

Diuretics Commonly Used in Dogs & Cats

David F. Senior, BVSc, DACVIM (SAIM), DECVIM-CA
Professor Emeritus, Louisiana State University

Diuretics increase tubular fluid flow rate and urine volume primarily by increasing the renal excretion of sodium and attendant anions. These characteristics allow diuretics to be useful in a number of clinical conditions (see **Common Indications for Treatment with Diuretics**) in which manipulation of renal function and extracellular fluid (ECF) volume and composition are indicated.

CLASSES OF DIURETICS & CLINICAL USE

Loop Diuretics

Loop diuretics, such as furosemide, bumetanide, and torsemide, inhibit the sodium-potassium-chloride (Na-K-Cl) symporter in the luminal membrane of the thick ascending limb of the loop of Henle, which induces the countercurrent multiplier effect. Inhibition of sodium reabsorption induces osmotic diuresis in more distal sections of the tubule, enhancing urinary excretion of sodium, chloride, potassium, calcium, and water.

Furosemide

Formulations → Injectable: 50 mg/mL solution; oral solution (syrup): 10 mg/mL in 60 mL; tablets: 12.5, 50 mg

For pulmonary edema & ascites associated with congestive heart failure (CHF)¹

Dose (dogs) → Injection: Start with 2 mg/kg q6-8h IV or IM; increase dose in increments of 1 mg/kg to effect (maximum, 5.5 mg/kg q6-8h); oral: up to 6 mg/kg PO q8h

Dose (cats) → Injection: Start with 0.5 mg/kg IV or IM q12h; increase dose in increments of 2.2 mg/kg to effect (maximum, 5 mg/kg q12-24h)

Maintenance dose → Oral: Start with 1 mg/kg PO every 2-3 days up to 2 mg/kg PO q8-12h, depending on response

Key Points

- ▶ Conservative doses should be implemented initially, then adjusted to the minimum effective dose based on a target respiration rate.¹
 - Ideal respiration rate varies based on the individual patient and environmental conditions and is achieved when the patient exhibits a steady, relaxed respiration pattern after stabilization.
- ▶ Parenteral furosemide is usually only used for a short period in patients with acute fluid accumulation.

- Single intravenous, subcutaneous, and oral administration may be equally effective to increase urine production in dogs.²

▶ Also see **General Comments**.

For fluid retention associated with glomerular disease³

Dose (dogs only) → 1 mg/kg IV or IM q6-12h, with incremental increases of 0.5-1 mg/kg IV or IM q6-12h

Key Points

- ▶ Use of diuretics for glomerular disease is reserved for patients with severe pulmonary edema or ascites that interferes with major organ function.³
- ▶ Mild peripheral edema is best left untreated in these patients.
- ▶ In patients with hypoalbuminemia, further ECF reduction with diuretics can cause severe hypovolemia and circulatory collapse.³
- ▶ Parenteral furosemide is usually used for a short period in patients with acute fluid accumulation.³
- ▶ Also see **General Comments**.

For acute management of moderate-to-severe or rapidly progressing hypercalcemia⁴

Dose (dogs only) → 2-4 mg/kg IV, SC, or PO q8-12h

Key Points

- ▶ Furosemide is a temporary supportive treatment for short-term control of hypercalcemia until the primary cause can be identified and corrected.⁴
- ▶ Full hydration should be maintained in patients being treated with furosemide for hypercalcemia.⁵
- ▶ Furosemide is usually reserved for patients that fail to respond to solute diuresis.
- ▶ Also see **General Comments**.

For prevention of cyclophosphamide-induced hemorrhagic cystitis⁵

Dose (dogs only) → 0.5-2.2 mg/kg PO or IV q24h

- ▶ Shown to be effective in reducing the incidence of sterile hemorrhagic cystitis in dogs currently receiving metronomic low-dose oral cyclophosphamide⁶

General Comments (Furosemide)

- ▶ Doses should be adjusted based on individual patient response.

COMMON INDICATIONS FOR TREATMENT WITH DIURETICS

- ▶ **Control of pulmonary edema by mobilization of fluid:** Both loop and thiazide diuretics reduce ECF volume, which in turn reduces intracapillary hydrostatic pressure, a Starling force that contributes to interstitial pulmonary edema.
- ▶ **Acute kidney injury:** Manipulation of fluid electrolyte and acid-base disturbances in patients with oliguric acute kidney injury is easier if urine output can be increased with administration of mannitol and/or loop diuretics.
- ▶ **Hypercalcemia:** Loop diuretics can be administered to increase renal calcium excretion, thereby addressing extreme, life-threatening hypercalcemia.
- ▶ **Control of hypertension:** The reduced ECF volume and reduced plasma volume produced by loop and thiazide diuretics can render them useful as adjunct therapy to control hypertension.
- ▶ **Control of cerebral edema and glaucoma:** By increasing plasma osmolality, IV boluses of mannitol can increase transfer of fluid from the intracellular fluid space and transcellular fluid space to ECF space, which can rapidly reduce cerebral swelling and intraocular pressure.
- ▶ **Calcium oxalate urolithiasis:** Because thiazide diuretics can decrease urine calcium excretion, they are indicated in long-term prevention of calcium oxalate urolithiasis.
- ▶ **Nephrogenic diabetes insipidus:** Loop diuretics combined with a low-sodium diet can reduce ECF volume so a greater proportion of glomerular filtrate is reabsorbed proximally, leaving less to be excreted in the absence of antidiuretic hormone activity, also known as vasopressin.
- ▶ **Prevention of cyclophosphamide-induced hemorrhagic cystitis:** Concurrent administration of furosemide can reduce the likelihood of cyclophosphamide-associated sterile hemorrhagic cystitis in dogs.

CHF = congestive heart failure
ECF = extracellular fluid

- ▶ Renal function and electrolytes, especially potassium, should be monitored to prevent prerenal azotemia.
- ▶ *In cats*: Ototoxicity and hearing loss can occur at high doses.
- ▶ Furosemide can potentiate the hypotensive effects of angiotensin-converting enzyme (ACE) inhibitors.
- ▶ Severe hypokalemia and hyponatremia can develop during treatment, particularly in patients with reduced food and water intake.
- ▶ *In cats*: Extreme dehydration and hypokalemia can occur when diuretics are administered long-term; careful monitoring is required.

Bumetanide

Formulations → Oral tablets: 0.5, 1, 2 mg; injection: 0.25 mg/mL

For cardiogenic or pulmonary edema, acute oliguric kidney failure, & moderate-to-severe hypercalcemia⁷⁻⁹

Dose (anecdotal; dogs, cats) → Definitive doses have not been published.

- ▶ Because bumetanide is 25 to 50 times more potent than furosemide on a mg/mL basis, furosemide doses can be divided by 25 or 50 to arrive at a best-guess dose.⁷⁻⁹

Key Points

- ▶ There seems to be little reason to use bumetanide instead of furosemide, as their modes of action are identical.
 - Furosemide is approved for use in dogs and cats; doses are anecdotal but well established in small animal medicine.
- ▶ Extreme dehydration can occur in cats receiving long-term diuretic therapy.

Torsemide

Formulations → Oral tablets: 5, 10, 20, 100 mg; injection: 10 mg/mL

For pulmonary edema & ascites associated with CHF¹⁰

Dose (dogs, cats) → 0.2-0.3 mg/kg PO q8-24h

Key Points

- ▶ Approximately 10 times more potent than furosemide
- ▶ Thought to be indicated in CHF patients that prove refractory to furosemide treatment¹⁰

ACE = angiotensin-converting enzyme

CHF = congestive heart failure

- ▶ Tablet size can make oral dosing difficult in small dogs and cats; however, compounded 5 mg/mL suspension remains stable for 90 days at room temperature.⁹
- ▶ Not as potassium-wasting as furosemide¹⁰
- ▶ Longer duration of action than furosemide; single-daily dosing has proven effective in dogs with degenerative mitral valve disease.¹¹
- ▶ Significant dehydration can occur when cats receive long-term diuretic therapy.

Osmotic Diuretic

Mannitol is a freely filtered, nonabsorbed 6-carbon sugar that promotes osmotic diuresis via retention of sodium and water throughout the nephron, resulting in enhanced excretion of sodium, chloride, potassium, and water.

Mannitol

Formulations → 5%, 10%, 15%, 20%, 25% IV solutions

For oliguric acute kidney injury¹²

Dose (dogs, cats) → 0.25-1 g/kg IV (slow bolus over 10-20 minutes) of 20%-25% solution

- ▶ If diuresis is induced within 30 to 60 minutes, continue administering at 60-120 mg/kg/hr IV CRI or 0.25-0.5 g/kg IV q4-6h.
- ▶ If diuresis fails to develop within 60 minutes, cautiously administer an additional 0.25-0.5 g/kg IV (slow bolus over 10-20 minutes) of 20%-25% solution.

Key Points

- ▶ Should only be administered when patients with acute kidney injury remain oliguric after complete rehydration
- ▶ Contraindicated in cases of ethylene glycol poisoning because of the preexisting hyperosmolar state
- ▶ Dose can be repeated once if initial administration fails to increase urine output.
 - Further administration of mannitol is contraindicated if diuresis fails to develop.
- ▶ *In dogs*: Short-lived impairment of platelet function may develop after mannitol administration.¹³
- ▶ Also see **General Comments**.

For acute glaucoma¹⁴

Dose (dogs, cats) → 0.5-1 g/kg IV (slow bolus over 10-20 minutes) of 20% solution

Key Points

- ▶ Mannitol use is indicated in patients with acute glaucoma that is refractory to topical medication.¹⁴
- ▶ Should be used only after correcting for fluid, electrolyte, and/or acid-base balance and if the patient is not anuric¹⁴
- ▶ Withholding water for 1 to 4 hours after treatment is recommended.
- ▶ Effect begins in 20 to 30 minutes and can persist for several hours.¹⁴
- ▶ Also see **General Comments**.

For increased CSF pressure/cerebral edema¹⁴

Dose (dogs, cats) → 0.5 g/kg IV (20% solution; slow bolus over 15-20 minutes)

- ▶ If required, repeat bolus at 0.5 g/kg IV q6-8h.

Key Points

- ▶ Should only be used after correcting for fluid, electrolyte, and/or acid-base balance and if the patient is not anuric¹⁵
- ▶ Contraindicated if ongoing intracranial hemorrhage is suspected
- ▶ Effect begins within 30 minutes and can persist for 6 hours.¹⁵
- ▶ Also see **General Comments**.

General Comments (Mannitol)

- ▶ Fluid, electrolyte, and acid-base status must be carefully monitored.^{12,14}
- ▶ Contraindications include CHF, fluid overload, and pulmonary edema.^{12,14}

Thiazide Diuretics

Thiazide diuretics, such as hydrochlorothiazide and chlorothiazide, inhibit the Na-Cl cotransport system in the early distal tubule. The consequences are similar to the action of loop diuretics in terms of increased sodium, chloride, potassium, and water excretion; however, because the effect is more distal, thiazides are not as powerful as loop diuretics and calcium excretion is reduced.

Hydrochlorothiazide

Formulations → Oral tablets: 12.5, 25, 50 mg; oral capsules: 12.5 mg; many combined formulations with other drugs

For prevention of recurrent calcium oxalate urolithiasis^{16,17}

Dose (dogs) → 2 mg/kg PO q12h

Dose (cats) → 1 mg/kg PO q12h

Key Points

- ▶ Used in conjunction with appropriate diets and medications to reduce calcium excretion and relative supersaturation of urine for calcium oxalate^{16,17}
- ▶ Usually only added to a preventive regimen if uroliths recur, even with appropriate dietary management and potassium citrate supplementation¹⁶
- ▶ Patients receiving long-term hydrochlorothiazide treatment should be monitored for hypercalcemia.
 - *In cats*: Extreme dehydration can occur when cats receive long-term diuretic therapy.¹⁷

For pulmonary edema & ascites associated with CHF¹⁸

Dose (dogs) → 1-4 mg/kg PO q12h

Dose (cats) → 1-2 mg/kg PO q12h

Key Point

- ▶ Doses should be started at the lower dose range and gradually increased until desired clinical outcome is achieved.¹⁸

For ascites secondary to liver disease¹⁹

Dose (dogs, cats) → 0.5-1 mg/kg PO q12h (in 1:1 combination with spironolactone)

Key Points

- ▶ Dose based on spironolactone content of the combined drug¹⁹
- ▶ The combination of spironolactone with hydrochlorothiazide reduces renal potassium loss.²⁰
- ▶ Doses should be started at the lower dose range and gradually increased until desired clinical outcome is achieved.¹⁹

For systemic hypertension²¹

Dose (dogs only) → 1 mg/kg PO q12-24h

Key Points

- ▶ Used as a second-choice/adjunct agent after ACE inhibitors and calcium-channel-blocking agents have been implemented
- ▶ Hydrochlorothiazide combined with spironolactone reduces renal potassium loss.

For nephrogenic diabetes insipidus²²

Dose (dogs only) → 2 mg/kg PO q12h

Key Point

- ▶ Should be combined with a low-sodium diet to reduce urine volume

Chlorothiazide

Formulations → Tablets: 250, 500 mg; oral suspension: 50 mg/mL; lyophilized powder for injection: 500 mg

For diuretic & nephrogenic diabetes insipidus²²

Dose (dogs, cats) → 20-40 mg/kg PO q12h

Key Point

- ▶ Should be combined with a low-sodium diet to reduce urine volume

General Comments (Thiazide Diuretics)

- ▶ Doses should be adjusted based on individual patient response.
- ▶ Renal function and electrolytes, especially potassium, should be monitored to prevent prerenal azotemia.
- ▶ Furosemide can potentiate the hypotensive effects of ACE inhibitors.
- ▶ Severe hypokalemia and hyponatremia can develop during treatment, particularly in patients with reduced food and water intake.
- ▶ Extreme dehydration and hypokalemia can occur when cats receive long-term diuretics; careful monitoring is required.
 - *In cats:* Ototoxicity and hearing loss can occur at high doses.

Aldosterone Antagonist

The aldosterone antagonist spironolactone inhibits the action of aldosterone on the collecting duct. Aldosterone normally stimulates Na/K-ATPase pumps on the basolateral membrane of the collecting duct cells; without this action, the tendency of potassium to passively diffuse into the tubular lumen is reduced. Thus, spironolactone can be used in combination with either loop or thiazide diuretics to reduce renal potassium excretion.

Spironolactone

Formulations → Tablets: 10, 40, 80 mg; chewable tablets: 10, 50, 100 mg; benazepril–spironolactone tablets: 2.5 mg/20 mg, 5 mg/40 mg, 10 mg/80 mg

ACE = angiotensin-converting enzyme
CHF = congestive heart failure

For adjunct treatment of CHF, ascites, & hypertension^{7,19,23,24}

Dose (dogs) → 1-2 mg PO q24h

Dose (anecdotal; cats) → Not well documented but most likely same dose as used for dogs⁷

Key Points

- ▶ Reduces potassium wasting caused by loop and thiazide diuretics
- ▶ Adjunct treatment only^{23,24}
- ▶ Additional benefit of adding spironolactone to a heart failure regimen for dogs and cats beyond the potassium-sparing effect is not clear.
- ▶ Ineffective as a sole agent to treat hypertension
- ▶ Used in combination with furosemide, ACE inhibitors, pimobendan, and amlodipine; spironolactone may increase survival time in dogs with CHF, although the positive effects appear unrelated to any diuretic action.²⁵

For fluid accumulation in glomerular disease^{7,23,24}

Dose (dogs) → 1-2 mg PO q24h

Dose (anecdotal; cats) → Not well documented but most likely same dose as used for dogs⁷

Key Points

- ▶ Reduces potassium wasting caused by loop and thiazide diuretics
- ▶ Adjunct treatment only^{23,24}

For hypokalemia associated with hyperaldosteronism in cats²⁶

Dose (cats only) → 1-2 mg/kg PO q12h

Key Points

- ▶ Spironolactone should be given in conjunction with oral potassium supplementation to control hypokalemia.
- ▶ Treatment usually must be continued for life.
- ▶ Concurrent treatment for hypertension with amlodipine or β blockers is usually indicated in patients with this condition.
- ▶ Severe facial ulcerative dermatitis can develop in cats treated with spironolactone.²⁷

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