AMMONIUM CHLORIDE

(ah-*moe*-nee-um) Uroeze®

ACIDIFYING AGENT

Prescriber Highlights

- Urinary acidifier; treatment of metabolic alkalosis
- Contraindicated in patients with hepatic failure or uremia
- Potential adverse effects are primarily GI distress; IV use may lead to metabolic acidosis
- May increase excretion of quinidine; decrease efficacy of erythromycin or aminoglycosides in urine

Uses/Indications

The veterinary indications for ammonium chloride are as a urinary acidifying agent to help prevent and dissolve certain types of uroliths (*e.g.*, struvite), to enhance renal excretion of some types of toxins (*e.g.*, strontium, strychnine) or drugs (*e.g.*, quinidine), or to enhance the efficacy of certain antimicrobials (*e.g.*, chlortetracycline, methenamine mandelate, nitrofurantoin, oxytetracycline, penicillin G or tetracycline) when treating urinary tract infections. Ammonium chloride has also been used intravenously for the rapid correction of metabolic alkalosis.

Because of changes in feline diets to restrict struvite and as struvite therapeutic diets (*e.g.*, s/d) cause aciduria, ammonium chloride is not commonly recommended for struvite uroliths in cats.

Pharmacology/Actions

The acidification properties of ammonium chloride are caused by its dissociation into chloride and ammonium ions *in vivo*. The ammonium cation is converted by the liver to urea with the release of a hydrogen ion. This ion combines with bicarbonate to form water and carbon dioxide. In the extracellular fluid, chloride ions combine with fixed bases and decrease the alkaline reserves in the body. The net effects are decreased serum bicarbonate levels and a decrease in blood and urine pH.

Excess chloride ions presented to the kidney are not completely reabsorbed by the tubules and are excreted with cations (principally sodium) and water. This diuretic effect is usually compensated for in the kidneys after a few days of therapy.

Pharmacokinetics

No information was located on the pharmacokinetics of this agent in veterinary species. In humans, ammonium chloride is rapidly absorbed from the GI.

Contraindications/Precautions/Warnings

Ammonium chloride is contraindicated in patients with severe hepatic disease as ammonia may accumulate and cause toxicity. In general, ammonium chloride should not be administered to uremic patients since it can intensify the metabolic acidosis already existing in some of these patients. As sodium depletion can occur, ammonium chloride should not be used alone in patients with severe renal insufficiency and metabolic alkalosis secondary to vomiting hydrochloric acid. In these cases, sodium chloride repletion with or without ammonium chloride administration should be performed to correct both sodium and chloride deficits. Ammonium chloride is contraindicated in patients with urate calculi or respiratory acidosis and high total CO_2 and buffer base. Ammonium chloride alone cannot correct hypochloremia with secondary metabolic alkalosis due to intracellular potassium chloride depletion; potassium chloride must be administered to these patients.

Do not administer subcutaneously, rectally or intraperitoneally.

Use ammonium chloride with caution in patients with pulmonary insufficiency or cardiac edema.

Adverse Effects

Development of metabolic acidosis (sometimes severe) can occur unless adequate monitoring is performed. When used intravenously, pain at the injection site can develop; slow administration lessens this effect. Gastric irritation, nausea and vomiting may be associated with oral dosing of the drug. Urinary acidification is associated with an increased risk for calcium oxalate urolith formation in cats.

Overdosage/Acute Toxicity

Clinical signs of overdosage may include: nausea, vomiting, excessive thirst, hyperventilation, bradycardias or other arrhythmias, and progressive CNS depression. Profound acidosis and hypokalemia may be noted on laboratory results.

Treatment should consist of correcting the acidosis by administering sodium bicarbonate or sodium acetate intravenously. Hypokalemia should be treated by using a suitable oral (if possible) potassium product. Intense acid-base and electrolyte monitoring should be performed on an ongoing basis until the patient is stable.

Reproductive/Nursing Safety

In humans, the FDA categorizes this drug as category ***B*** for use during pregnancy (*Animal studies have not yet demonstrated risk to the fetus, but there are no adequate studies in pregnant women; or animal studies have shown an adverse effect, but 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.*) In a separate system evaluating the safety of drugs in canine and feline pregnancy (Papich 1989), this drug is categorized as in class: ***B*** (*Safe for use if used cautiously. Studies in laboratory animals may have uncovered some risk, but these drugs appear to be safe in dogs and cats or these drugs are safe if they are not administered when the animal is near term.*)

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving ammonium chloride or other urinary acidifying agents 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

Doses

- **DOGS:**

  For urine acidification:

  a) As adjunctive therapy for struvite uroliths: 20 mg/kg PO three times daily (Labato 2002b)

  b) To enhance the renal elimination of certain toxins/drugs: 200 mg/kg/day divided four times daily (Grauer and Hjelle 1988)

  c) To enhance elimination of strontium: 0.2–0.5 grams PO 3–4 times a day (used with calcium salts) (Bailey 1986)

  For ATT (ammonia tolerance testing):

  a) 2 mL/kg of a 5% solution of ammonium chloride deep in the rectum, blood sampled at 20 minutes and 40 minutes; or oral challenge with ammonium chloride 100 mg/kg (maximum dose = 3 grams) either in solution: dissolved in 20–50 mL warm water or in gelatin capsules, blood sampled at 30 and 60 minutes. Test may also be done by comparing fasting and

6–hour postprandial samples without giving exogenous ammonium chloride. (Center 2004)

- **CATS:**

For urine acidification:

a) In struvite dissolution therapy if diet and antimicrobials do not result in acid urine or to help prevent idiopathic FUS in a non-obstructed cat: 20 mg/kg PO twice daily (Lage, Polzin, and Zenoble 1988)

b) As adjunctive therapy for struvite uroliths: 20 mg/kg PO twice daily (Labato 2002b)

c) 800 mg per day given in the food once daily (if diet and antimicrobials do not reduce pH) (Lewis, Morris, and Hand 1987)

- **HORSES:**

a) 4–15 grams PO (Swinyard 1975)

b) Ammonium chloride as a urinary acidifier: 60–520 mg/kg PO daily. Ammonium salts are unpalatable and will have to be dosed via stomach tube or dosing syringe. Alternatively, ammonium sulfate at 165 mg/kg PO per day is more palatable and may be accepted when mixed with grain or hay. (Jose-Cunilleras and Hinchcliff 1999)

c) As a urinary acidifier to enhance renal excretion of strychnine: 132 mg/kg PO (Schmitz 2004)

- **CATTLE:**

For urolithiasis prevention:

a) 200 mg/kg PO (Howard 1986)

b) 15–30 grams PO (Swinyard 1975)

- **SHEEP & GOATS:**

For urolithiasis prevention:

a) 200 mg/kg PO (Howard 1986)

b) 1–2 grams PO (Swinyard 1975)

Monitoring

- Urine pH (Urine pH's of ≤6.5 are recommended as goals of therapy)
- Blood pH if there are clinical signs of toxicity or treating metabolic alkalosis
- Serum electrolytes, if using chronically or if treating metabolic acidosis
- Prior to IV use, it is recommended that the carbon dioxide combining power of the patient's serum be measured to insure that serious acidosis is prevented

Client Information

- Contact veterinarian if animal exhibits signs of nausea, vomiting, excessive thirst, hyperventilation or progressive lethargy
- Powders may have a bitter taste and patients may not accept their food after mixing

Chemistry/Synonyms

An acid-forming salt, ammonium chloride occurs as colorless crystals or as white, fine or course, crystalline powder. It is somewhat hygroscopic, and has a cool, saline taste. When dissolved in water, the temperature of the solution is decreased. One gram is soluble in approximately 3 mL of water at room temperature; 1.4 mL at 100°C. One gram is soluble in approximately 100 mL of alcohol.

One gram of ammonium chloride contains 18.7 mEq of ammonium and chloride ions. The commercially available concentrate for injection (26.75%) contains 5 mEq of each ion per mL and contains disodium edetate as a stabilizing agent. The pH of the concentrate for injection is approximately 5.

Ammonium chloride may also be known as muriate of ammonia and sal ammoniac.

Storage/Stability/Compatibility

Ammonium chloride for injection should be stored at room temperature; avoid freezing. At low temperatures, crystallization may occur; it may be resolubolized by warming to room temperature in a water bath.

Ammonium chloride should not be titrated with strong oxidizing agents *etc.* potassium chlorate) as explosive compounds may result.

Ammonium chloride is reported to be physically **compatible** with all commonly used IV replacement fluids and potassium chloride. It is **incompatible** with codeine phosphate, dimenhydrinate, methadone HCl, nitrofurantoin sodium, sulfisoxazole diolamine, and warfarin sodium. It is also reportedly **incompatible** with alkalis and their hydroxides.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Ammonium Chloride Tablets: 200 mg, 400 mg; *UriKare® 200, 400 Tablets* (Neogen); (Rx). Approved for use in cats and dogs.

Ammonium Chloride Granules: 200 mg per ¼ teaspoonful powder; *Uroeze® 200* (Virbac), *UriKare® 200* (Neogen); (Rx) Approved for cats and dogs.

Ammonium Chloride Granules: 400 mg per ¼ teaspoonful powder; *Uroeze®* (Virbac), *UriKare® 400* (Neogen); (Rx) Approved for cats and dogs.

Ammonium chloride is also found in some veterinary labeled cough preparations *e.g., Spect-Aid® Expectorant* Granules (7% guaifenesin, 75% ammonium chloride, potassium iodide 2%) and in some cough syrups (also containing guaifenesin, pyrilamine and phenylephrine).

When used in large animals, feed grade ammonium chloride can be obtained from feed mills.

HUMAN-LABELED PRODUCTS:

Ammonium Chloride Injection: 26.75% (5 mEq/mL) in 20 mL (100 mEq) vials. Must be diluted before infusion; generic; (Rx). Preparation of solution for IV administration: Dilute 1 or 2 vials (100–200 mEq) in either 500 or 1000 mL of sodium chloride 0.9% for injection. Do not administer at a rate greater than 5 mL/min (human adult).

AMMONIUM MOLYBDATE AMMONIUM TETRATHIOMOLYBDATE

(ah-***moe***-nee-um moe-***lib***-date; tet-ra-***thye***-oh-moe-***lib***-date)

Molypen®

COPPER POISONING TREATMENT

Prescriber Highlights

- **Used primarily to treat copper poisoning in food animals (esp. sheep)**
- **Consider contacting FDA for guidance in treating food animals**