ASCORBIC ACID
VITAMIN C

(a-***skor***-bik)

Prescriber Highlights

- Prevention/treatment of scurvy in Guinea pigs most accepted use
- At usual dosages, little downside to use; may exacerbate liver injury in copper toxicosis
- Some drug interactions, primarily due to its urinary acidification qualities
- May alter some lab results (urine glucose, occult blood in stool, serum bilirubin)

Uses/Indications
Ascorbic acid is used to prevent and treat scurvy in guinea pigs. It has been used as a urinary acidifier in small animals, but its efficacy is in question. Sodium ascorbate does not acidify the urine. In the past, it was used to treat copper-induced hepatopathy in dogs but this use has fallen into disfavor (see Contraindications below).

Pharmacology/Actions
Exogenously supplied ascorbic acid is a dietary requirement in some exotic species (including rainbow trout, Coho salmon), guinea pigs, and in primates. The other domestic species are able to synthesize *in vivo* enough Vitamin C to meet their nutritional needs. Vitamin C is used for tissue repair and collagen formation. It may be involved with some oxidation-reduction reactions, and with the metabolism of many substances (iron, folic acid, norepinephrine, histamine, phenylalanine, tyrosine, some drug enzyme systems). Vitamin C is believed to play a role in protein, lipid and carnitine synthesis, maintaining blood vessel integrity and immune function.

Pharmacokinetics
Vitamin C is generally well absorbed in the jejunum (human data) after oral administration, but absorption may be reduced with high doses as an active process is involved with absorption. Ascorbic acid is widely distributed and only about 25% is bound to plasma proteins. Vitamin C is biotransformed in the liver. When the body is saturated with vitamin C and blood concentrations exceed the renal threshold, the drug is more readily excreted unchanged into the urine.

Contraindications/Precautions/Warnings
Vitamin C (high doses) should be used with caution in patients with diabetes mellitus due to the laboratory interactions (see below), or in patients susceptible to urolithiasis.

Because there is some evidence that it may increase copper's oxidative damage to the liver, avoid vitamin C's use in animals with copper-associated hepatopathy.

Adverse Effects
At usual doses vitamin C has minimal adverse effects. Occasionally GI disturbances have been noted in humans. At higher dosages there is an increased potential for urate, oxalate or cystine stone formation, particularly in susceptible patients.

Reproductive/Nursing Safety
The reproductive safety of vitamin C has not been studied, but it is generally considered safe at moderate dosages. In humans, the FDA categorizes this drug as category ***A*** for use during pregnancy (*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.*) But in dosages greater than the RDA, the FDA categorizes vitamin C 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.*)

Overdosage/Acute Toxicity
Very large doses may result in diarrhea and potentially urolithiasis. Generally, treatment should consist of monitoring and keeping the patient well hydrated.

Drug Interactions
The following drug interactions have either been reported or are theoretical in humans or animals receiving ascorbic acid (high dosages) and may be of significance in veterinary patients:

- **AMINOGLYCOSIDES:** (*e.g.*, **gentamicin**) and **ERYTHROMYCIN:** Are more effective in an alkaline medium; urine acidification may diminish these drugs' effectiveness in treating bacterial urinary tract infections
- **QUINIDINE:** Urine acidification may increase renal excretion
- **DEFEROXAMINE:** While vitamin C may be synergistic with deferoxamine in removing iron, it may lead to increased iron tissue toxicity, especially in cardiac muscle. It should be used with caution, particularly in patients with preexisting cardiac disease.

Laboratory Considerations
- **URINE GLUCOSE:** Large doses of vitamin C may cause false-negative values
- **STOOL OCCULT BLOOD:** False-negative results may occur if vitamin C is administered within 48–72 hours of an amine-dependent test
- **BILIRUBIN, SERUM:** Vitamin C may decrease concentrations

Doses
- **CATS:**
  a) For adjunctive treatment of FIP: 125 mg PO q12h (Weiss 1994)
  b) For adjunctive treatment of toxic (*e.g.*, acetaminophen) methemoglobinemia (with oxygen, acetylcysteine): 30 mg/kg PO q6h (Macintire 2006b)
- **RABBITS/RODENTS/SMALL MAMMALS:**
  a) Rabbits: For soft stools (may reduce cecal absorption of clostridial endotoxins): 100 mg/kg PO q12h (Ivey and Morrisey 2000)
- **GUINEA PIGS:**
  For treatment of scurvy:
  a) During pregnancy: 30 mg/kg either parenterally or PO (in feed or water) (Fish and Besch-Williford 1992)
  b) 25–50 mg (total dose) parenterally once daily until improvement is noted, then give oral supplemental vitamin C (daily requirement is 15 mg/day) (Wilson 2005)
  c) 10 mg/kg daily, by injection if necessary, plus supportive care. Recovery is relatively rapid, usually within a week. Prevention is adequate daily intake of vitamin C. (Burke 1999)
  d) 50 mg/kg PO, IM or SC (Adamcak and Otten 2000)
  For prevention of scurvy:
  a) Add 200 mg vitamin C to one liter of dechlorinated water and add to water bottle. 10–30 mg/kg PO, SC or IM (Adamcak and Otten 2000)

■ **HORSES:**

a) For replacement therapy after stress (*e.g.*, strenuous exercise): 20 grams PO daily (Ferrante and Kronfeld 1992)

b) For adjunctive treatment of erythrocyte oxidative injury (*e.g.*, red maple toxicity): 10–20 grams PO once daily (Davis and Wilkerson 2003)

c) As a urinary acidifier: 1–2 g/kg PO daily (Jose-Cunilleras and Hinchcliff 1999)

d) As adjunctive therapy for perinatal asphyxia syndrome in foals: 100 mg/kg per day IV (Slovis 2003b)

■ **CATTLE:**

a) For vitamin C-responsive dermatitis in calves: 3 grams SC once or twice (Miller 1993)

Chemistry/Synonyms

A water-soluble vitamin, ascorbic acid occurs as white to slightly yellow crystal or powder. It is freely soluble in water and sparingly soluble in alcohol. The parenteral solution has a pH of 5.5–7.

Ascorbic acid may also be known as: acidum ascorbicum, L-ascorbic acid, cevitamic acid, E300, or vitamin C; many trade names are available.

Storage/Stability/Compatibility

Protect from air and light. Ascorbic acid will slowly darken upon light exposure; slight discoloration does not affect potency. Because with time ascorbic acid will decompose with the production of CO_2, open ampules and multidose vials carefully. To reduce the potential for excessive pressure within ampules, store in refrigerator and open while still cold.

Ascorbic acid for injection is **compatible** with most commonly used IV solutions, but is **incompatible** with many drugs when mixed in syringes or IV bags. 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:

Parenteral Injection: 250 mg/mL (as sodium ascorbate) in 100 and 250 mL vials; generic; (Rx or OTC depending on labeling)

Ascorbic Acid Powder: 442.25 g/lb *Vita-Flex Pure C*® (Vita-Flex); 50 grams/lb *Mega-C Powder*® (AHC); 146 g/pack *Stabilized C*® (Alpharma); (OTC)

HUMAN-LABELED PRODUCTS:

As ascorbic acid or sodium ascorbate—Tablets & Capsules: 250 mg, 500 mg, 1000 mg & 1500 mg; *Cevi-Bid*® (Lee); generic; (OTC);

Oral Extended-release Tablets: 500 mg & 1000 mg; generic; (OTC)

Crystals: 1000 mg per ¼ tsp. in 120g and 1 lb; *Vita-C*® (Freeda); (OTC)

Powder: 1060 mg per ¼ tsp. in 120 g and 1 lb; 60 mg per ¼ tsp. in 454 g; *Dull-C*® (Freeda); Ascorbic Acid (Humco); (OTC)

Liquid/Solution: 100 mg/mL in 50 mL and 500 mg/5 mL in 120 mL and 480 mL; *Cecon*® (Abbott); generic; (OTC)

Parenteral Injection: 500 mg/mL in 50 mL vials; *Ascor L 500*® (McGuff); generic; (Rx)

ASPARAGINASE

(a-***spar***-a-gin-ase) L-Asparaginase, Elspar®

ANTINEOPLASTIC

Prescriber Highlights

- **Antineoplastic useful in treating lymphoid malignancies in dogs/cats**
- **Two primary adverse effects: hypersensitivity & effects on protein synthesis (usually manifested by: GI effects, hemorrhagic pancreatitis, hepatotoxicity or coagulation disorders); bone marrow suppression is more rare**

Uses/Indications

Asparaginase has been useful in combination with other agents in the treatment of lymphoid malignancies. The drug is most useful in inducing remission of disease but is occasionally used in maintenance or rescue protocols.

Use of asparaginase as part of an initial treatment lymphosarcoma protocol is now somewhat controversial, as one study (MacDonald, Thamm et al. 2005) in dogs showed no statistical difference for response rates, remission or survival rate, remission or survival duration, or prevalence of toxicity and treatment delay in dogs treated with or without asparaginase as part of a standard CHOP protocol.

Pharmacology/Actions

Some malignant cells are unable to synthesize asparagine and are dependent on exogenous asparagine for DNA and protein synthesis. Asparaginase catalyzes asparagine into ammonia and aspartic acid. The antineoplastic activity of asparaginase is greatest during the post mitotic (G_1) cell phase. While normal cells are able to synthesize asparagine intracellularly, some normal cells having a high rate of protein synthesis, require some exogenous asparagine and may be adversely affected by asparaginase.

Resistance to asparaginase can develop rapidly, but apparently, there is no cross-resistance between asparaginase and other antineoplastic agents.

Asparaginase possesses antiviral activity, but its toxicity prevents it from being clinically useful in this regard.

Pharmacokinetics

Asparaginase is not absorbed from the GI tract and must be given either IV or IM. After IM injection, serum levels of asparaginase are approximately ½ of those after IV injection. Because of its high molecular weight, asparaginase does not diffuse readily out of the capillaries and about 80% of the drug remains within the intravascular space.

In humans after IV dosing, serum levels of asparagine fall almost immediately to zero and remain that way as long as therapy continues. Once therapy is halted, serum levels of asparagine do not recover for at least 23 days.

The metabolic fate of asparaginase is not known. In humans, the plasma half-life is highly variable and ranges from 8–30 hours.

Contraindications/Precautions/Warnings

Asparaginase is contraindicated in patients who have exhibited anaphylaxis to it, or those with pancreatitis or a history of pancreatitis. Asparaginase should be used with caution in patients with preexisting hepatic, renal, hematologic, gastrointestinal, or CNS dysfunction.