Sildenafil may also be known as UK 92480, UK 92480-10, *Aphrodil*®, *Revatio*®, or *Viagra*®.

Storage/Stability
Sildenafil tablets should be stored at room temperature (25°C; 77°F); excursions permitted to 15–30°C (59–86°F).

Dosage Forms/Regulatory Status
VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Sildenafil Citrate Tablets: 20 mg (of sildenafil); *Revatio*® (Pfizer); (Rx)

Sildenafil Citrate Tablets: 25 mg, 50 mg & 100 mg (of sildenafil); *Viagra*® (Pfizer); (Rx)

SILYMARIN
MILK THISTLE

(sill-e-***mar***-in) Marin®

NUTRACEUTICAL HEPATO-PROTECTANT

Prescriber Highlights

- Nutraceutical that may be useful for treatment of chronic & acute liver disease, cirrhosis; as a hepato-protective agent when hepatotoxins (*e.g.*, *Aminita phalloide*) ingested
- Appears well-tolerated; potentially could cause GI effects
- Do not confuse Milk Thistle with Blessed Thistle
- Potential drug interactions

Uses/Indications
While controlled studies demonstrating efficacy and a standardized form and concentration of silymarin are lacking, it is being used to treat a variety of liver diseases in humans and domestic companion animals (birds, dogs, cats, horses, rabbits). It is mostly of interest in treating chronic and acute liver disease, cirrhosis, and as a hepato-protective agent when hepatotoxic agents are ingested (*e.g.*, *Aminita phalloide*; "Death Cap Mushrooms").

Pharmacology/Actions
Silymarin has a variety of pharmacologic actions that may contribute to its apparent effects in treating liver disease. It inhibits lipid peroxidase and beta-glucoronidase and acts as an anti-oxidant and free radical scavenger. Silymarin also inhibits the cytotoxic, inflammatory, and apoptotic effects of tumor necrosis factor (TFN). It apparently can alter outer hepatocyte cell membranes that can prevent toxin penetration. Silymarin is thought to reduce hepatic collagen formation and increase hepatic glutathione content.

Pharmacokinetics
In humans, silymarin has an oral bioavailability of less than 50% and peak levels occur 2–4 hours post-dose. When silibinin (silybin, sylibin) is complexed with phosphatidylcholine, oral absorption can be increased. The drug undergoes extensive enterohepatic circulation and has significantly higher concentrations in liver cells and bile than in plasma. Elimination half-life in humans averages 6 hours. The majority of the drug is eliminated unchanged in the feces, but 20–40% is converted into glucuronide and sulfate conjugates which are eliminated in the feces; only about 8% is excreted in the urine.

Contraindications/Precautions/Warnings
There are no reported absolute contraindications to silymarin in animals. Extracts from the plant parts of Milk Thistle (not the seeds which are used to make the extract silymarin), may possess estrogen-like activity and should not be used in patients where exogenous estrogens would be contraindicated.

Adverse Effects
Silymarin is apparently well tolerated when administered orally. In humans, GI disturbances have been reported on occasion (nausea to diarrhea). Patients who have allergies to other members of the Asteraceae/Compositae plant family (includes ragweed, marigolds, daisies, etc.) may exhibit allergic reactions to Milk Thistle derivatives. Do not confuse Milk Thistle with Blessed Thistle.

Reproductive/Nursing Safety
Data on the safety of silymarin use during pregnancy or nursing is not available; its potential benefit must be weighed against the uncertainty of its safety.

Overdosage/Acute Toxicity
Overdoses are unlikely to cause significant morbidity. Gastrointestinal effects may be seen and treated in a supportive manner.

Drug Interactions
While no specific drug interactions have been reported, silymarin may inhibit cytochrome P450 isoenzyme 2C9 (CYP2C9). Drugs with narrow therapeutic indexes that are metabolized by this isoenzyme should be used with caution when using silymarin. Drugs that could be affected include: **warfarin, amitriptyline, verapamil,** etc.

Silymarin also may inhibit CYP3A4, but thus far this interaction does not appear to be clinically significant. Silymarin may increase the clearance of drugs that undergo hepatic glucuronidation (not cats), including: **acetaminophen, diazepam, morphine, and lamotrigine.** Clinical significance has not been determined for this interaction and the usefulness of silymarin for treating acetaminophen toxicity has not been determined.

Laboratory Considerations
No interactions with laboratory tests are reported.

Doses
- **DOGS & CATS:**
  a) Therapeutic dosage is unknown, but suggested doses range from 50–250 mg/day (Twedt 2004)
  b) For adjunctive therapy for chronic liver disease: 20–50 mg/kg per day (extrapolated from human, monkey, rodent and dog research) (Center 2002)
  c) For chronic liver disease and ameliorating the effects of anticonvulsants: Dosages vary from 50–200 mg given every 12–24 hours (Tams 2001)
  d) For hepatotoxicity, hepatic recovery/regeneration, hepatic fibrosis: 20–50 mg/kg/day. (Webb 2007b)
  e) Cats: 4–8 mg/kg/day (Zoran 2006b)

Monitoring
- Clinical efficacy

Client Information
- Because silymarin experience in animals is limited, clients should understand the "investigational nature" of its use

Chemistry/Synonyms
Milk Thistle, the common name for *Silybum marianum*, has been used as a medicinal agent for at least two thousand years. The me-

dicinal extract from the seeds of the plant is silymarin that contains the four flavolignans: silichristin (sylichristin), isosilibinin, silydianin (silidianin), and the most biological active component, silibinin (sylibin, silybin, silibide). Milk Thistle extract contains approximately 70% silymarin of which about 70% is silibinin. Silymarin is reportedly fairly insoluble in water.

Silymarin or Milk thistle may also be known as *Carduus marianus*, Holy Thistle, Legalon, or Marian Thistle. Blessed Thistle is a different compound.

Storage/Stability

Unless otherwise labeled, commercially available products containing silymarin should be stored at room temperature in tight containers. Avoid storing the products in areas of high humidity.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Milk Thistle or silymarin is considered a nutritional supplement by the FDA. No standards have been accepted for potency, etc. by regulatory bodies. Supplements are available from a wide variety of sources and dosage forms include tablets and capsules in a variety of concentrations (150–1000 mg). When choosing a product it is recommended to purchase ones that state the concentration (usually 70–80%) of silymarin contained in the product.

Silybin A+B 9 mg (in a phosphatidylcholine complex) & Vitamin E 50 IU Tablets: *Marin® for Cats* (Nutramax); Not considered a drug by the FDA.

Silybin A+B 24 mg (in a phosphatidylcholine complex), Vitamin E 105 IU, & Zinc 17 mg Chewable Tablets: *Marin® for Dogs* (Nutramax); Not considered a drug by the FDA. Labeled for use in small to medium dogs.

Silybin A+B 70 mg (in a phosphatidylcholine complex), Vitamin E 300 IU, & Zinc 45 mg Chewable Tablets: *Marin® for Dogs* (Nutramax); not considered a drug by the FDA. Labeled for use in large dogs.

A combination product (*Denamarin®*, Nutramax) containing SAMe and silybin (silymarin) is also labeled for use in dogs and cats.

HUMAN-LABELED PRODUCTS: None as pharmaceuticals

SODIUM BICARBONATE

(soe-***dee***-um bye-***kar***-boe-nate) Neut®

ALKALINIZER

Prescriber Highlights

- Alkalinizing agent used to treat metabolic acidosis & alkalinize urine; may be used adjunctively for hypercalcemic or hyperkalemic crises
- Contraindications: Parenteral bicarbonate is generally contraindicated in patients with metabolic or respiratory alkalosis, excessive chloride loss secondary to vomiting or GI suction, at risk for development of diuretic-induced hypochloremic alkalosis, or with hypocalcemia where alkalosis may induce tetany
- Extreme Caution: Hypocalcemia Caution: CHF, nephrotic syndrome, hypertension, oliguria or volume overload
- Adverse Effects: Especially with parenteral (high dose): metabolic alkalosis, hypokalemia, hypocalcemia, "overshoot" alkalosis, hypernatremia, volume overload, congestive heart failure, shifts in the oxygen dissociation curve causing decreased tissue oxygenation, & paradoxical CNS acidosis leading to respiratory arrest. If used during CPR: hypercapnia, if the patient is not well ventilated; patients may be predisposed to ventricular fibrillation.
- Drug Interactions

Uses/Indications

Sodium bicarbonate is indicated to treat metabolic acidosis and alkalinize the urine. It is also used as adjunctive therapy in treating hypercalcemic or hyperkalemia crises.

Pharmacology/Actions

Bicarbonate ion is the conjugate base component of bicarbonate:carbonic acid buffer, the principal extracellular buffer in the body.

Contraindications/Precautions/Warnings

Parenterally administered sodium bicarbonate is considered generally contraindicated in patients with metabolic or respiratory alkalosis, excessive chloride loss secondary to vomiting or GI suction, at risk for development of diuretic-induced hypochloremic alkalosis, or with hypocalcemia where alkalosis may induce tetany.

Use with extreme caution and give very slowly in patients with hypocalcemia. Because of the potential sodium load, use with caution in patients with CHF, nephrotic syndrome, hypertension, oliguria, or volume overload.

Adverse Effects

Sodium bicarbonate therapy (particularly high-dose parenteral use) can lead to metabolic alkalosis, hypokalemia, hypocalcemia, "overshoot" alkalosis, hypernatremia, volume overload, congestive heart failure, shifts in the oxygen dissociation curve causing decreased tissue oxygenation, and paradoxical CNS acidosis leading to respiratory arrest.

When sodium bicarbonate is used during cardiopulmonary resuscitation, hypercapnia may result if the patient is not well ventilated; patients may be predisposed to ventricular fibrillation.

Oral and parenteral bicarbonate (especially at higher doses) may contribute significant amounts of sodium and result in hyper-