ANNEXE I

SUMMARY OF PRODUCT CHARACTERISTICS

Mis en forme : Police :11 pt

Mis en forme : Police :11 pt, Gras

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prilactone Next 50 mg chewable tablets for dogs
Prilactone vet 50 mg chewable tablets for dogs (FI)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains
Active substance:
Spironolactone.....50 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

~~For the full list of excipients, see section 6.1.~~

~~3. PHARMACEUTICAL FORM~~

~~Chewable tablet~~
Clover-shaped scored beige chewable tablet. The tablet can be divided into four equal parts.

34. CLINICAL ~~PARTICULARS~~INFORMATION

34.1 Target species

Dog~~s~~s

34.2 Indications for use~~, specifying the~~ 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.

34.3 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 34.7.

34.4 Special warnings ~~for each target species~~

None.

34.5 Special precautions for use

Special precautions for safe use in ~~animals~~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 34.3).

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 sensiti~~z~~sation. 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.

34.6 Adverse ~~reactions (frequency and seriousness)~~events

Dogs:

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

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Mis en forme : Police :(Par défaut) Times New Roman, Non Gras, Soulignement

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Mis en forme : Police :(Par défaut) Times New Roman, Non Gras, Soulignement

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Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman, 11 pt

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :Times New Roman, Non Gras, Soulignement

Mis en forme : Police :Times New Roman, Non Gras, Soulignement

Mis en forme : Police :Times New Roman

Mis en forme : Police :Times New Roman

treated):	

[1]in entire male dogs, reversible

~~Canine~~

~~Common~~ ~~(1 to 10 animals / 100 animals treated):~~	~~Vomiting, Diarrhoea~~

~~A reversible prostatic atrophy is often observed in entire male dogs.~~

~~Dogs:~~

~~A reversible prostatic atrophy is often observed in entire male dogs. Vomiting and diarrhoea may commonly occur.~~

~~The frequency of adverse reactions is defined using the following convention:~~

~~- very common (more than 1 in 10 animals treated displaying adverse reaction(s))~~

~~- common (more than 1 but less than 10 animals in 100 animals treated)~~

~~- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)~~

~~- rare (more than 1 but less than 10 animals in 10,000 animals treated)~~

~~- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).~~

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 ~~also the last section of~~ the package leaflet for respective contact details.

34.7 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.

~~**Pregnancy and lactation:**~~

~~Spironolactone had developmental toxicity in laboratory animals.~~
~~The safety of the product has not been assessed in pregnant and lactating bitches.~~
~~Do not use during pregnancy and lactation.~~

34.8 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 34.5).

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Mis en forme : Police :Non Italique

Mis en forme : Police :(Par défaut) Times New Roman, Gras

Mis en forme : Police :(Par défaut) Times New Roman

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 ~~Amounts to be administered and a~~Administration routes and dosage

Oral use.

2 mg of spironolactone per kg of body weight once daily, i.e. 1 tablet per 25 kg of body weight~~, by oral route~~. The product should be administered with meal.

Dog weight (kg)	Prilactone Next 50 mg Number of tablets per day
> 3.0 to 6.0	¼
> 6.0 to 12.5	½
> 12.5 to 18.0	¾
> 18.0 to 25.0	1
> 25.0 to 31.0	1 ¼
> 31.0 to 37.0	1 ½
> 37.0 to 43.0	1 ¾
> 43.0 to 50.0	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.

Instruction on how to divide the tablet: Put the tablet on an even surface, with its scored side facing down (convex face up). With the tip of the forefinger, exert slight vertical pressure on the middle of the tablet to break it along its width into halves. Then, in order to obtain quarters, exert slight pressure on the middle of one half with the forefinger to break it into two parts.

3.10 Symptoms of ~~O~~overdose (~~symptoms~~and where applicable, emergency procedures, and antidotes)~~, if necessary~~

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~~4~~.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~~1~~ Withdrawal period~~(s)~~

Not applicable.

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Mis en forme : Police :Non Italique

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman, Non souligné

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman

45. PHARMACOLOGICAL ~~PROPERTIES~~INFORMATION

~~Pharmacotherapeutic group: Aldosterone antagonist.~~

4.1 ATC vet code:

QC03DA01

45.21 Pharmacodynamics ~~properties~~

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.

45.32 Pharmacokinetics ~~particulars~~

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

Mis en forme : Police :(Par défaut) Times New Roman, Gras, Français (France)
Mis en forme : Police :(Par défaut) Times New Roman, Français (France)
Mis en forme : Police :(Par défaut) Times New Roman, Français (France)
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman

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

56. PHARMACEUTICAL PARTICULARS

~~**6.1 List of excipients**~~

~~Artificial chicken flavour~~
~~Yeast~~
~~Crospovidone type A~~
~~Sodium lauryl sulfate~~
~~Maltodextrine~~
~~Magnesium stearate~~
~~Silica, colloidal anhydrous~~
~~Silicified microcrystalline cellulose~~
~~Lactose monohydrate~~

~~6.~~12 Major incompatibilities

~~None~~ Not applicable.

56.~~23~~ Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging: 72 hours.

56.~~34.~~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 72 hours.

56.~~45~~ 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 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.

56.~~56~~ 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.

Mis en forme : Police :(Par défaut) Times New Roman

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.

~~Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.~~

6~~7~~. NAME OF THE MARKETING AUTHORISATION HOLDER

7~~8~~. MARKETING AUTHORISATION NUMBER(S)

8~~9~~. DATE OF FIRST AUTHORISATION~~/RENEWAL OF THE AUTHORISATION~~

Date of first authorisation: {DD/MM/YYYY}

9.~~10~~ DATE OF THE LAST REVISION OF THE ~~TEXT~~SUMMARY OF THE PRODUCT CHARACTERISTICS

{~~DD/MM/YYYY~~mm/yyyy}

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.(https://medicines.healthe.europa.eu/veterinary)

~~**PROHIBITION OF SALE, SUPPLY AND/OR USE**~~

~~To be completed in accordance with national requirements~~

Mis en forme : Police :(Par défaut) Times New Roman, Anglais (États-Unis)

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman, Anglais (États-Unis)

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman, Non souligné

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Gauche, Taquets de tabulation : 7,17 cm,Gauche

ANNEX III

LABELLING AND PACKAGE LEAFLET

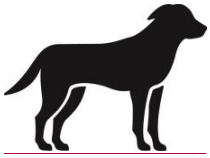
A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prilactone Next 50 mg chewable tablets ~~tablets for dogs~~
Prilactone vet 50 mg chewable tablets ~~tablets for dogs~~ (FI)
~~Spironolactone~~



2. STATEMENT OF ACTIVE SUBSTANCES

One tablet contains
Active substance:
Spironolactone.....50 mg

~~3. PHARMACEUTICAL FORM~~

~~Chewable tablet~~

34. PACKAGE SIZE

10 tablets
20 tablets
30 tablets
100 tablets
180 tablets

45. TARGET SPECIES

Dog~~s~~

56. INDICATION~~(S)~~

67. ~~METHOD AND~~ ROUTE~~(S)~~ OF ADMINISTRATION

For oral administration.

~~Read the package leaflet before use.~~

Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Police :(Par défaut) Times New Roman, Non Surlignage
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Police :(Par défaut) Times New Roman

78. WITHDRAWAL PERIODS (S)

~~9. SPECIAL WARNING(S), IF NECESSARY~~

~~Read the package leaflet before use.~~

810. EXPIRY DATE

Exp.{mm/yyyy}
~~EXP {month/year}~~
Once divided, use within 72 hours

911. SPECIAL STORAGE ~~CONDITIONS~~PRECAUTIONS

~~This veterinary medicinal product does not require any special storage conditions.~~
Store in the original package.
~~For shelf life of divided tablets: see package leaflet.~~

102. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE" ~~SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY~~

Read the package leaflet before use.
~~Disposal: read the package leaflet before use.~~

113. THE WORDS "FOR ANIMAL TREATMENT ONLY" ~~AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable~~

For animal treatment only ~~- to be supplied only on veterinary prescription.~~

124. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

135. NAME ~~AND ADDRESS~~ OF THE MARKETING AUTHORISATION HOLDER

146. MARKETING AUTHORISATION NUMBER(S)

Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait), Taquets de tabulation : 8,01 cm, Centré

Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)

Mis en forme : Police :Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)

Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)

Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)

Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)

Mis en forme : Police :(Par défaut) Times New Roman, Anglais (États-Unis)

Mis en forme : Police :(Par défaut) Times New Roman, Bordure : : (Simple, Automatique, 0,5 pt Épaisseur du trait)

Mis en forme : Police :(Par défaut) Times New Roman

157. ~~MANUFACTURER'S~~ BATCH NUMBER

Lot {number}
~~Batch:~~

Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)

~~Veterinary Medicinal product~~

~~PRILACTONE NEXT 50 MG CHEWABLE TABLETS FOR DOGS~~

~~**PART IB**~~

~~**A – LABELLING – BLISTER**~~

~~Pharmaceutical form~~

~~Chewable Tablet~~

Mis en forme : Gauche

Mis en forme : Police :(Par défaut) Times New Roman, 11 pt

Mis en forme : Gauche, Interligne : Exactement 13 pt

Mis en forme : Gauche

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Police :(Par défaut) Times New Roman, 11 pt

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Gauche, Bordure : Haut: (Pas de bordure), Bas: (Pas de bordure), Gauche: (Pas de bordure), Droite: (Pas de bordure)

Mis en forme : Police :(Par défaut) Times New Roman, 11 pt

Mis en forme : Police :(Par défaut) Times New Roman

Mis en forme : Gauche

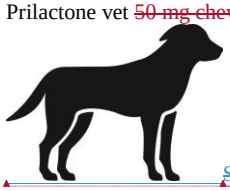
Mis en forme : Police :(Par défaut) Times New Roman, 11 pt

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Aluminium Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prilactone Next ~~50 mg chewable tablets for dogs~~
Prilactone vet ~~50 mg chewable tablets for dogs~~ (FI)



~~Spironolactone~~

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE ~~NAME OF THE MARKETING AUTHORISATION HOLDER~~

~~Ceva logo~~50 mg of spironolactone

3. BATCH NUMBER

Lot {number}

~~4~~3. EXPIRY DATE

Exp. {mm/yyyy}
~~EXP {month/year}~~

~~**4. BATCH NUMBER**~~

~~Batch:~~

~~**5. THE WORDS "FOR ANIMAL TREATMENT ONLY"**~~

~~For animal treatment only.~~

Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Police :(Par défaut) Times New Roman, Non souligné
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Police :Times New Roman
Mis en forme : Bordure : Encadrement : (Simple, Automatique, 0,5 pt Épaisseur du trait)
Mis en forme : Police :(Par défaut) Times New Roman

~~Veterinary Medicinal product~~

~~PRILACTONE NEXT 50 MG CHEWABLE TABLETS FOR DOGS~~

~~PART IB~~

~~B – PACKAGE LEAFLET~~

~~Pharmaceutical form~~

~~Chewable Tablet~~

Mis en forme : Centré, Droite : 0,2 cm, Interligne : simple, Taquets de tabulation : Pas à 1 cm

Mis en forme : Police :(Par défaut) Times New Roman, 11 pt

Mis en forme : Droite : 0,2 cm, Interligne : simple, Taquets de tabulation : Pas à 1 cm

Mis en forme : Droite : 0,2 cm, Taquets de tabulation : Pas à 1 cm

Mis en forme : Droite : 0,2 cm, Bordure : Haut: (Pas de bordure), Bas: (Pas de bordure), Gauche: (Pas de bordure), Droite: (Pas de bordure), Taquets de tabulation : Pas à 1 cm

Mis en forme : Droite : 0,2 cm, Interligne : simple, Taquets de tabulation : Pas à 1 cm

Mis en forme : Interligne : simple, Taquets de tabulation : Pas à 1 cm

Mis en forme : Police :(Par défaut) Times New Roman

B. PACKAGE LEAFLET

PACKAGE LEAFLET

~~PRILACTONE NEXT 50 MG CHEWABLE TABLETS FOR DOGS~~

~~1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT~~

~~Marketing authorisation holder~~

~~Manufacturer for the batch release:~~
~~Ceva Santé Animale~~
~~Boulevard de la Communication~~
~~Zone Autoroutière~~
~~53950 LOUVERNE~~
~~FRANCE~~

12. Name of the veterinary medicinal product

Prilactone Next 50 mg chewable tablets for dogs
Prilactone vet 50 mg chewable tablets for dogs (FI)
~~Spironolactone~~

~~23.~~ ~~STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)~~Composition

One tablet contains
Active substance:
Spironolactone.....50 mg
~~Chewable tablet~~
Clover-shaped scored beige chewable tablet. The tablet can be divided into four equal parts.

3. Target species

Dog~~ss~~

4. Indication~~(s)~~ for use

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.

5. Contraindications

Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman, 11 pt
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman
Mis en forme : Police :(Par défaut) Times New Roman

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 "Pregnancy and lactation".

~~12~~6. S~~s~~pecial warnings

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 section "Contraindications").
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 sensitis~~z~~ation. 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~~

Pregnancy and lactation:
The safety of the product has not been assessed in pregnant and lactating bitches.
Laboratory studies in laboratory animals have shown evidence of developmental toxicity.
Do not use during pregnancy and lactation.
~~Pregnancy and lactation~~
~~Spironolactone had developmental toxicity in laboratory animals.~~
~~The safety of the product has not been assessed in pregnant and lactating bitches.~~
~~Do not use during pregnancy and lactation.~~

Interaction with other medicinal products and other forms of interaction:

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Mis en forme : Police :(Par défaut) Times New Roman
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Mis en forme : Police :(Par défaut) Times New Roman, Non Gras, Soulignement , Anglais (États-Unis)
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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 section "Special precautions for use").
Spironolactone may cause both induction and inhibition of cytochrome P450 enzymes and could therefore affect the metabolism of other drugs utilizing these metabolic pathways.

Overdose:
After administration of up to 5 times the recommended dose (10 mg/kg) to healthy dogs, dose-dependent adverse effects were noted, See section "Adverse reactions".
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.

76. Adverse ~~reactions~~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. If you notice any side effects, even those not already listed in the package leaflet, or you think that the medicine has not worked, please contact, in the first instance, you veterinarian. You can also report any adverse events to the marketing authorization holder or its local representative using the contact details at the end of the leaflet, or via your national system details.
~~Dogs:~~

~~A reversible prostatic atrophy is often observed in entire male dogs. Vomiting and diarrhoea may commonly occur.~~
~~The frequency of adverse reactions is defined using the following convention:~~
~~- very common (more than 1 in 10 animals treated displaying adverse reaction(s))~~
~~- common (more than 1 but less than 10 animals in 100 animals treated)~~
~~- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)~~
~~- rare (more than 1 but less than 10 animals in 10,000 animals treated)~~
~~- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).~~

~~If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.~~
~~Alternatively you can report via your national reporting system {national system details}.~~

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~~7. TARGET SPECIES~~

~~Dogs~~

8. Dosage for each species, route~~(s)~~ and method of administration

Oral use.

2 mg of spironolactone per kg of body weight once daily, ~~i.e.~~i.e., 1 tablet per 25 kg of body weight~~, by oral route~~. The product should be administered with meal.

Dog weight (kg)	Prilactone Next 50 mg Number of tablets per day
> 3.0 to 6.0	¼
> 6.0 to 12.5	½
> 12.5 to 18.0	¾
> 18.0 to 25.0	1
> 25.0 to 31.0	1 ¼
> 31.0 to 37.0	1 ½
> 37.0 to 43.0	1 ¾
> 43.0 to 50.0	2

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

9. Advice on correct administration

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.
As feeding significantly increases the oral bioavailability of spironolactone it is recommended to administer the product during the meal.
Instruction on how to divide the tablet: Put the tablet on an even surface, with its scored side facing down (convex face up). With the tip of the forefinger, exert slight vertical pressure on the middle of the tablet to break it along its width into halves. Then, in order to obtain quarters, exert slight pressure on the middle of one half with the forefinger to break it into two parts.

10. Withdrawal period~~(s)~~

Not applicable

11. Special storage precautions

Keep out of the sight and reach of children.
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 72 hours.

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Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.

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12. SPECIAL WARNING(S)

Special precautions for use in animals

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 section "Contraindications").

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 sensitization. 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.

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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.

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

Pregnancy and lactation

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Spironolactone had developmental toxicity in laboratory animals.

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

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Do not use during pregnancy and lactation.

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 section "Special precautions for use").

~~Spironolactone may cause both induction and inhibition of cytochrome P450 enzymes and could therefore affect the metabolism of other drugs utilizing these metabolic pathways.~~

~~**Overdose (symptoms, emergency procedures, antidotes), if necessary**~~
~~After administration of up to 5 times the recommended dose (10 mg/kg) to healthy dogs, dose-dependent adverse effects were noted, See section "Adverse reactions".~~
~~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.~~

12~~3~~. Special precautions for ~~the~~ disposal ~~of unused product or waste materials, if any~~

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon how to dispose of medicines no longer required.

~~Medicines should not be disposed of via wastewater. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.~~

13. 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.

14. Marketing authorization numbers and pack sizes

(MA)

Pack sizes:
Cardboard box with 10 tablets
Cardboard box with 20 tablets
Cardboard box with 30 tablets
Cardboard box with 100 tablets
Cardboard box with 180 tablets

Not all pack sizes may be marketed.

15~~4~~. Date on which the package leaflet was last ~~approved~~revised

{~~DD/MM/YYYY~~mm/yyyy}
Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).
~~Detailed information on this veterinary medicinal product is available in the Union Product Database.~~

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
(Name and address to be completed nationally)
Tel: +800 35 22 11 51
Email: pharmacovigilance@ceva.com

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~~Marketing authorisation holder~~

Manufacturer for the batch release:
Ceva Santé Animale
Boulevard de la Communication
Zone Autoroutière
53950 LOUVERNE
FRANCE

175. Other information

~~Pack sizes:~~
~~Cardboard box with 10 tablets~~
~~Cardboard box with 20 tablets~~
~~Cardboard box with 30 tablets~~
~~Cardboard box with 100 tablets~~
~~Cardboard box with 180 tablets~~

~~Not all pack sizes may be marketed.~~

~~For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.~~

~~Local representative:~~

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