30 mL, 60 mL & 120 mL; 798 IU/30 mL in 473 mL; Vitamin E (Freeda); *Nutr-E-Sol*® (Advanced Nutritional Technology); (OTC)

Topicals are available. There are no approved vitamin E/selenium products, but there are many products that contain either vitamin E (alone, or in combination with other vitamins ± minerals) or selenium (as an injection alone or in combination with other trace elements) available.

VORICONAZOLE

(vor-ih-*koh*-nah-zohl) Vfend®

SECOND GENERATION TRIAZOLE ANTIFUNGAL

Prescriber Highlights

- Broad-spectrum oral/parenteral triazole antifungal
- Very little clinical experience thus far in veterinary medicine; extremely expensive
- Like other compounds in this class, there are many potential drug interactions

Uses/Indications

Voriconazole may be a useful treatment for a variety of fungal infections in veterinary patients, particularly against *Blastomyces*, *Cryptococcus*, and *Aspergillus*. It has high oral bioavailability in a variety of species and can cross into the CNS. Currently available human dosage forms are extremely expensive, however, and little clinical experience has occurred using voriconazole in veterinary patients. There is considerable interest in using voriconazole for treating aspergillosis in pet birds as their relative small size may allow the drug to be affordable; additional research must be performed before dosing regimens are available.

Pharmacology/Actions

Voriconazole a synthetic derivative of fluconazole, has broad-spectrum antifungal activity against a variety of organisms, including *Candida*, *Aspergillus*, *Trichosporon*, *Histoplasma*, *Cryptococcus*, *Blastomyces*, and *Fusarium* species. Like the other azole/triazole antifungals it inhibits cytochrome P-450-dependent 14-alpha-sterol demethylase which is required for ergosterol biosynthesis in fungal cell walls. Unlike fluconazole, voriconazole also inhibits 24-methylene dehydrolanosterol demethylation in molds such as *Aspergillus* giving it more activity against these fungi.

Pharmacokinetics

In dogs, voriconazole is rapidly and essentially completely absorbed after oral administration. Peak levels occur about 3 hours after oral dosing. Voriconazole is only moderately (51%) bound to canine plasma proteins and volume of distribution is about 1.3 L/kg. It is metabolized in the liver to a variety of metabolites with the N-oxide metabolite being the primary circulating metabolite. This metabolite has only weak (<100X as active as the parent) antifungal activity. The elimination pharmacokinetics of voriconazole in dogs is very complex. Both dose-dependent non-linear elimination and auto-induced metabolism after multiple dosages are seen complicating any dosage regimen scenarios; dosages may need to be increased over time. Auto-induction of metabolism apparently does not occur in humans, rabbits or guinea pigs.

In horses, voriconazole is well absorbed after oral administration with peak levels occurring at approximately 3 hours post-dose. Voriconazole has low protein binding (31%); volume of distribution is about 1.35 L/kg. Elimination half-life is quite long—approximately 13 hours after oral dosing. It is not known if voriconazole self-induces hepatic metabolism after multiple doses in the horse.

Contraindications/Precautions/Warnings

Voriconazole is contraindicated in patients hypersensitive to it other azole antifungals. It should be given with caution to patients with hepatic dysfunction, or proarrhythmic conditions.