For symptomatic therapy of idiopathic feline lower urinary tract disease:

a) 2.5–12.5 mg (total dose) PO once daily at night (Bartges 2006e)
b) 5–10 mg (total dose) PO once daily at night; the drug is in popular use at present and further studies are needed (Senior 2006)
c) Reserved for cases with severe, recurrent signs; 2.5–12.5 mg (total dose) PO at the time the owner retires for the night. Dosage is adjusted to produce a barely perceptible calming effect on the cat. If no improvement is seen within 2 months, the medication may be gradually tapered and then stopped. (Buffington 2006)

For neuropathic pain:

a) 2.5–12.5 mg/cat PO once daily (Hardie 2000)
b) 0.5–2 mg/kg PO once daily; may be a useful addition to NSAIDs for chronic pain. (Lascelles, Robertson et al. 2003)

■ **BIRDS:**

For adjunctive treatment of feather plucking:

a) 1–2 mg/kg PO q12–24 hours. Anecdotal reports indicate some usefulness. Barring side effects, may be worth a more prolonged course of therapy to determine efficacy. (Lightfoot 2001)

Monitoring

- Efficacy
- Adverse effects; it is recommended to perform a cardiac evaluation, CBC and serum chemistry panel prior to therapy
- For cats, some clinicians recommend that liver enzymes be measured prior to therapy, one month after initial therapy, and yearly, thereafter

Client Information

- All tricyclics should be dispensed in child-resistant packaging and kept well away from children or pets.
- Several weeks may be required before efficacy is noted and to continue dosing as prescribed. Do not abruptly stop giving medication without veterinarian's advice.

Chemistry/Synonyms

A tricyclic dibenzocycloheptene-derivative antidepressant, amitriptyline HCl occurs as a white or practically white, odorless or practically odorless crystalline powder that is freely soluble in water or alcohol. It has a bitter, burning taste and a pK_a of 9.4.

Amitriptyline may also be known as amitriptylini hydrochloridum; many trade names are available.

Storage/Stability

Amitriptyline tablets should be stored at room temperature. The injection should be kept from freezing and protected from light.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 2 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Amitriptyline HCl Tablets: 10, 25, 50, 75, 100, 150 mg; generic; (Rx)

There are also fixed dose oral combination products containing amitriptyline and chlordiazepoxide, and amitriptyline and perphenazine.

AMLODIPINE BESYLATE

(am-loe-***di***-peen) Norvasc®

CALCIUM CHANNEL BLOCKER

Prescriber Highlights

- Calcium channel blocker used most often for treating hypertension, especially in cats
- Slight negative inotrope; use with caution in patients with heart disease, hepatic dysfunction
- Potentially may cause anorexia & hypotension in cats early in therapy
- Hypertension may rapidly reoccur if dosages are missed

Uses/Indications

Oral amlodipine appears to be a useful agent in the treatment of hypertension in cats and many consider it the drug of choice for this indication. In pharmacokinetic studies, amlodipine has decreased blood pressure in dogs with chronic renal disease, but its efficacy in treating hypertensive dogs has been disappointing.

Hypertension in cats is usually secondary to other diseases (often renal failure or cardiac causes such as thyrotoxic cardiomyopathy or primary hypertrophic cardiomyopathy, etc.) and is most often seen in middle-aged or geriatric cats. These animals often present with acute clinical signs such as blindness, seizures, collapse or paresis. A cat is generally considered hypertensive if systolic blood pressure is >160 mmHg. Early reports indicate that if antihypertensive therapy is begun acutely, some vision may be restored in about 50% of cases of blindness secondary to hypertension.

Pharmacology/Actions

Amlodipine inhibits calcium influx across cell membranes in both cardiac and vascular smooth muscle. It has a greater effect on vascular smooth muscle, thereby acting as a peripheral arteriolar vasodilator and reducing afterload. Amlodipine also depresses impulse formation (automaticity) and conduction velocity in cardiac muscle.

Pharmacokinetics

No feline-specific data on the drug's pharmacokinetics was located. In humans, amlodipine's bioavailability does not appear to be altered by the presence of food in the gut. The drug is slowly but almost completely absorbed after oral administration. Peak plasma concentrations occur between 6–9 hours post-dose and effects on blood pressure are correspondingly delayed. The drug has very high plasma protein binding characteristics (approximately 93%). However, drug interactions associated with potential displacement from these sites have not been elucidated. Amlodipine is slowly, but extensively metabolized to inactive compounds in the liver. Terminal plasma half-life is approximately 35 hours in healthy humans, but is prolonged in the elderly and in those patients with hypertension or hepatic dysfunction.

Contraindications/Precautions/Warnings

Because amlodipine may have slight negative inotropic effects, it should be used cautiously in patients with heart failure or cardiogenic shock. It should also be used cautiously in patients with hepatic disease or at risk for developing hypotension. A relative contraindication for amlodipine exists for humans with advanced aortic stenosis.

There is concern that using amlodipine alone for treating hypertension in cats with renal disease may expose glomeruli to higher pressures secondary to efferent arteriolar constriction. This is caused by localized increases in renin-angiotensin-aldosterone axis activity thereby allowing progressive damage to glomeruli. It is postulated that using an ACE inhibitor with amlodipine may help prevent this occurrence (Stepian 2006a).

Adverse Effects

Because of amlodipine's relatively slow onset of action, hypotension and inappetence is usually absent in cats. Infrequently, cats may develop azotemia, lethargy, hypokalemia, reflex tachycardia and weight loss. In humans taking amlodipine, headache (7.3% incidence) is the most frequent problem reported.

Reproductive/Nursing Safety

While no evidence of impaired fertility was noted in rats given 8X overdoses, amlodipine has been shown to be fetotoxic (intrauterine death rates increased 5 fold) in laboratory animals (rats, rabbits) at very high dosages. No evidence of teratogenicity or mutagenicity was observed in lab animal studies. In rats, amlodipine prolonged labor. It is unknown whether amlodipine enters maternal milk. 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.*)

Overdosage/Acute Toxicity

There were 69 exposures to amlodipine reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2005–2006. In these cases 59 were dogs with 7 showing clinical signs; the remaining 10 cases were cats with 2 showing clinical signs. Common findings in dogs, recorded in decreasing frequency included anorexia, lethargy, tachycardia, acidosis and bradycardia. Common findings in cats, recorded in decreasing frequency included lethargy and polydipsia.

Limited experience with other calcium channel blockers in humans has shown that profound hypotension and bradycardia may result. When possible, massive overdoses should be managed with gut emptying and supportive treatment. Beta-agonists and intravenous calcium may be beneficial.

Drug Interactions

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

No clinically significant drug-drug interactions have been noted specifically with amlodipine at this time. However, concomitant use of **diuretics**, **beta-blockers**, other **vasodilators or other agents that may reduce blood pressure** (*e.g.*, **fentanyl**) may cause hypotension if used with amlodipine. **Grapefruit juice/powder** may alter bioavailability.

Laboratory Considerations

No specific concerns were noted

Doses

- **CATS:**

For treatment of systemic hypertension:

a) 0.625 mg (1/4 of a 2.5 mg tablet) PO once daily; some larger cats (>4 kg) or those with severe hypertension may require doses as high as 1.25 mg PO twice daily. Titrate dosage carefully, based upon BP determinations. (Brown and Henik 2000); (Trepanier 1999)

b) 0.625–1.25 mg (total dose) PO once daily. Drug of choice; often successful as a single agent. Can be combined with an ACEI, beta-blocker or diuretic if needed. Maximum effect seen within 7 days of therapy. (Sparkes 2003a)

- **DOGS:**

For adjunctive therapy for refractory heart failure:

a) For treatment of advanced mitral valve degeneration as an afterload reducer after ACE inhibitor maintenance therapy has been established: 0.2–0.4 mg/kg PO twice daily. Initiate therapy at 0.1 mg/kg PO twice daily and up-titrate weekly while monitoring blood pressure. (Kraus 2003)

b) As an arterial vasodilator particularly in dogs moderately refractory, or recurrent CHF secondary to mitral regurgitation and maintained blood pressures: 0.1 mg/kg q12–24h initially; titrate up as needed to 0.25 mg/kg PO q12–24h; monitor blood pressure. (DeFrancesco 2006)

For treatment of systemic hypertension in dogs with chronic renal disease:

a) 0.05–0.25 mg/kg PO once daily. In many dogs, amlodipine appears to be less effective, even at high doses (1 mg/kg/day). (Brown, Brown et al. 2006)

b) 0.1–0.2 mg/kg PO q12–24h (Stepian 2006a)

Monitoring

- Blood pressure
- Ophthalmic exam
- Adverse effects

Client Information

- May give with food
- Missing dosages can cause rapid redevelopment of symptoms and damage secondary to hypertension

Chemistry/Synonyms

Amlodipine besylate, a dihydropyridine calcium channel-blocking agent, occurs as a white crystalline powder that is slightly soluble in water and sparingly soluble in alcohol.

Amlodipine Besylate may also as: amlodipini besilas, UK-48340-26, or UK-48340-11 (amlodipine maleate); many trade names are available.

Storage/Stability

Store amlodipine tablets at room temperature, in tight, light resistant containers.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

The ARCI (Racing Commissioners International) has designated this drug as a class 4 substance. See the appendix for more information.

HUMAN-LABELED PRODUCTS:

Amlodipine Tablets: 2.5 mg, 5 mg, 10 mg; *Norvasc*® (Pfizer); *Amvaz*® (Reddy); (Rx)

Fixed-dose combination products with benazepril (*Lotrel*®) or atorvastatin (*Caduet*®) are available.

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