eight weeks. Prednisolone is given concurrently starting at 2 mg/kg/day, tapering to 0.5 mg/kg day. (Davies, Wyatt et al. 2002)

c) For lymphoma and mastocytoma: 2 mg/m2 weekly. For lymphosarcoma and various carcinomas: 2.5 mg/m2 IV weekly (MacEwen and Rosenthal 1989), (Rosenthal 1985)

- **CATS:**

For susceptible neoplastic diseases:

a) For lymphosarcoma and mast cell neoplasms: 2 mg/m2 IV every 7–14 days (Couto 1989b)

b) 2 mg/m2 slow IV every 7–14 days (Golden and Langston 1988)

Monitoring

- Efficacy
- Toxicity (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
- Contact the veterinarian if the patient exhibits any symptoms of profound depression, abnormal bleeding (including bloody diarrhea) and/or bruising

Chemistry/Synonyms

Commonly referred to as a Vinca alkaloid, vinblastine 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. The commercially available injection has a pH of 3–5.5.

Vinblastine may also be known as: 29060-LE, NSC-49842, sulfato de vimblastina, vinblastini sulfas, vincaleukoblastine sulphate, VBL, *Alkaban®*, *Blastovin®*, *Cellblastin®*, *Cytoblastin®*, *Ifabla®*, *Lemblastine®*, *Periblastine®*, *Serovin®*, *Solblastin®*, *Velban®*, *Velbe®*, *Velsar®*, or *Xintoprost®*.

Storage/Stability/Compatibility

The sterile powder for injection, solution for injection and reconstituted powder for injection should all be protected from light. The powder for injection and injection should be stored in the refrigerator (2–8°C). The intact powder for injection is stable at room temperature for at least one month. After reconstituting with bacteriostatic saline, the powder for injection is stable for 30 days if refrigerated.

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

Vinblastine sulfate **compatibility information conflicts** or is dependent on diluent or concentration factors with the following drugs or solutions: doxorubicin HCl and heparin sodium (in syringes).

Vinblastine 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:

Vinblastine Sulfate Injection: 1 mg/mL in 10 mL and 25 mL vials; generic; (Rx)

Vinblastine Powder for Injection: 10 mg in vials; *Velban®* (Lilly); generic; (Rx)

VINCRISTINE SULFATE

(vin-***kris***-teen) **Oncovin®**

ANTINEOPLASTIC

Prescriber Highlights

- **A Vinca alkaloid antineoplastic used for a variety of tumors in dogs & cats (primarily lymphoid & hematopoietic neoplasms); also used for the treatment of immune-mediated thrombocytopenia**
- **Caution: Hepatic disease, leukopenia, infection, or preexisting neuromuscular disease; reduce dose if hepatic disease**
- **Adverse Effects: Much less myelosuppressive than vinblastine, but may cause more peripheral neurotoxic effects; neuropathic clinical signs can include proprioceptive deficits, spinal hyporeflexia, or paralytic ileus with resulting constipation; 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**

Uses/Indications

Vincristine is used as an antineoplastic primarily in combination drug protocols in dogs and cats in the treatment of lymphoid and hematopoietic neoplasms. In dogs, it may be used alone in the therapy of transmissible venereal neoplasms.

Because vincristine can induce thrombocytosis (at low doses) and has some immunosuppressant activity, it may also be employed in the treatment of immune-mediated thrombocytopenia.

Pharmacology/Actions

Vincristine apparently binds to microtubular proteins (tubulin) in the mitotic spindle, thereby preventing cell division during metaphase. It also interferes with amino acid metabolism by inhibiting glutamic acid utilization and preventing purine synthesis, citric acid cycle and urea formation. Tumor resistance to one Vinca alkaloid does not imply resistance to another.

Vincristine can induce thrombocytosis (mechanism unknown) and has some immunosuppressant activity.

Pharmacokinetics

Vincristine is administered IV as it is unpredictably absorbed from the GI tract. After injection it is rapidly distributed to tissues. In humans, approximately 75% is bound to tissue proteins and the drug does not appreciably enter the CNS.

Vincristine is extensively metabolized, presumably by the liver and primarily excreted in the bile/feces; lesser amounts are eliminated in the urine. The elimination half-life in dogs is reportedly biphasic with an alpha half-life of 13 minutes and a beta half-life of 75 minutes.

Contraindications/Precautions/Warnings

Vincristine should be used with caution in patients with hepatic disease, leukopenia, infection, or preexisting neuromuscular disease.

Doses of vincristine should be reduced in patients with hepatic disease. A 50% reduction in dose should be considered if serum bilirubin levels are greater than 2 mg/dl.

Because vincristine is potentially a neurotoxic substrate of P-glycoprotein, it should be used with caution in those herding breeds (*e.g.*, Collies) that may have the gene mutation that causes a nonfunctional protein

As vincristine may be a skin irritant, gloves and protective clothing should be worn when preparing or administering the medication. If skin/mucous membrane exposure occurs, thoroughly wash area with soap and water.

Adverse Effects

Although structurally related to and having a similar mechanism of action as vinblastine, vincristine has a different adverse reaction profile. Vincristine is much less myelosuppressive (mild leukopenia) at usual doses than is vinblastine, but may cause more peripheral neurotoxic effects. Neuropathic clinical signs may include proprioceptive deficits, spinal hyporeflexia, or paralytic ileus with resulting constipation. In humans, vincristine commonly causes mild sensory impairment and peripheral paresthesias. These may also occur in animals, but are not usually noted due to difficulty in detection. Cats, however, can develop neurotoxicity that can be associated with constipation or paralytic ileus thereby aggravating anorexia. They can develop reversible axon swelling and paranodal demyelination.

Additionally, in small animals, vincristine may cause impaired platelet aggregation, increased liver enzymes, inappropriate ADH secretion, jaw pain, alopecia, stomatitis, or seizures.

Extravasation injuries associated with perivascular injection of vincristine can range from irritation to necrosis and tissue sloughing. Because of the vesicant action of this drug, it is recommended to use a different needle for injecting the drug than the one used to withdraw it from the vial. Recommendations of therapy for extravasation include discontinuing the infusion immediately at that site and applying moderate heat to the area to help disperse the drug. Injections of hyaluronidase have been suggested to help diffuse the drug. Others have suggested applying ice to the area to limit the drug's diffusion and minimize the area affected. Topical dimethyl sulfoxide (DMSO) has also been recommended by some to treat the area involved.

Reproductive/Nursing Safety

Little is known about the effects of vincristine on developing fetuses, but it is believed that the drug possesses some teratogenic and embryotoxic properties. It may also cause aspermia in males. In humans, the FDA categorizes this drug as category ***D*** for use during pregnancy (*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.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as in class: ***C*** (*These drugs may have potential risks. Studies in people or laboratory animals have uncovered risks, and these drugs should be used cautiously as a last resort when the benefit of therapy clearly outweighs the risks.*)

It is not known whether this drug is excreted in milk. Because of the potential for serious adverse reactions in nursing offspring, consider using milk replacer if dams are being given this drug.

Overdosage/Acute Toxicity

In dogs, it is reported that the maximally tolerated dose of vincristine is 0.06 mg/kg every 7 days for 6 weeks. Animals receiving this dose showed signs of slight anemia, leukopenia, increased liver enzymes, and neuronal shrinkage in the peripheral and central nervous systems.

In cats, the lethal dose of vincristine is reportedly 0.1 mg/kg. Cats receiving toxic doses showed clinical signs of weight loss, seizures, leukopenia, and general debilitation.

In humans, cardiovascular and hematologic monitoring are performed after an overdose. Treatment can include anticonvulsants, and prevention of ileus. Additionally, an attempt is made to prevent the effects associated with the syndrome of inappropriate antidiuretic hormone (SIADH) with fluid restriction and loop diuretics to maintain serum osmolality. There have been some reports of leucovorin calcium being used to treat vincristine overdoses in humans, but efficacy of this treatment has not yet been confirmed.

Drug Interactions

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

- **ASPARAGINASE**: Additive neurotoxicity may occur; is apparently less common when asparaginase is administered after vincristine
- **MITOMYCIN**: In humans who have previously or simultaneously received mitomycin-C with Vinca alkaloids, severe bronchospasm has occurred

Caution is advised if using other drugs that can inhibit **p-glycoprotein** particularly in those dogs at risk for MDR1-allele mutation (Collies, Australian Shepherds, Shelties, Long-haired Whippet, etc. "white feet"), unless tested "normal". Drugs and drug classes involved include:

- **AMIODARONE**
- **AZOLE ANTIFUNGALS** (*e.g.*, **ketoconazole**)
- **CARVEDILOL**
- **CYCLOSPORINE**
- **DILTIAZEM**
- **ERYTHROMYCIN; CLARITHROMYCIN**
- **QUINIDINE**
- **SPIRONOLACTONE**
- **TAMOXIFEN**
- **VERAPAMIL**

Laboratory Considerations

- Vincristine may significantly increase both blood and urine concentrations of **uric acid**

Doses

For more information on using vincristine as part of chemotherapy protocols such as COP, VELCAP, etc, refer to the protocols found in the appendix or other dosages/protocols found in numerous references, including: *Withrow and MacEwen's Small Animal Clinical Oncology, 4th Ed.* (Withrow and Vail 2007); *Canine and Feline Geriatric Oncology* (Villalobos 2007); *Small Animal Internal Medicine, 3rd Edition* (Nelson and Couto 2003); *Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat 6th Edition* (Ettinger and Feldman 2005); and *The 5-Minute Veterinary Consult Canine & Feline, 3rd Ed.* (Tilley and Smith 2004).

■ **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