

Which Drugs Can Control Systemic Arterial Hypertension in Dogs & Cats?

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CALCIUM-CHANNEL BLOCKER

Amlodipine Besylate

Amlodipine besylate, a dihydropyridine calcium-channel blocker with vascular selectivity, is the preferred medication for treatment of systemic hypertension. Several studies have documented the efficacy of oral amlodipine in decreasing arterial blood pressure in both hypertensive cats¹⁻⁴ and dogs.⁵ Amlodipine also can be used for crisis therapy (see **Hypertensive Crisis Therapy**, page 45).

Formulation → Oral (tablet, chewable)

Dose (dogs) → 0.1-0.2 mg/kg PO once or twice a day⁶

- Rarely, up to 0.4 mg/kg PO twice a day required in dogs with resistant hypertension

Dose (cats) → 0.625 mg/cat PO once or twice a day (roughly 0.1 mg/kg/day)

- Higher doses occasionally required for cats with resistant hypertension (rarely exceed 0.4 mg/kg/day)
- **Note:** Transdermal administration is not commercially available, but in 1 pilot study in cats, 0.1-0.4 mg/kg/day formu-

lated per cat at 0.625 mg amlodipine per 0.1 mL ointment was described, although this formulation did not appear to be as effective as the oral formulation.⁷

Key Points

- New chewable formulation was recently reported, with voluntary acceptance in 73% of cats.⁸
- In both dogs and cats, side effects are rare.⁹⁻¹¹
 - Gingival hyperplasia and peripheral edema have been reported in dogs.⁹⁻¹¹
 - Both side effects resolve with drug cessation.
 - Systemic hypotension is a rare but potential side effect.¹²

CAUTION: Because of profound efficacy in lowering arterial blood pressure and altering renal perfusion, amlodipine is optimally given with an angiotensin-converting enzyme (ACE) inhibitor to blunt potential renin-angiotensin-aldosterone activation.^{13,14}

ANGIOTENSIN-CONVERTING ENZYME INHIBITORS

ACE inhibitors promote vasodilation by preventing production

of angiotensin II, a potent vasoconstrictor. ACE inhibitors are seldom potent enough to control arterial blood pressure in patients with severe hypertension (eg, >180 mm Hg).^{14,15}

Enalapril & Benazepril

Enalapril, the most studied ACE inhibitor in clinical veterinary medicine, is commonly used in animals with cardiovascular and renal diseases.¹⁶ Benazepril, however, has been suggested as the preferred ACE inhibitor for animals with renal dysfunction, as it is partially metabolized by the liver rather than solely cleared by the kidneys, resulting in more predictable pharmacokinetics in animals with renal disease.¹⁷

Formulation → Oral (tablet)

Dose (standard & starting; dogs & cats) → 0.25-0.5 mg/kg PO once to twice a day¹⁴

- ▶ Once-daily dosing appears appropriate for benazepril based on pharmacokinetics studies in dogs¹⁸ and cats.¹⁹
- ▶ Lower starting dose of 0.1-0.2 mg/kg PO once to twice a day is advised in animals with renal dysfunction.
 - Escalate to full standard dose in 10-14 days if renal function remains stable.

Key Points

- ▶ By themselves, ACE inhibitors have weak antihypertensive properties in cats and should not be used as sole therapy for systemic hypertension.^{15,20,21}
- ▶ In dogs, ACE inhibitors are often given as initial therapy, with reduction in arterial blood pressure documented in dogs with renal disease.^{22,23}
- ▶ Adverse events from ACE inhibitors relate to impaired renal function, particularly if the animal is dehydrated at the time medication is initiated.¹⁴
 - Normalization of hydration status and close monitoring of renal values is advised for dehydrated animals or those on chronic diuretic therapy while receiving benazepril or enalapril.

ADRENERGIC RECEPTOR BLOCKERS (ALPHA & BETA)

Prazosin

Prazosin, an α_1 -adrenergic receptor blocker, can be an effective vasodilator in both dogs and cats.²⁴ Activation of the α_1 -adrenergic receptor in the peripheral vasculature results in vasoconstriction by action on the vascular smooth muscle;

blockade of this receptor by prazosin results in vasodilation and reduction in systemic arterial blood pressure.²⁵

Formulation → Oral (capsule)

Dose (dogs) → Typical dose of 0.25-1 mg/kg PO 2-3 times a day¹⁴

- ▶ Conservative doses of 1 mg PO 3 times a day also reported in dogs weighing <15 kg and 2 mg PO 3 times a day in dogs weighing >15 kg

CAUTION: Administer initial dose cautiously, as potent vasodilation may occur.

- Start with low end of dose range and/or administer first dose while monitoring patients in a clinic or hospital setting.

Dose (cats) → 0.25-0.5 mg/cat PO 2-3 times a day²⁶

- ▶ Compounded capsules typically required

CAUTION: Administer initial dose cautiously, as potent vasodilation may occur.

- Start with dose of 0.25 mg/cat and/or administer first dose while monitoring patients in a clinic or hospital setting.

Key Points

- ▶ Except for lethargy, side effects are not reported in the veterinary literature.²⁷
- In the author's experience, acute hypotension during initiation of therapy can occur as previously noted.

CAUTION: Because of profound efficacy in lowering arterial blood pressure and altering renal perfusion, prazosin is typically given with an ACE inhibitor to blunt potential renin-angiotensin-aldosterone activation.

By themselves, ACE inhibitors have weak antihypertensive properties in cats and should not be used as sole therapy for systemic hypertension.^{15,20,21}

ACE = angiotensin-converting enzyme

Atenolol

Atenolol is the most common β -adrenergic receptor blocker used in animals. Generally, β -blockers are considered complementary agents in animals with systemic arterial hypertension and normal cardiac function. Antihypertensive effects derive from reduction in cardiac output caused by both negative inotropic and negative chronotropic effects.

Formulation → Oral (tablet, suspension)

Dose (dogs) → Most commonly prescribed at 0.5-1 mg/kg PO twice a day^{14,28}

Dose (cats) → 6.25 mg/cat PO twice a day

Key Points

- In 1 study of hyperthyroid cats with hypertension,²⁹ atenolol administered at 1-2 mg/kg PO twice a day did not reduce arterial blood pressure to <160 mm Hg in 70% of cats.
 - Atenolol cannot, therefore, be recommended as sole therapy for hyperthyroid cats with hypertension.
- The primary side effects of excessive β -blockade are lethargy and bradycardia.

ANGIOTENSIN RECEPTOR BLOCKERS

Similar to ACE inhibitors, angiotensin receptor blockers (ARBs), such as irbesartan, losartan, and telmisartan, are antagonists of the angiotensin II receptor and thus result in vasodilation. These agents commonly used in humans have not been sufficiently studied in dogs or cats.

Irbesartan

Formulation → Oral (tablet)

Dose (dogs only; do not use in cats) → Experimental studies found that a single dose of 5 mg/kg PO had an antihypertensive effect in normal beagles.³⁰

Losartan

Formulation → Oral (tablet)

Dose (dogs; do not use in cats) → 0.125-0.25 mg/kg once a day in azotemic dogs; 0.5-1 mg/kg once a day in nonazotemic dogs³¹

ACE = angiotensin-converting enzyme

ARB = angiotensin receptor blocker

Telmisartan

Formulation → Oral (tablet, solution)

Dose (dogs) → Clinical case report describes variable dose administration starting at 0.4 mg/kg PO once a day and increasing to 0.9 mg/kg PO once a day.³²

Dose (cats) → 1 mg/kg PO once a day³³

Key Points (irbesartan, losartan, telmisartan)

- Until further studies are performed, the utility of ARBs for antihypertensive therapy is uncertain.
- Adverse events in humans include angioedema, deterioration in renal function, and hyperkalemia.³⁴
- Progression of renal dysfunction was reported in 2 of 112 cats treated with telmisartan.³³

DIRECT ARTERIAL VASODILATOR Hydralazine

Hydralazine is a direct arterial vasodilator, working via an endothelial pathway and associated with membrane hyperpolarization of the vascular smooth muscle.³⁵ With the increased use of amlodipine (calcium-channel blocker) and ACE inhibitors, hydralazine is less commonly used for antihypertensive therapy in dogs and cats, although it can be used in refractory cases and for crisis therapy (see **Hypertensive Crisis Therapy**).

Formulation → Oral (tablet)

Dose (dogs) → 0.5-2 mg/kg PO twice a day^{14,36}

- Lower doses initially advised until clinical response observed

Dose (cats) → 2.5 mg/cat PO once or twice a day¹⁴

- Lower doses initially advised until clinical response observed

Key Points

- Side effects may include anorexia and reflex tachycardia.³⁷

CAUTION: Because of profound efficacy in lowering arterial blood pressure and altering renal perfusion, hydralazine is typically given with an ACE inhibitor to blunt potential renin-angiotensin-aldosterone activation.

HYPERTENSIVE CRISIS THERAPY

In a clinical setting, a hypertensive crisis develops when an animal presents with signs of target organ damage (eg, retinal detachment or hyphema, aortic dissection, neurologic impairment) and markedly elevated (typically >200 mm Hg) systemic arterial blood pressure. During a hypertensive crisis in dogs and cats, acute control of arterial blood pressure to values of 170 to 180 mm Hg is advised. Rapid restoration of arterial blood pressure to normal values (eg, 120-140 mm Hg) should not be the goal of therapy, as cerebral autoregulation resets to higher pressures with chronic systemic hypertension. Cerebral ischemia may occur if sufficient time is not given for the cerebral vasculature to readjust to blood pressure normalization.³⁸ After 48 to 72 hours in a range of 160 to 180 mm Hg, further reduction to normal values using oral antihypertensive agents may be pursued.

Sodium Nitroprusside

Although this is the most potent and easily titrated agent to lower arterial blood pressure in dogs and cats, its cost has greatly increased in recent years because of limited manufacturers.

Formulation → IV (infusion)

Dose (dogs & cats) → Typically, 0.5-10 µg/kg/min³⁹⁻⁴¹

- ▶ Start at lowest end of dose range; increase gradually, pending response every 3-5 minutes.

Key Points

- ▶ Administer in a critical care setting, with monitoring of direct (invasive) arterial pressure.
- ▶ Infusion line should be protected from light and drug administered for no longer than 48 hours to avoid potential thiocyanate and cyanide accumulation and/or toxicity.
- ▶ Side effects may include hypotension.
- ▶ With prolonged use, methemoglobinemia, lactic acidosis, and other signs of cyanide intoxication may develop.⁴¹

Hydralazine

Formulation → IV (infusion)

Dose (dogs & cats) → 0.1-0.2 mg/kg IV up to every 2 hours¹⁴

Key Points

- ▶ Administer in a critical care setting, with monitoring of direct (invasive) arterial pressure.

- ▶ Reflex tachycardia and hypotension are potential side effects.

Amlodipine Besylate

Formulation → Oral (tablet, chewable)

Dose (dogs) → 0.1-0.25 mg/kg PO once or twice a day¹⁴

- ▶ Can be used in acute hypertensive setting for dogs, particularly if IV agents as described earlier are not available

Dose (cats) → 0.625-1.25 mg/cat PO once or twice a day¹⁴

- ▶ Although an oral medication, often used for acute hypertensive crises in cats because of its efficacy and safety profile

Key Points

- ▶ As previously noted for standard therapy (see **Amlodipine Besylate**, page 42).

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