1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prilactone Next 10 mg chewable tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains
Active substance:
Spironolactone.....10 mg

Excipient(s):

Qualitative composition of excipients and other constituents
Artificial chicken flavour
Yeast
Crospovidone type A
Sodium lauryl sulfate
Maltodextrine
Magnesium stearate
Silica, colloidal anhydrous
Silicified microcrystalline cellulose
Lactose monohydrate

Oblong scored beige chewable tablet. The tablets can be divided into two equal parts.

3. CLINICAL INFORMATION

3.1 Target species

Dogs

3.2 Indications for use for each target species

For use in combination with standard therapy (including diuretic support, where necessary) for the treatment of congestive heart failure caused by degenerative mitral valve disease in dogs.

3.3 Contraindications

Do not use in animals used for or intended for use in breeding.
Do not use in dogs suffering from hypoadrenocorticism, hyperkalaemia or hyponatraemia.
Do not administer spironolactone in conjunction with NSAIDs to dogs with renal insufficiency.
Do not use in cases of hypersensitivity to spironolactone or any of the excipients.
See section 3.7.

3.4 Special warnings

None

3.5 Special precautions for use

Special precautions for safe use in the target species:

Kidney function and plasma potassium levels should be evaluated before initiating combined treatment with spironolactone and ACE inhibitors. Unlike in humans, an increased incidence of hyperkalaemia was not observed in clinical trials performed in dogs with this combination. However, in dogs with renal impairment, regular monitoring of renal function and plasma potassium levels is recommended as there may be an increased risk of hyperkalaemia.

Dogs treated concomitantly with spironolactone and NSAIDs should be correctly hydrated. Monitoring of their renal function and plasma potassium levels is recommended before initiation and during treatment with combined therapy (see 3.3).
As spironolactone has an antiandrogenic effect, it is not recommended to administer the product to growing dogs.
As spironolactone undergoes extensive hepatic biotransformation, care should be taken when using the product to treat dogs with hepatic dysfunction.
The chewable tablets are flavoured. In order to avoid accidental ingestion, store these tablets out of the reach of animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

The product may cause skin sensitisation. Persons known to be allergic to spironolactone or other components of the final formulation should not handle this product.

Handle this product with great care to avoid unnecessary exposure, taking all recommended precautions.

Wash hands after use.

If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs :

Very common (>1 animal / 10 animals treated):	Prostatic atrophy[1]
Common (1 to 10 animals / 100 animals treated):	Vomiting, Diarrhoea

[1]in entire male dogs, reversible

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the product has not been assessed in pregnant and lactating bitches.

Pregnancy and lactation:

Laboratory studies in laboratory animals have shown evidence of developmental toxicity.
Do not use during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

In clinical studies, the product was co-administered with ACE-inhibitors, furosemide and pimobendan without evidence of associated adverse reactions.
Spironolactone decreases digoxin elimination and hence raises digoxin plasma concentration. As the therapeutic index for digoxin is very narrow, it is advisable to monitor closely dogs receiving both digoxin and spironolactone.
The administration of either deoxycorticosterone or NSAIDs with spironolactone may lead to a moderate reduction of the natriuretic effects (reduction of urinary sodium excretion) of spironolactone.
Concomitant administration of spironolactone with ACE-inhibitors and other potassium-sparing drugs (as angiotensin receptor blockers, ß-blockers, calcium channels blockers, etc..) may potentially lead to hyperkalaemia (see 3.5).
Spironolactone may cause both induction and inhibition of cytochrome P450 enzymes and could therefore affect the metabolism of other drugs utilizing these metabolic pathways.

3.9 Administration routes and dosage

Oral use.
2 mg of spironolactone per kg of body weight once daily, i.e. 1 tablet per 5 kg of body weight. The product should be administered with meal.

Dog weight (kg)	Prilactone Next 10 mg Number of tablets per day
> 1 to 2.5	½
> 2.5 to 5	1
> 5 to 7.5	1 ½
> 7.5 to 10	2

To ensure a correct dosage, body weight should be determined as accurately as possible.

The tablets are flavoured. If the dog does not accept the tablet from hand or bowl, then the tablets may be mixed with a small amount of food offered prior to the main meal, or administered directly into the mouth after feeding.

3.10 Symptoms of overdose (and where applicable, emergency procedures, and antidotes)

After administration of up to 5 times the recommended dose (10 mg/kg) to healthy dogs, dose-dependent adverse effects were noted, see section 3.6.
In case of an accidental massive ingestion by a dog, there is no specific antidote or treatment. It is therefore recommended to induce vomiting, lavage the stomach (depending on risk assessment) and monitor electrolytes. Symptomatic treatment, e.g., fluid therapy, should be provided.

3.11. Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATC vet code:

QC03DA01

4.2 Pharmacodynamics

Spironolactone and its active metabolites (including 7α-thiomethyl-spironolactone and canrenone) act as specific antagonists of aldosterone, and exert their effects by binding competitively to the mineralocorticoid receptor located in the kidneys, heart and blood vessels.
Spironolactone is a natriuretic drug (historically described as a soft diuretic). In the kidney, spironolactone inhibits the aldosterone-induced sodium retention leading to increase in sodium and subsequently water excretion, and potassium retention. The renal effects of spironolactone and its metabolites lead to a decrease in extracellular volume and consequently in a decrease of cardiac preload and left atrial pressure. The result is an improvement in heart function.
In the cardiovascular system, spironolactone prevents the detrimental effects of aldosterone. Although the precise mechanism of action is not yet clearly defined, aldosterone promotes myocardial fibrosis, myocardial and vascular remodelling and endothelial dysfunction.
In experimental models in dogs, it was shown that long term therapy with an aldosterone antagonist prevents progressive left ventricle dysfunction and attenuates left ventricle remodelling in dogs with chronic heart failure.
When used in combination with ACE-inhibitors, spironolactone may counteract the effects of "aldosterone escape".
A slight increase in aldosterone blood levels may be observed in animals on treatment. This is thought to be due to activation of feedback mechanisms without adverse clinical consequence. There may be a dose related hypertrophy of the adrenal zona glomerulosa at high dose rates.

4.3 Pharmacokinetics

The pharmacokinetics of spironolactone are based on its metabolites, as the parent compound is rapidly metabolised.
Absorption
In dogs, oral bioavailability of spironolactone as measured by canrenone AUCs was 83% relative to the iv route. It has been shown that feeding significantly increases the oral bioavailability of all measured metabolites resulting from dosing dogs with spironolactone. After multiple oral doses of 2 mg spironolactone per kg for 5 consecutive days, steady-state conditions are reached by day 3 and only a slight accumulation of canrenone is observed. After oral administration of spironolactone in dogs at 2 mg/kg, a mean Cmax of 41 ng/mL is achieved for the primary metabolites, canrenone, after 4 hours.
Distribution
The mean apparent volume of distribution during elimination phase after oral dosing in dogs was 41 L/kg for canrenone.
The mean residence time of the metabolites ranges from 11 hours.
The protein binding is about 90%.
Metabolism
Spironolactone is rapidly and completely metabolised by the liver into its active metabolites, canrenone, 7α-thiomethyl-spironolactone and 6β-hydroxy-7α-thiomethyl-spironolactone, which are the primary metabolites in the dog.
Elimination
Spironolactone is mainly excreted via its metabolites. Plasma clearance of canrenone is 3 L/h/kg for canrenone, in dogs. After oral administration of radiolabelled spironolactone to the dog, 66 % of the dose is recovered in faeces and 12 % in the urine. 74% of the dose is excreted within 48 hours

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf-life after first opening the immediate packaging: 24 hours.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions.
Store in the original package.
Any part-used tablet should be returned to the opened blister and used within 24 hours.

5.4 Nature and composition of immediate packaging

(PA-AL-PVC – aluminium heat sealed) containing 10 tablets per blister
Cardboard box of 10 tablets containing 1 blister of 10 tablets
Cardboard box of 20 tablets containing 2 blisters of 10 tablets
Cardboard box of 30 tablets containing 3 blisters of 10 tablets
Cardboard box of 60 tablets containing 6 blisters of 10 tablets
Cardboard box of 100 tablets containing 10 blisters of 10 tablets
Cardboard box of 180 tablets containing 18 blisters of 10 tablets

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Ceva Santé Animale

7. MARKETING AUTHORISATION NUMBER(S)

VPA10815/035/001

8. DATE OF FIRST AUTHORISATION

22/04/2016

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

23/07/2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
Detailed information on this veterinary medicinal product is available in the Union Product Database (http://medicines.health.europa.eu/veterinary)