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-

natremia and volume overload; use with caution in patients with CHF, or acute renal failure.

Reproductive/Nursing Safety

Reproductive safety studies have not been performed. Assess risk versus benefit before using.

Overdosage/Acute Toxicity

Sodium bicarbonate can cause severe alkalosis, with irritability or tetany if overdosed or given too rapidly. Dosages should be thoroughly checked and frequent monitoring of electrolyte and acid/base status performed.

Treatment may consist of simply discontinuing bicarbonate if alkalosis is mild or by using a rebreathing mask. Severe alkalosis may require intravenous calcium therapy. Sodium chloride or potassium chloride may be necessary if hypokalemia is present.

Drug Interactions

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

- **ANTICHOLINERGIC AGENTS**: Concomitant oral sodium bicarbonate may reduce absorption; administer separately
- **AZOLE ANTIFUNGALS** (**ketoconazole, itraconazole**): Concomitant oral sodium bicarbonate may reduce absorption; administer separately
- **CIPROFLOXACIN; ENROFLOXACIN**: The solubility of ciprofloxacin and enrofloxacin is decreased in an alkaline environment; patients with alkaline urine should be monitored for signs of crystalluria
- **CORTICOSTEROIDS**: Patients receiving high dosages of sodium bicarbonate and ACTH or glucocorticoids may develop hypernatremia
- **DIURETICS** (*e.g.*, **thiazides, furosemide**): Concurrent use of sodium bicarbonate in patients receiving potassium-wasting diuretics may cause hypochloremic alkalosis
- **EPHEDRINE**: When urine is alkalinized by sodium bicarbonate, excretion may be decreased
- **HISTAMINE$_2$ BLOCKING AGENTS** (*e.g.*, **cimetidine**, **ranitidine**): Concomitant oral sodium bicarbonate may reduce absorption; administer separately
- **IRON PRODUCTS**: Concomitant oral sodium bicarbonate may reduce absorption; administer separately
- **ORAL MEDICATIONS**: Because oral sodium bicarbonate can either increase or reduce the rate and/or extent of absorption of many orally administered drugs, it is recommended to avoid giving other drugs within 1–2 hours of sodium bicarbonate
- **QUINIDINE**: When urine is alkalinized by sodium bicarbonate, excretion may be decreased
- **SALICYLATES**: When urine is alkalinized by sodium bicarbonate, excretion of weakly acidic drugs may be increased
- **SUCRALFATE**: Oral sodium bicarbonate may reduce the efficacy of sucralfate if administered concurrently
- **TETRACYCLINES**: Concomitant oral sodium bicarbonate may reduce absorption; administer separately

Doses

- **DOGS & CATS:**

For severe metabolic acidosis:

a) Main therapeutic goal should be to eliminate the underlying cause of acidosis. If causes are not readily reversible, arterial pH is <7.2 (7.1 if diabetic ketoacidosis), and ventilatory procedures have not reduced acidemia, bicarbonate therapy should be considered. mEq of bicarbonate required = 0.5 x body weight in kgs. x (desired total CO_2 mEq/L minus measured total CO_2 mEq/L). Give 1/2 of the calculated dose slowly over 3–4 hours IV. Recheck blood gases and assess the clinical status of the patient. Avoid over-alkalinization. (Schaer 1986)

For adjunctive therapy of diabetic ketoacidosis:

Note: Use of bicarb for this indication is somewhat controversial

a) If plasma bicarbonate is ≤11 mEq/L give bicarbonate therapy. Dose (in mEq) = body weight in kgs. x 0.4 x (12 – patient's bicarbonate) x 0.5. Give above dose over 6 hours in IV fluids and then recheck plasma bicarbonate or total venous CO2. If still ≤11 mEq/L, recalculate dose and repeat therapy. (Nelson and Feldman 1988)

For metabolic acidosis in acutely critical situations (cardiac arrest):

a) 1 mEq/kg IV initially, followed by 0.5 mEq/kg at 10–15 minute intervals during CPR (Moses 1988)
b) Give none during the first 5–10 minutes of arrest, then 0.5 mEq/kg every 5 minutes of cardiac arrest thereafter (Haskins 1989)

For adjunctive treatment of hypercalcemic crisis:

a) The mEq of bicarbonate required = 0.3 x body weight in kgs. x (desired plasma bicarbonate mEq/L – measured plasma bicarbonate mEq/L); or 1 mEq/kg IV every 10–15 minutes; maximum total dose: 4 mEq/L (Kruger, Osborne, and Polzin 1986)

For adjunctive therapy for hyperkalemic crises:

a) If serum bicarbonate or total CO_2 is unavailable: 2–3 mEq/kg IV over 30 minutes if patient has decreased tissue perfusion or renal failure and does not have diabetic ketoacidosis. Must be used judiciously. (Willard 1986)
b) 1–2 mEq/kg IV slowly (Macintire 2006a)

Metabolic acidosis secondary to renal failure:

a) Dogs: Initial dose: 8–12 mg/kg PO q8h; adjust dosage to attain blood total CO_2 concentrations to 18–24 mEq/L for renal failure. Although, inferior to monitoring total CO_2; urine pH may be used as a guideline for adjusting dosage. Urine pH should be between 6.5–7. (Polzin and Osborne 1985)
b) Initial dose: 8–12 mg/kg q8h; adjust dosage to attain blood total CO_2 concentrations to 18–24 mEq/L (Allen 1989)
c) 8–12 mg/kg PO q8–12h (Vaden 2007)

To alkalinize the urine:

a) Dosage must be individualized to the patient. Initially give 10–90 grains (650 mg–5.85 grams) PO per day, depending on the size of the patient and the pretreatment urine pH value. Goal of therapy is to maintain a urine pH of about 7; avoid pH >7.5. (Osborne et al. 1989)
b) For adjunctive therapy in dissolution and/or prevention of urate urolithiasis in dogs: 0.5–1 gram (1/8–1/4 tsp.) per 5 kg of body weight three times daily PO. Goal of therapy is to attain a urine pH of from 7–7.5. (Senior 1989)

- **HORSES:**

For metabolic acidosis:

a) Associated with colic; if pH is <7.3 and base deficit is >10 mEq/L estimate bicarbonate requirement using the formula: bicarbonate deficit (HCO^{-3} mEq) = base deficit (mEq/L) x 0.4 x body weight (kg). May administer as a 5% sodium bicarbonate solution. Each L of solution contains 600 mEq of bicarbonate (hypertonic) and should not be administered any faster than 1–2 L/hr. Because acidotic horses with colic tend also to be dehydrated, may be preferable to give as isotonic sodium bicarbonate (150 mEq/L). (Stover 1987)

■ **RUMINANTS:**

For acidosis:

a) 2–5 mEq/kg IV for a 4–8 hour period (Howard 1986)

b) For severely dehydrated (10–16% dehydrated) acidotic calves (usually comatose): Use isotonic sodium bicarbonate (156 mEq/L). Most calves require about 2 liters of this solution given over 1–2 hours, then change to isotonic saline and sodium bicarbonate or a balanced electrolyte solution. Isotonic sodium bicarbonate may be made by dissolving 13 grams of sodium bicarbonate in 1 L of sterile water. Isotonic saline and sodium bicarbonate may be made by: mixing 1 L of isotonic saline with 1 L of isotonic sodium bicarbonate. (Radostits 1986)

■ **BIRDS:**

For metabolic acidosis:

a) 1 mEq/kg initially IV (then SC) for 15–30 minutes to a maximum of 4 mEq/kg (Clubb 1986)

Monitoring

■ Acid/base status
■ Serum electrolytes
■ Urine pH (if being used to alkalinize urine)

Chemistry/Synonyms

An alkalinizing agent, sodium bicarbonate occurs as a white, crystalline powder having a slightly saline or alkaline taste. It is soluble in water and insoluble in alcohol. One gram of sodium bicarbonate contains about 12 mEq each of sodium and bicarbonate; 84 mg of sodium bicarbonate contains 1 mEq each of sodium and bicarbonate. A 1.5% solution of sodium bicarbonate is approximately isotonic. An 8.4% solution of sodium bicarbonate can be made isotonic by diluting each mL with 4.6 mL of sterile water for injection.

Sodium Bicarbonate may also be known as: baking soda, E500, monosodium carbonate, natrii bicarbonas, natrii hydrogenocarbonas, sal de vichy, sodium acid carbonate, $NaHCO_3$, sodium hydrogen carbonate; many trade names are available.

Storage/Stability/Compatibility

Sodium bicarbonate tablets should be stored in tight containers, preferably at room temperature (15–30°C). Sodium bicarbonate injection should be stored at temperatures less than 40°C and preferably at room temperature; avoid freezing.

Sodium bicarbonate powder is stable in dry air, but will slowly decompose upon exposure to moist air.

Sodium bicarbonate is reportedly physically **compatible** with the following intravenous solutions and drugs: Dextrose in water, dextrose/saline combinations, dextrose-Ringer's combinations, sodium chloride injections, amikacin sulfate, aminophylline, amobarbital sodium, amphotericin B, atropine sulfate, bretylium tosylate, carbenicillin disodium, cefoxitin sodium, cephalothin sodium, cephapirin sodium, chloramphenicol sodium succinate, chlorothiazide sodium, cimetidine HCl, clindamycin phosphate, ergonovine maleate, erythromycin gluceptate/lactobionate, *Innovar*®, heparin sodium, hyaluronidase, hydrocortisone sodium succinate, kanamycin sulfate, lidocaine HCl, metaraminol bitartrate, methotrexate sodium, methyldopate HCl, nafcillin sodium, netilmicin sulfate, oxacillin sodium, oxytocin, phenobarbital sodium, phenylephrine HCl, phenytoin sodium, phytonadione, potassium chloride, prochlorperazine edisylate, and sodium iodide.

Sodium bicarbonate **compatibility information conflicts** or is dependent on diluent or concentration factors with the following drugs or solutions: lactated Ringer's injection, Ringer's injection, sodium lactate 1/6 M, ampicillin sodium, calcium chloride/gluconate, methicillin sodium, penicillin G potassium, pentobarbital sodium, promazine HCl, thiopental sodium, vancomycin HCl, verapamil HCl, and vitamin B-complex with C. Consult specialized references or a hospital pharmacist for more specific information.

Sodium bicarbonate is reportedly physically **incompatible** with the following solutions or drugs: alcohol 5%/dextrose 5%, D_5 lactated Ringer's, amrinone lactate, ascorbic acid injection, carmustine, cisplatin, codeine phosphate, corticotropin, dobutamine HCl, epinephrine HCl, glycopyrrolate, hydromorphone HCl, imipenem-cilastatin, regular insulin, isoproterenol HCl, labetolol HCl, levorphanol bitartrate, magnesium sulfate, meperidine HCl, methadone HCl, metoclopramide HCl, norepinephrine bitartrate, oxytetracycline HCl, pentazocine lactate, procaine HCl, secobarbital sodium, streptomycin sulfate, succinylcholine chloride, tetracycline HCl.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Sodium Bicarbonate Injection: 8.4% (1 mEq/mL) in 50 mL (50 mEq/vial), 100 mL (100 mEq/vial) and 500 mL (500 mEq/vial) vials; available generically labeled; (Rx)

HUMAN-LABELED PRODUCTS:

Injectable Products:

Sodium Bicarbonate Neutralizing Additive Solution: 4% (0.48 mEq/mL) in 5 mL (2.4 mEq) vials; 4.2% (0.5 mEq/mL) in 5 mL fill in 6 mL vials (2.5 mEq); *Neut*® (Abbott); Sodium Bicarbonate (American Pharmaceutical Partners); (Rx)

Sodium Bicarbonate Injection: 4.2% (0.5 mEq/mL) in 10 mL (5 mEq) syringes, 10 mL (5 mEq) *Bristoject* syringes; generic, (Hospira, American Pharmaceutical Partners); (Rx)

Sodium Bicarbonate Injection: 5% (0.6 mEq/mL) in 500 mL vials (297.5 mEq); generic, (Hospira, Baxter, McGaw); (Rx)

Sodium Bicarbonate Injection: 7.5% (0.9 mEq/mL) in 50 mL (44.6 mEq) amps, syringes, vials, *Bristoject* syringes and 200 mL (179 mEq) *MaxiVials*; generic (Hospira, American Regent, American Pharmaceutical Partners); (Rx)

Sodium Bicarbonate Injection: 8.4% (1 mEq/mL) in 10 mL (10 mEq) and 50 mL (50 mEq) syringes and 50 mL vials (50 mEq/vial); generic (Hospira, American Regent, American Pharmaceutical Partners); (Rx)

Oral Products:

Tablets: 325 mg & 650 mg; (1 g sodium bicarbonate provides 11.9 mMol sodium and 11.9 mMol bicarbonate); generic; (OTC)

Powder: 120 g, 300 g & 1 lb; generic; (OTC)

Omeprazole/Sodium Bicarbonate Capsules (immediate release): 20 mg omeprazole/1,100 mg sodium bicarbonate) & 40 mg omeprazole/1,100 mg sodium bicarbonate; *Zegerid*® (Santarus); (Rx)

Omeprazole/Sodium Bicarbonate Powder for Oral Suspension: 20 mg omeprazole/1,680 mg sodium bicarbonate & 40 mg omeprazole/1,680 mg sodium bicarbonate; *Zegerid*® (Santarus); (Rx)

Sodium Bromide—see Bromides
Sodium Chloride Injections—see the Intravenous Fluids section in the appendix
Sodium Citrate—see Citrate Salts
Sodium Hyaluronate—see Hyaluronate Sodium
Sodium Iodide—see Iodide, Sodium
Sodium Nitroprusside—See Nitroprusside Sodium
Sodium Phosphate—see Phosphate, Parenteral

SODIUM POLYSTYRENE SULFONATE

(soe-***dee***-um pol-ee-***stye***-reen ***sulf***-foe-nate)

Kayexalate®, SPS

CATIONIC EXCHANGE RESIN (HYPERKALEMIA)

Prescriber Highlights

- Cation exchange resin used to treat hyperkalemia
- Contraindications: Patients who cannot tolerate a large sodium load
- Cause of hyperkalemia must be addressed
- Adverse Effects: Constipation, anorexia, vomiting, or nausea. Overdosage/overuse may lead to hypokalemia, hypocalcemia & hypomagnesemia.
- If given PO, often mixed with sorbitol to expedite removal of resin (& potassium)
- Drug Interactions

Uses/Indications

SPS is indicated as adjunctive treatment of hyperkalemia. The cause of the hyperkalemia should be elucidated and corrected if possible.

Pharmacology/Actions

SPS is a resin that exchanges sodium for other cations. After being given orally, hydrogen ions will be exchanged for sodium (in an acidic environment). As the resin travels through the intestinal tract, the hydrogen ions will be exchanged with other more concentrated cations. Primary exchange with potassium occurs predominantly in the large intestine. When given as a retention enema, SPS generally exchanges sodium for potassium directly in the colorectum. While theoretically, up to 3.1 mEq of potassium could be exchanged per gram of SPS, it is unlikely that more than one mEq will be exchanged per gram of resin administered.

Pharmacokinetics

SPS is not absorbed from the GI tract. Its onset of action may be from hours to days; so severe hyperkalemia may require other treatments (*e.g.*, dialysis) in the interim.

Contraindications/Precautions/Warnings

Because large quantities of sodium may be released and absorbed, patients on severely restricted sodium diets (severe CHF, hypertension, oliguria) may benefit from alternative methods of treatment. Overdosage/overuse may lead to hypokalemia, hypocalcemia and hypomagnesemia.

Adverse Effects

Large doses may cause constipation (fecal impactions have been reported rarely), anorexia, vomiting or nausea. Dose related hypocalcemia, hypokalemia and sodium retention have also been noted. To hasten the drug's action and prevent constipation, SPS is generally mixed with 70% sorbitol (3–4 mL per one gram of resin) when dosed orally.

Reproductive/Nursing Safety

While reproductive studies have apparently not been performed, it is unlikely the drug carries much teratogenic potential. In humans, the FDA categorizes this drug 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.*)

As SPS is not absorbed, it should be safe to use during nursing.

Overdosage/Acute Toxicity

Overdosage may cause the adverse effects noted (above); treat symptomatically.

Drug Interactions

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

- **ANTACIDS, LAXATIVES** (**calcium**- or **magnesium**-**containing**): SPS may bind with magnesium or calcium found in laxatives (milk of magnesia, magnesium sulfate, etc.) or antacids which can prevent bicarbonate ion neutralization and lead to metabolic alkalosis. Concurrent use is not recommended during SPS therapy.

Doses

If dosed orally, to hasten the drug's action and to prevent constipation SPS is generally mixed with 70% sorbitol (3–4 mL per one gram of resin); shake well before using.

- **DOGS:**
  a) For hyperkalemia: 2 grams of resin/kg of body weight (each gram should be suspended in 3–4 mL of water; or use commercially prepared suspension products) divided into 3 daily doses. If given orally, give with a cathartic. Do not use a cathartic if using as a retention enema as it must be in the colon for at least 30 minutes. To prepare a retention enema from the powder: add 15 grams per 100 mL of a 1% methylcellulose solution or 10% dextrose. If hyperkalemia is severe: 3–4 times the normal amount of resin may be given. (Willard 1986)
  b) For mild hyperkalemia (<6 mEq/L): 2 grams/kg PO in 3–4 divided doses with 20% sorbitol; may also be give as an enema without sorbitol. (Cowgill and Francey 2005)
- **HORSES:**
  a) For life-threatening hyperkalemia in neonatal foals: 15 grams of resin in 100 mL of 10% dextrose via enema. Monitor serum potassium and sodium closely. (Madigan 2002b)

Monitoring

- Serum electrolytes (sodium potassium (at least once a day), calcium, magnesium
- Acid/base status, ECG, if warranted

Chemistry/Synonyms

A sulfonated cation exchange resin, sodium polystyrene sulfonate (SPS) occurs as a golden brown, fine powder. It is odorless and tasteless. Each gram contains 4.1 mEq of sodium and has an *in vitro* exchange capacity of about 3.1 mEq of potassium (in actuality a maximum of 1 mEq is usually exchanged).

Sodium Polystyrene Sulfonate may also be known as: natrii polystyrenesulfonas, sodium polystyrene sulphonate, *Elutit-Natrium®*, *K-Exit®*, *Kayexalate®*, *Kexelate®*, *Kionex®*, *Resinsodio®*, *Resonium®*, *Resonium A®*, or *SPS®*.

Storage/Stability

Store products in well-closed containers at room temperature; do not heat. Suspensions made from powder should be freshly prepared and used within 24 hours.