

UpCard[®]-CA1

(torsemide oral solution)

Couch cuddles

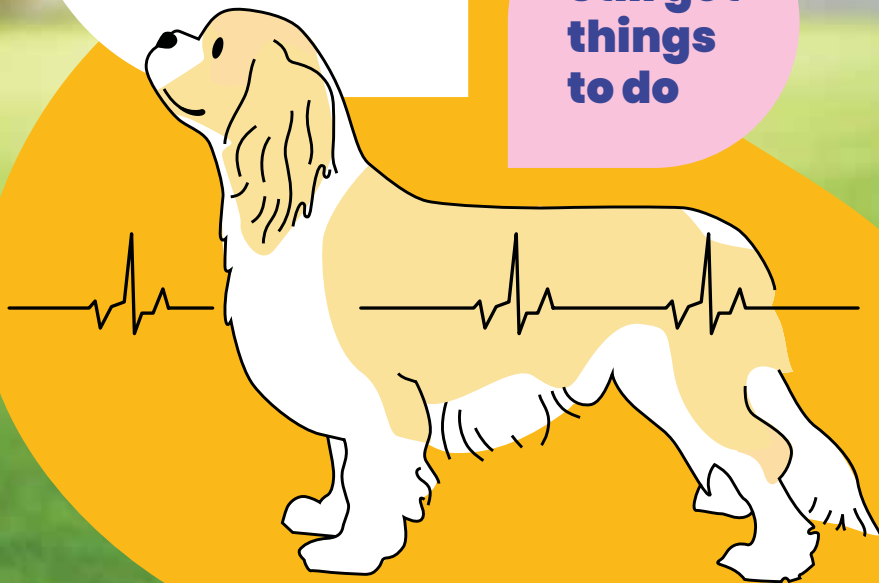
Sunbathing

Belly rubadubs

Squirrelveillance

**Advanced
Diuresis with
Once Daily Dosing
for Dogs with CHF
due to MMVD**

**Still got
things
to do**



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For full prescribing information, see page 10.

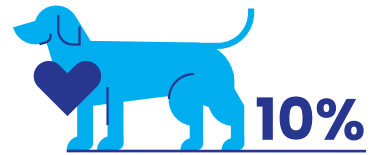


UpCard-CA1
(torsemide oral solution)

Innovative new option for managing CHF.

UpCard-CA1 contains torsemide and is a potent loop diuretic conditionally approved by the FDA for the management of pulmonary edema in dogs with congestive heart failure (CHF) caused by myxomatous mitral valve disease (MMVD).¹

Congestive heart failure is a complex clinical syndrome.



Approximately 10% of dogs visiting general veterinary practices have heart disease.²

Myxomatous mitral valve disease (MMVD) is the most common cause, accounting for approximately 75% of cases.²



TRICUSPID

While myxomatous mitral valve disease affects the left atrioventricular (mitral) valve, the tricuspid valve also has myxomatous disease in 30% of the cases.²

Diuretics are a cornerstone of CHF treatment.

Treatment for CHF typically involves diuretics to reduce fluid buildup, as well as medications to improve heart function and reduce blood pressure.³

Loop diuretics, such as furosemide, are often prescribed to reduce intravascular fluid volume, which helps decrease preload, venous/capillary pressures, and relieve clinical signs of volume overload.⁴

The need for multiple daily doses, however, can negatively impact owner compliance and, therefore, patient outcomes.

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Veterinarians need new tools to manage diuretic resistance.

As CHF progresses, some dogs may develop diuretic resistance, where they stop responding adequately to their prescribed dose.⁴ It often manifests as persistent or recurrent signs of CHF despite therapy.⁴

To overcome diuretic resistance, options include progressively increasing the dose, combining different types of diuretics, or adding medications like ACE inhibitors to counteract RAAS activation.⁴

Now, a new FDA conditionally approved potent diuretic option, torsemide, may also help combat resistance. Torsemide has been shown to have a longer half-life, higher potency, and longer duration of action compared to furosemide, the most commonly used loop diuretic.¹

Veterinarians need an effective diuretic that also aids in compliance.

Main Barriers for Current Loop Diuretics⁵

Requires multiple daily doses	73%
Several side effects	62%
Difficult administration for pet owners	51%
Higher likelihood to develop diuretic resistance	44%
Low treatment compliance	38%

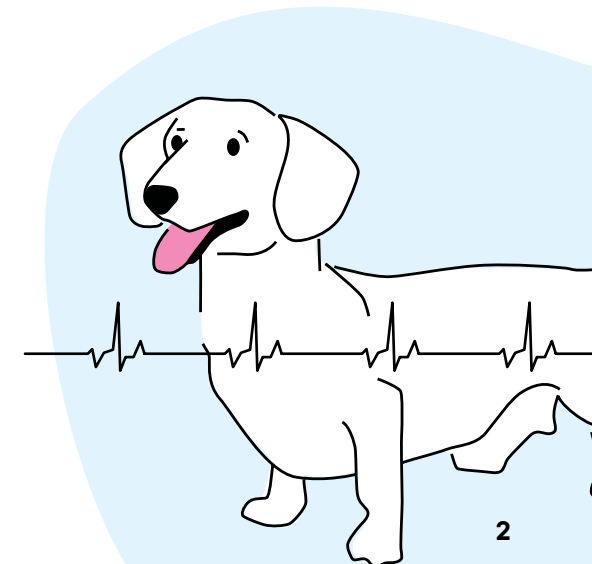
Most Important Treatment Selection Factors⁵

Improvement in quality of life for patient and owner	85%
Favorable safety profile	62%
High treatment compliance	60%
Efficacy in treating fluid retention	60%
Convenient administration for pet owners	59%

In a survey, the main barriers to using current loop diuretics were mostly associated with difficulty in pet owners complying with treatment due to challenging administration and multiple daily dosing.⁵

Veterinarians stated that the most important factors when determining the choice of a CHF treatment included safety, convenience, compliance, and efficacy.⁵

This drug has not been evaluated in dogs used for breeding, pregnant or lactating bitches. The most common side effects seen in dogs with CHF due to MMVD while taking UpCard-CA1 are cough, dyspnea, pulmonary edema, and cardiac arrest. Adverse reactions not related to disease progression in dogs receiving UpCard-CA1 include polyuria and polydipsia, renal insufficiency, increased BUN and serum creatinine, urinary incontinence, hypokalemia, hypochloremia, hypercalcemia, hypomagnesemia, diarrhea, vomiting, and inappetence. **For full prescribing information, see page 10.**

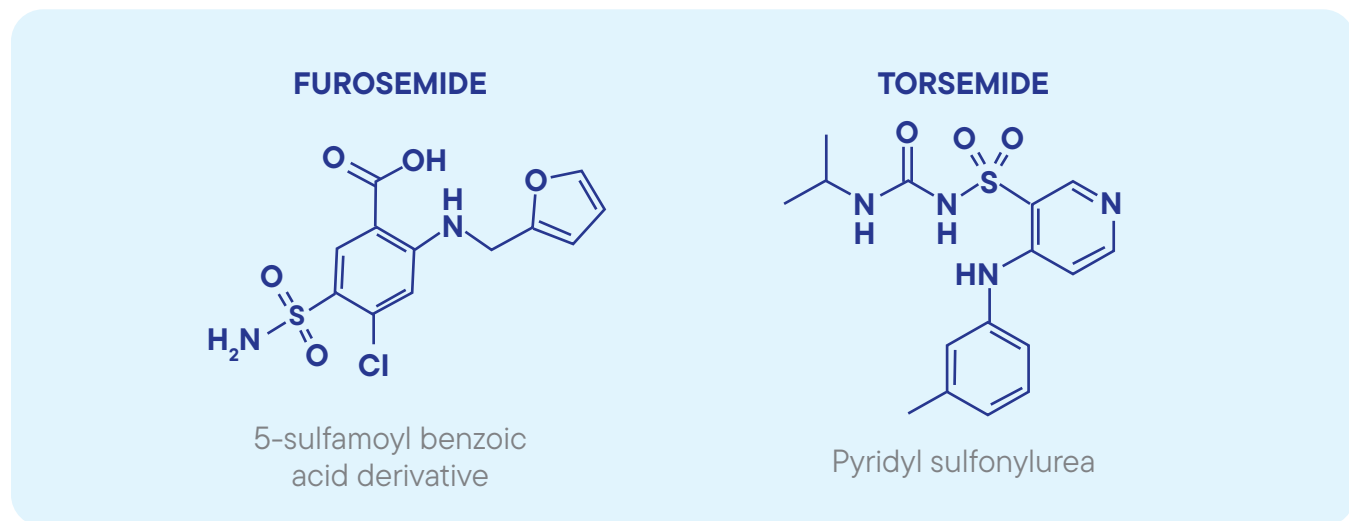


UpCard-CA1 is structurally different.

UpCard-CA1
(torsemide oral solution)

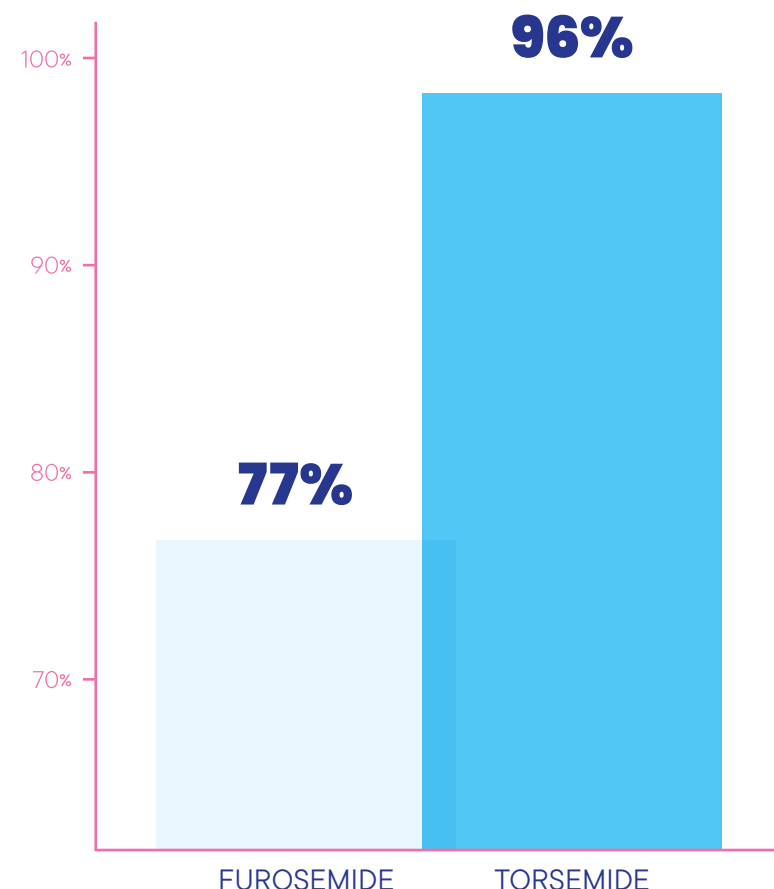
The active ingredient in UpCard-CA1 is torsemide, a potent loop diuretic of the pyridyl sulfonylurea class.⁶

Torsemide has a chemical structure different from furosemide and possesses a longer half-life, higher bioavailability, and greater potency and duration of diuretic action.³



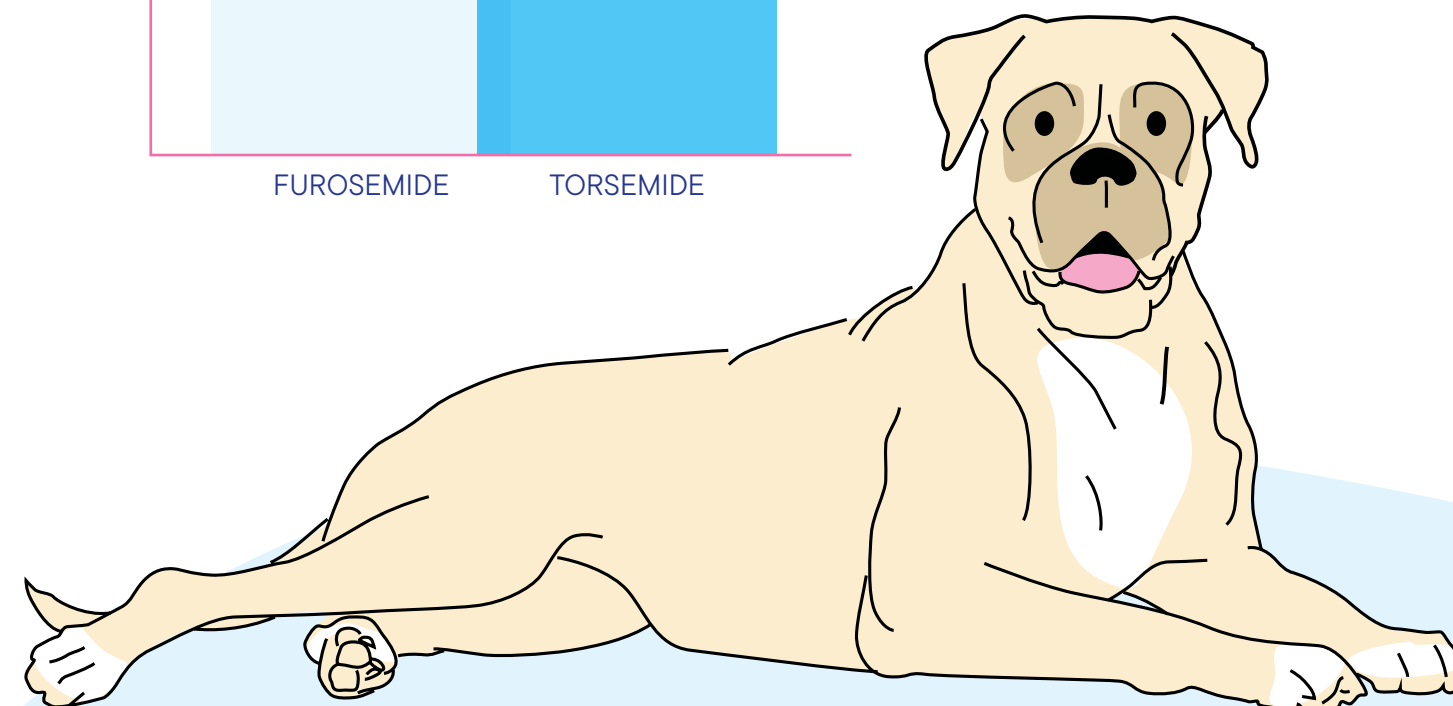
Bioavailability⁴

Bioavailability of Torsemide Compared to Furosemide



Torsemide tablets and solution behave similarly.

A pharmacokinetic (PK) study demonstrated similar bioavailability between the tablet formulation of torsemide used in earlier studies and the oral solution of UpCard-CA1!



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Half-life⁴

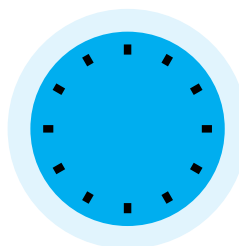
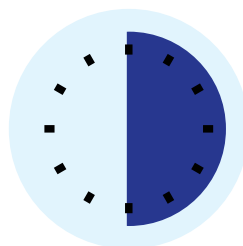
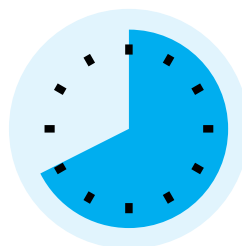
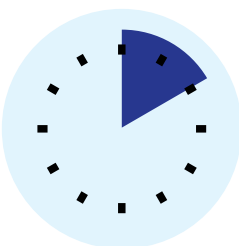
Duration⁴

FUROSEMIDE

TORSEMIDE

FUROSEMIDE

TORSEMIDE



1-2 HRS

8 HRS

6 HRS

12 HRS

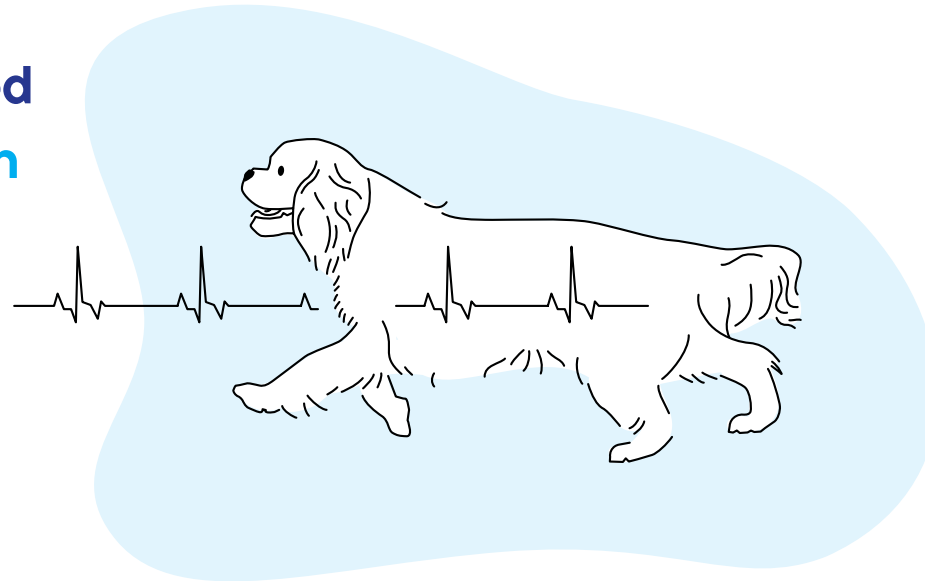
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UpCard®-CA1
(torsemide oral solution)

Feel empowered with potent diuresis.

In studies, a single daily dose of UpCard-CA1 was shown to have a reasonable expectation of efficacy and was non-inferior in comparison to furosemide for managing pulmonary edema in dogs with CHF caused by MMVD.¹

Torsemide was associated with a two-fold reduction in the risk of reaching composite cardiac endpoint compared to furosemide.⁴



UpCard-CA1 increased urine output.

Single oral dose.¹

0.05-0.10 mg/kg dose

50% increase

> The greatest mean percentage was observed at 5 mg/kg.

Doses between 0.15 and 4.5 mg/kg/day administered over 5 days.¹

0.15 mg/kg dose

33-50% increase

4.5 mg/kg dose

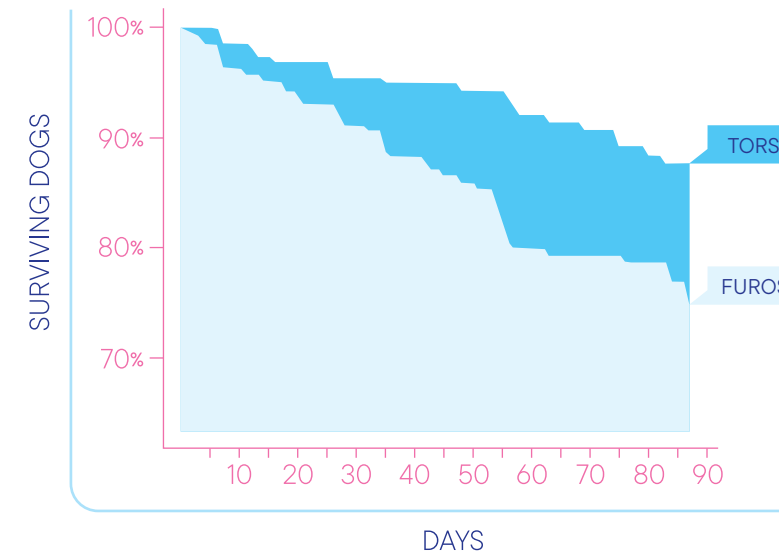
181-328% increase

> At a dose of **0.75 mg/kg**, urine output was not significantly different than 1.5 mg/kg and 4.5 mg/kg.

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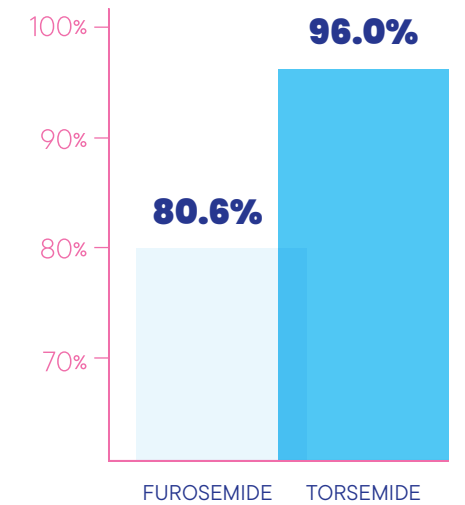
Results of a multisite European field study.¹

Cardiac Endpoint Comparison



Kaplan-Meier plot of percentage of dogs that have not yet met the composite cardiac endpoint as a function of time, in 366 dogs with congestive heart failure attributable to degenerative mitral valve disease and treated with either torsemide (n = 180) or furosemide (n = 186). The composite cardiac endpoint was a composite of spontaneous cardiac death, euthanasia for heart failure, and congestive heart failure class worsening. As compared to furosemide, torsemide was associated with a 2-fold reduction in the risk of reaching the endpoint (adjusted HR = 0.47; 95% CI 0.27-0.82; P = 0.0077).

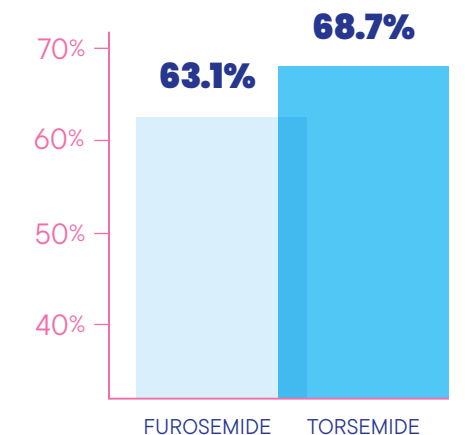
Success Rates¹



Primary endpoint was response rate at Day 84 with a successful response to treatment if pulmonary edema and/or pleural effusion or ascites had not worsened compared to Day 0.

Efficacy of Torsemide Tablets Compared to Furosemide

In a field study using torsemide (torasemide tablets), 132 dogs with congestive heart failure were included in the effectiveness analysis.¹



Torasemide is the EU spelling of Torsemide.

The most common side effects seen in dogs with CHF due to MMVD while taking UpCard-CA1 are cough, dyspnea, pulmonary edema, and cardiac arrest. Adverse reactions not related to disease progression in dogs receiving UpCard-CA1 include polyuria and polydipsia, renal insufficiency, increased BUN and serum creatinine, urinary incontinence, hypokalemia, hypochloremia, hypercalcemia, hypomagnesemia, diarrhea, vomiting, and inappetence. **For full prescribing information, see page 10.**

Prescribe confidently.

Torsemide (also known as torasemide) tablets have been approved for use as a veterinary diuretic in the European Union (EU) since 2015.



In a six-month study, UpCard-CA1 was well tolerated in healthy dogs even when given at 1.5 times (0.66 mg/kg) the maximum conditionally approved dose.¹

- No mortality, moribundity, or serious adverse reactions observed
- Clinical observations included reduced fecal amounts, lower body condition scores, inappetence, lethargy, and dehydration
- These clinical observations were not unusual for loop diuretics in healthy dogs

NOTE: Because loop diuretics have a well-characterized safety profile and can cause serious adverse events at high doses, the safety of UpCard-CA1 was evaluated using doses lower than the standard 1X, 3X, and 5X treatment groups.¹

In a 13-week study, results showed that the drug has an adequate margin of safety when administered at a daily dose of 0.1 mg/kg.¹

- The clinical pathology, gross necropsy, and histopathology findings were related to the expected pharmacological effects of a loop diuretic

While there were similar responses between torsemide and furosemide tablets in an efficacy study of 176 dogs, there was an increased frequency of renal adverse events with torsemide-treated dogs.¹



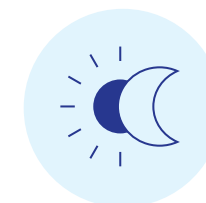
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Innovation meets compliance.

When managing the complexity of giving pills two to three times per day, choosing UpCard-CA1 gives veterinarians and their clients the benefit of a once daily, easily titratable oral solution.



No splitting or crushing of pills



Once daily administration

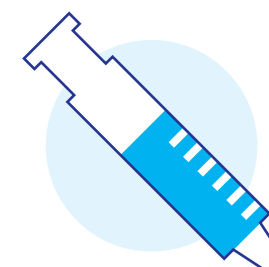


In a study with 319 dogs, torsemide achieved higher owner compliance³

Precise, consistent dosing.

UpCard-CA1 should be administered at 0.05 to 0.2 mg/lb. (0.11 to 0.44 mg/kg) of body weight once daily.⁶

With UpCard-CA1, there's no over or underdosing.



Comparison of dosing a dog weighing 18 lbs. – a common weight for dogs with CHF.⁷

Torsemide 0.9 mg – available in a precise dose of 0.45 mL of UpCard-CA1

Furosemide 16.36 mg – available in either a 12.5 mg tablet or a 20 mg tablet

It's easy to make the switch.

UpCard-CA1 can be used with common CHF therapies.

UpCard-CA1 is conditionally approved by the FDA for use with concurrent therapy with pimobendan, spironolactone, and an angiotensin converting enzyme (ACE) inhibitor for the management of pulmonary edema in dogs with congestive heart failure caused by myxomatous mitral valve disease (MMVD).¹

There is no washout period required when switching to UpCard-CA1 from another diuretic.¹

Potent new torsemide loop diuretic for dogs with CHF.



Potent diuresis

Studies show torsemide is associated with a two-fold reduction in risk of reaching cardiac endpoint vs. furosemide and higher success rates (96% vs. 81%).^{1,4}



Once daily dosing

The 8-hour half-life and 12-hour duration of action of torsemide allows for convenient once daily administration, improving owner compliance.^{3,4}



Easy titration

No over or underdosing. The oral solution allows for precise and consistent dosing compared to splitting tablets.



Structurally different

Torsemide has a longer half-life, higher bioavailability, greater potency, and longer duration of action compared to furosemide.³

UpCard-CA1 is brought to you by Vetoquinol, the same company that brings you other innovative medications like Clevor[®] (ropinirole ophthalmic solution) and is backed by our Satisfaction Guarantee.

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SOURCES

¹UpCard-CA1 Freedom of Information summary.

²Keene BW, et al. ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs. *J Vet Intern Med.* 2019;33:1127-1140.

³Besche B, et al. Efficacy of oral torasemide in dogs with degenerative mitral valve disease and new onset congestive heart failure: The CARPODIEM study. *J Vet Intern Med.* 2020;34(5):1746-1758.

⁴Chetboul V, et al. Short-Term Efficacy and Safety of Torasemide and Furosemide in 366 Dogs with Degenerative Mitral Valve Disease: The TEST Study. *J Vet Intern Med.* 2017;31(6):1629-1642.

⁵UpCard-CA1 Market study.

⁶UpCard-CA1 Product label.

⁷Data on file.

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