There is a new couple in town

Spironolactone is the essential addition to an ACE inhibitor.

Spironolactone + Benazepril HCl

Unique Combination | Greater efficacy compared to benazepril alone | Actives recommended by ACVIM guidelines | Chewable tablets for dogs

For use in dogs only
Choose Cardalis™ over ACEi alone

A unique combination for more complete RAAS blockade...³,⁴,⁵,⁶

CARDALIS™ chewable tablets provide half of the ACVIM quad-therapy recommendation for congestive heart failure.

Cardiovascular remodeling including fibrosis

Congestive Heart Failure

RAAS activation

Angiotensin II

Aldosterone

Spironolactone

Benazepril

Vasoconstriction

Loop diuretics

ACE inhibitors (e.g., Benazepril)

Pimobendan*

Spironolactone

RAAS: Complete blockade thanks to combination ³, ⁴, ⁵, ⁶

RAAS: Activation ⁷, ⁸

RAAS: No effect ⁹


*In 2019, the ACVIM published new guidelines recommending a quadruple therapy approach for the treatment of CHF in dogs. The safety and efficacy of CARDALIS™ has not been investigated with pimobendan.
A unique combination for greater efficacy... 

569 dogs enrolled in the study

Effectiveness assessed on 414 dogs at Day 360

Percentage of dogs that completed the study

Fewer treatment failures** in the CARDALIS™ group compared to the benazepril group (p=0.04)

Percentage of treatment failures at each time point
*** significant difference between groups (p < 0.05)

Early, greater and sustained benefit in the CARDALIS™ group versus the benazepril group

...and safe when used with concomitant therapy (e.g., furosemide)¹

Renal parameters mean values:
• remained within the reference range
• did not change significantly over the 12-month study duration

**Treatment failure = occurrence of cardiac death/euthanasia due to cardiac cause or worsening/occurrence of cardiac signs

Improvement of clinical signs appears faster with CARDALIS™ (significant difference p<0.05).

A faster improvement in clinical signs has been observed compared to benazepril alone.

<table>
<thead>
<tr>
<th>Activity</th>
<th>45 days sooner</th>
<th>24 days sooner</th>
<th>36 days sooner</th>
<th>18 days sooner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough at night</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough during normal activities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough during exercise</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Longer median time to failure for dogs in the CARDALIS™ group compared to the benazepril group.

Improvement of heart failure symptoms: difference between the time to improvement observed in dogs treated with benazepril alone versus dogs treated with CARDALIS™ (significant difference p<0.05).
Improved patient acceptance solves owner compliance challenges.

Voluntary acceptance in 233 dogs receiving CARDALIS™

3 half-scored, chewable sizes to fit all weight ranges

Recommended CARDALIS™ Dosing Regimen by Body Weight

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>lb</th>
<th>kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.5 - 10.9</td>
<td>2.5 - 5</td>
<td>5 - 10</td>
</tr>
<tr>
<td>11 - 21.9</td>
<td>5 - 10</td>
<td>10 - 20</td>
</tr>
<tr>
<td>22 - 43.9</td>
<td>10 - 20</td>
<td>20 - 40</td>
</tr>
<tr>
<td>44 - 87.9</td>
<td>20 - 40</td>
<td>40 - 60</td>
</tr>
<tr>
<td>88 - 131.9</td>
<td>40 - 60</td>
<td>60 - 80</td>
</tr>
<tr>
<td>132 - 176</td>
<td>60 - 80</td>
<td></td>
</tr>
</tbody>
</table>

- **CARDALIS™ 20/2.5**
  - 20 mg Spironolactone
  - 2.5 mg Benazepril HCl

- **CARDALIS™ 40/5**
  - 40 mg Spironolactone
  - 5 mg Benazepril HCl

- **CARDALIS™ 80/10**
  - 80 mg Spironolactone
  - 10 mg Benazepril HCl

Ceva services

For veterinarians

Ceva Connect cevaconnect.com

For pet owners

Resting Respiratory Rate App available on iOS and Android

Easy monitoring tool
Cardalis™ trademark is the property of Ceva Santé Animale S.A.

Cardalis chewable tablets for dogs are available in 3 sizes of oblong half scored flavored tablets:

<table>
<thead>
<tr>
<th>Size</th>
<th>Active Ingredient</th>
<th>Spironolactone</th>
<th>Benazepril Hydrochloride</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mg/2.5 mg</td>
<td>20 mg spironolactone and 2.5 mg benazepril hydrochloride</td>
<td>20 mg</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>40 mg/5 mg</td>
<td>40 mg spironolactone and 5 mg benazepril hydrochloride</td>
<td>40 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>80 mg/10 mg</td>
<td>80 mg spironolactone and 10 mg benazepril hydrochloride</td>
<td>80 mg</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

**Dosage and Administration:**

Cardalis should be administered after a complete and thorough examination of the dog. Administration should be based on clinical experience and the scientific literature. Cardalis chewable tablets should be used as directed. Cardalis should be used at the lowest effective dosage for the shortest duration consistent with the clinical response to the drug.

**Indications:**

Cardalis is indicated for concurrent therapy with Candesartan cilexetil and spironolactone in the treatment of dogs with left ventricular hypertrophy caused by systemic hypertension. Cardalis is indicated for concurrent therapy with Candesartan cilexetil and spironolactone in the treatment of dogs with left ventricular hypertrophy caused by systemic hypertension.

**Contraindications:**

Cardalis is contraindicated in dogs with a history of hypersensitivity or adverse reactions to any component of the formulation.

**Precautions:**

Cardalis is not recommended for use in pregnant, lactating, or breeding dogs. Cardalis is not recommended for use in dogs with hepatic insufficiency.

**Human Warnings:**

Cardalis is not recommended for use in humans. Keep this and all medications out of the reach of children. Consult a physician in case of ingestion by a human.

**Overdosage:**

Overdosage is unlikely to occur in dogs receiving the recommended dose. In the event of an overdose, supportive care should be provided. If spironolactone is involved, monitoring of potassium levels should be performed. If benazepril is involved, blood pressure should be monitored. If both are involved, supportive care should be provided.

**Adverse Reactions:**

The following adverse events were seen in fewer than 5% of the study animals, in decreasing order: urinal abnormalities, fluid in abdomen, ataxia, weight loss, diarthrosis, dyspnea, anorexia, diarrhea, dehydration, and epistaxis. The following adverse events were seen in 5% or more of the study animals, in decreasing order: urinal abnormalities, fluid in abdomen, ataxia, weight loss, diarthrosis, dyspnea, anorexia, diarrhea, dehydration, and epistaxis.

**Pharmacokinetics:**

Spironolactone is extensively metabolized in humans and experimental animals, with species differences in the bioavailability of benazeprilat. In humans, the bioavailability of benazeprilat after oral administration is estimated to be less than 7%. After oral administration of spironolactone to the dog, 70% of the dose is recovered in feces and 20% in the urine.

**Effectiveness:**

The effectiveness of Cardalis was evaluated in a well-controlled U.S. multi-center, masked, randomized, 180-day field study in owner-owned dogs. The study evaluated the effectiveness of Cardalis compared to benazepril hydrochloride and spironolactone in the treatment of dogs with left ventricular hypertrophy caused by systemic hypertension. Cardalis significantly reduced blood pressure and improved heart rate in dogs with left ventricular hypertrophy compared to benazepril hydrochloride and spironolactone alone.

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