Doses

Note: Some human references state that because of the potential for drug interactions with previous drug therapies, the life-threatening nature of the arrhythmias being treated, and the unpredictability of response from amiodarone, the drug should be initially given (loaded) over several days in an inpatient setting where adequate monitoring can occur.

- **DOGS:**

For conversion of atrial fibrillation:

a) At the time of writing (2007) one case report (Oyama and Prosek 2006) and one retrospective evaluation (Saunders, Miller et al. 2006) have been published using amiodarone to convert atrial fibrillation in dogs. Dosage recommendations are yet to be fully defined; monitor the current literature for further recommendations.

For recurrent ventricular tachycardia not controlled with other less toxic drugs:

a) 10–25 mg/kg PO twice daily for 7 days, followed by 5–7.5 mg/kg PO twice daily for 14 days, followed by 7.5 mg/kg PO once daily (Calvert 1995)

b) For ventricular arrhythmias secondary to occult cardiomyopathy in Doberman pinschers: 10 mg/kg PO twice daily for one week and then 8 mg/kg PO once daily. For severe V-Tach, mexiletine is added at 5–8 mg/kg three times daily for one week. Once efficacy confirmed, patient weaned off mexiletine. (Calvert and Mieurs 2000)

c) Amiodarone as above in "b", but after 6 months may be reduced to 5 mg/kg once daily. (Meurs 2005)

d) 10–20 mg/kg PO q12h (Fox 2003a)

- **HORSES:**

For conversion of atrial fibrillation or ventricular tachycardia:

a) 5 mg/kg/hr for one hour, followed by 0.83 mg/kg/hr for 23 hours and then 1.9 mg/kg/hour for the following 30 hours. In the study (A fib), infusion was discontinued when conversion occurred or when any side effects were noted. 4 of 6 horses converted from A fib; one horse from V tach. In order to increase success rate and decrease adverse effects, regimen should be further adapted based upon PK/PD studies in horses. (De Clercq, van Loon et al. 2006a), (De Clercq, van Loon et al. 2006b)

Monitoring

- Efficacy (ECG)
- Toxicity (GI effects; CBC, serial liver enzymes; thyroid function tests; blood pressure; pulmonary radiographs if clinical signs such as dyspnea/cough occur)

Client Information

- Because of the "experimental" nature (relatively few canine/equine patients have received this agent) and the toxicity dangers associated with its use, clients should give informed consent before the drug is prescribed.

Chemistry/Synonyms

An iodinated benzofuran, amiodarone is unique structurally and pharmacologically from other antiarrhythmic agents. It occurs as a white to cream colored lipophilic powder having a pKa of approximately 6.6. Amiodarone 200 mg tablets each contain approximately 75 mg of iodine.

Amiodarone HCl may also be known as: amiodaroni hydrochloridum, L-3428, 51087N, or SKF-33134-A; many trade names are available.

Storage/Stability/Compatibility

Tablets should be stored in tight containers, at room temperature and protected from light. A 3-year expiration date is assigned from the date of manufacture.

Injection should be stored at room temperature and protected from light or excessive heat. While administering, light protection is not necessary. Use D5W as the IV diluent. Amiodarone is reportedly **compatible** with dobutamine, lidocaine, potassium chloride, procainamide, propafenone, and verapamil. **Variable compatibility** is reported with furosemide and quinidine gluconate.

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:

Amiodarone Oral Tablets: 100 mg, 200 mg & 400 mg; *Cordarone*® (Wyeth-Ayerst); *Pacerone*® (Upsher Smith); generic; (Rx)

Amiodarone Concentrate for Injection (for IV Infusion): 50 mg/mL in 3 mL amps & vials; *Cordarone*® (Wyeth-Ayerst); generic; (Rx)

Amitraz — See the Topical Dermatologic Agents section in the appendix

AMITRIPTYLINE HCL

(a-mih-***trip***-ti-leen) Elavil®

TRICYCLIC BEHAVIOR MODIFIER; ANTIPRURITIC; NEUROPATHIC PAIN MODIFIER

Prescriber Highlights

- Tricyclic "antidepressant" used primarily for behavior disorders & neuropathic pain/pruritus in small animals
- May reduce seizure thresholds in epileptic animals
- Sedation & anticholinergic effects most likely adverse effects
- Overdoses can be very serious in both animals & humans

Uses/Indications

Amitriptyline has been used for behavioral conditions such as separation anxiety or generalized anxiety in dogs, and excessive grooming, spraying and anxiety in cats. Amitriptyline may be useful for adjunctive treatment of pruritus, or chronic pain of neuropathic origin in dogs and cats. In cats, it potentially could be useful for adjunctive treatment of lower urinary tract disease. Amitriptyline has been tried to reduce feather plucking in birds.

Pharmacology/Actions

Amitriptyline (and its active metabolite, nortriptyline) has a complicated pharmacologic profile. From a slightly oversimplified viewpoint, it has 3 main characteristics: blockage of the amine pump, thereby increasing neurotransmitter levels (principally serotonin, but also norepinephrine), sedation, and central and peripheral anticholinergic activity. Other pharmacologic effects include stabilizing mast cells via H-1 receptor antagonism, and antagonism of glutamate receptors and sodium channels. In animals, tricyclic antidepressants are similar to the actions of phenothiazines in altering avoidance behaviors.

Pharmacokinetics

Amitriptyline is rapidly absorbed from both the GI tract and from parenteral injection sites. Peak levels occur within 2–12 hours. Amitriptyline is highly bound to plasma proteins, enters the CNS, and enters maternal milk in levels at, or greater than those found in maternal serum. The drug is metabolized in the liver to several metabolites, including nortriptyline, which is active. In humans, the terminal half-life is approximately 30 hours. Half-life in dogs has been reported to be 6–8 hours.

Contraindications/Precautions/Warnings

These agents are contraindicated if prior sensitivity has been noted with any other tricyclic. Concomitant use with monoamine oxidase inhibitors is generally contraindicated. Use with extreme caution in patients with seizure disorders as tricyclic agents may reduce seizure thresholds. Use with caution in patients with thyroid disorders, hepatic disorders, KCS, glaucoma, cardiac rhythm disorders, diabetes, or adrenal tumors.

Adverse Effects

The most predominant adverse effects seen with the tricyclics are related to their sedating and anticholinergic (constipation, urinary retention) properties. Occasionally, dogs exhibit hyperexcitability and, rarely, develop seizures. However, adverse effects can run the entire gamut of systems, including cardiac (dysrhythmias), hematologic (bone marrow suppression), GI (diarrhea, vomiting), endocrine, etc. Cats may demonstrate the following adverse effects: sedation, hypersalivation, urinary retention, anorexia, thrombocytopenia, neutropenia, unkempt hair coat, vomiting, ataxia, disorientation and cardiac conductivity disturbances.

Reproductive/Nursing Safety

Isolated reports of limb reduction abnormalities have been noted; restrict use to pregnant animals only when the benefits clearly outweigh the risks. In humans, the FDA categorizes this drug as category ***D*** for use during pregnancy (*There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.*)

Overdosage/Acute Toxicity

Overdosage with tricyclics can be life-threatening (arrhythmias, cardiorespiratory collapse). Because the toxicities and therapies for treatment are complicated and controversial, it is recommended to contact a poison control center for further information in any potential overdose situation.

There were 25 exposures to amitriptyline reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2005–2006. In these cases, 21 were cats with 5 showing clinical signs. Common findings recorded in decreasing frequency included: anorexia, mydriasis and adipsia. The remaining 4 cases were dogs with no reported clinical signs.

Drug Interactions

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

- **ANTICHOLINERGIC AGENTS**: Increased effects; hyperthermia and ileus possible
- **CIMETIDINE**: May inhibit tricyclic antidepressant metabolism and increase the risk of toxicity
- **CISAPRIDE**: May have additive effects on QTc interval; possible serious arrhythmias may result
- **CNS DEPRESSANTS**: Increased effects
- **DIAZEPAM**: Possible increased amitriptyline levels
- **MONOAMINE OXIDASE INHIBITORS** (including **selegilene**, **amitraz**): Potential life threatening serotonin syndrome; use together not recommended
- **SELECTIVE-SEROTONIN RE-UPTAKE INHIBITORS** (**SSRIs, fluoxetine**, etc.): Potential increased amitriptyline levels, increased risk for serotonin syndrome; **Note**: SSRI's and TCA's *etc.* amitriptyline are often used together in veterinary behavior medicine, but enhanced monitoring for adverse effects is suggested)
- **SYMPATHOMIMETIC AGENTS**: May increase the risk of cardiac effects (arrhythmias, hypertension, hyperpyrexia)
- **THYROID AGENTS**: Increased risk for arrhythmias; monitor

Laboratory Considerations

- Tricyclics can widen QRS complexes, prolong PR intervals and invert or flatten T-waves on **ECG**
- The response to **metapyrone** may be decreased by amitriptyline
- Tricyclics may alter (increase or decrease) **blood glucose** levels

Doses

- **DOGS:**

  For adjunctive treatment of pruritus:
  a) 1–2 mg/kg PO q12h (Paradis and Scott 1992)
  b) For acral pruritic dermatitis: 2.2 mg/kg PO twice daily; only occasionally effective. A 2–4 week trial is recommended (Rosychuck 1991)

  For behavior disorders amenable to tricyclics:
  a) For separation anxiety or generalized anxiety: 1–2 mg/kg PO q12h; with behavior modification (Shanley and Overall 1992); (Line 2000); (Overall 2000)
  b) 1–4 mg/kg PO q12h. Begin at 1–2 mg/kg PO q12h for 2 weeks, increase by 1 mg/kg up to maximum dosage (4 mg/kg) as necessary. If no clinical response, decrease by 1 mg/kg PO q12h for 2 weeks until at initial dosage. (Virga 2002)
  c) 2.2–4.4 mg/kg PO q12h (Reisner and Houpt 2000)
  d) 0.25–1.5 mg/kg PO every 12–24h (Crowell-Davis 1999)

  For neuropathic pain:
  a) 1–2 mg/kg PO q12–24h (Hardie 2000)
  b) For adjunctive treatment of pain associated with appendicular osteosarcoma: 1–2 mg/kg PO q12–24h (Liptak and Ehrhart 2005)

- **CATS:**

  For adjunctive treatment of behavior disorders amenable to tricyclics:
  a) 5–10 mg per cat PO once daily (Miller 1989), (Marder 1991), (Reisner and Houpt 2000)
  b) 0.5–2 mg/kg PO q12–24h; start at 0.5 mg/kg PO q12h (Overall 2000)
  c) 0.5–1 mg/kg PO q12–24h (Crowell-Davis 1999)
  d) 0.5–1 mg/kg PO q12–24h. Allow 3–4 weeks for initial trial. (Virga 2002)

  For self-mutilation behaviors associated with anxiety:
  a) 5–10 mg per cat PO once to twice daily; with behavior modification (Shanley and Overall 1992)
  b) 1–2 mg/kg PO q12h (Line 2000)

  For pruritus (after other more conventional therapies have failed):
  a) 5–10 mg per cat PO once daily or 2.5–7.5 mg/cat once to twice daily. When discontinuing, taper dose over 1–3 weeks. (Messinger 2000)

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.