[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vasotop P 0.625 mg tablets for dogs (CMS: AT, BE, DE, EL, ES, IT, LU, NL)
Vasotop 0.625 mg tablets for dogs (NO)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Ramipril 0.625 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Brown ferric oxide (E172)	1.0 mg
Hydroxypropylmethylcellulose	
Starch, pregelatinised	
Cellulose, microcrystalline	
Sodium stearyl fumarate	
Artificial powdered beef flavour	
Silica colloidal anhydrous	

Brownish orange flavoured oblong tablet with dark spots and with a score line on both sides.
Embossing: One side: V on both sides of the score line.
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 treatment of congestive heart failure (according to New York Heart Association (NYHA) classification grade II, III & IV) caused by valvular insufficiency due to chronic degenerative valvular heart disease (endocardiosis) or cardiomyopathy, with or without adjunct therapy with the diuretic furosemide and/or the cardiac glycosides digoxin or methyldigoxin.

Class	Clinical signs
II	Fatigue, shortness of breath, coughing etc. become evident when ordinary exercise is exceeded. Ascites may appear at this stage.
III	Comfortable at rest, but exercise capacity is minimal.

IV	No capacity for exercise. Disabling clinical signs are present even at rest.

In patients treated concurrently with the veterinary medicinal product and furosemide, the dose of the diuretic can be reduced to achieve the same diuretic effect as treatment with furosemide alone.

3.3 Contraindications

Do not use in any dog with haemodynamically relevant stenosis (e.g. aortic stenosis, mitral valve stenosis) or obstructive hypertrophic cardiomyopathy.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

If signs of apathy or ataxia (potential signs of hypotension) occur during treatment with the veterinary medicinal product, the drug should be discontinued and treatment resumed at 50% of the original dose once symptoms have subsided.

The use of ACE inhibitors in dogs with hypovolaemia/dehydration (e.g. as a result of diuretic treatment, vomiting or diarrhoea) can lead to acute hypotension. In such cases the fluid and electrolyte balance should be restored immediately and treatment with this veterinary medicinal product suspended until it has been stabilised.

In patients at risk of hypovolaemia, the veterinary medicinal product should be introduced gradually over one week (starting with half the normal dose).

1-2 days before and after commencement of treatment with ACE inhibitors, the patient's hydration status and renal function should be checked. This is also necessary after the veterinary medicinal product dose has been increased or if a diuretic is given concurrently.

Use according to the benefit/risk assessment in dogs with renal and hepatic failures.

In dogs with kidney problems, renal function should be monitored during therapy with the veterinary medicinal product.

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

Wash hands after use. In case of accidental ingestion seek immediately medical advice 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:

Rare	Low blood pressure[1] (visible as fatigue, lethargy or ataxia)

(1 to 10 animals / 10,000 animals treated):	

[1] At the start of treatment with ACE inhibitors or after a dosage increase. In such cases treatment should be discontinued until the patient's condition has returned to normal and then resumed with 50% of the original dose. As high doses of diuretics can also lead to a fall in blood pressure, the concurrent administration of diuretics in the early phase of treatment with ACE inhibitors should be avoided in these patients.

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

As no data are available on the use of the veterinary medicinal product during pregnancy and lactation, the veterinary medicinal product should not be used in pregnant or lactating bitches.

3.8 Interaction with other medicinal products and other forms of interaction

Both diuretics and a low-sodium diet potentiate the action of ACE inhibitors by activating the renin-angiotensin-aldosterone system (RAAS). Large doses of diuretics and a low-sodium diet should therefore be avoided during treatment with ACE inhibitors in order to prevent hypotension (with symptoms such as apathy, ataxia and more rarely syncope or acute renal failure).

The concomitant administration of potassium or potassium-sparing diuretics should be avoided because of the risk of hyperkalaemia.

3.9 Administration routes and dosage

For oral use.

The therapeutic dose in the dog is a single daily oral administration of 0.125 mg ramipril per kg body weight (1 tablet of veterinary medicinal product 0.625 mg per 5 kg bodyweight).

To ensure accurate dosing, each individual should be carefully weighed before calculating the dose.

Treatment should always be started with this lowest recommended dose. The dose should only be increased if the animal does not respond to the recommended initial dosage of 0.125 mg ramipril per kg bodyweight.

Depending on the severity of the pulmonary congestion in patients with cough or pulmonary oedema, the dose may be increased after 2 weeks to 0.25 mg ramipril per kg BW and day.

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

Oral doses of up to 2.5 mg ramipril per kg bodyweight (10-times the recommended highest dose) have been well tolerated in healthy young dogs.

Hypotension may occur as a symptom of overdose with signs of apathy and ataxia.

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 ATCvet code: QC09AA05

4.2 Pharmacodynamics

Ramipril is hydrolysed by esterases in the liver to its active metabolite ramiprilat. Ramiprilat inhibits the enzyme dipeptidylcarboxypeptidase I, also called angiotensin-converting enzyme (ACE). This enzyme catalyses the conversion of angiotensin I to angiotensin II in the blood plasma and endothelia and the breakdown of bradykinin. As angiotensin II has a potent vasoconstrictive action, while bradykinin is a vasodilator, the reduced formation of angiotensin II and the inhibition of bradykinin breakdown lead to vasodilation.

In addition, plasma angiotensin II causes the release of aldosterone (in the renin-angiotensin-aldosterone system - RAAS). Ramiprilat therefore also reduces the secretion of aldosterone. This leads to an increase in the serum potassium concentration.

The inhibition of tissue ACE causes a reduction of local angiotensin II, especially in the heart, and enhances the action of bradykinin. Angiotensin II induces cell division in smooth muscle, while bradykinin causes a local increase in prostacyclins (PGI_2) and NO, which in turn inhibit the proliferation of smooth muscle. These two synergistic effects of local ACE inhibition are synonymous with a reduction of myotropic factors and lead to a marked reduction in the proliferation of smooth muscle cells in cardiac muscle and blood vessels. Ramipril thus prevents or substantially reduces myogenic hypertrophy in congestive heart failure (CHF) and leads to a reduction in peripheral resistance.

The plasma ACE activity was measured as a criterion of the pharmacodynamic action of ramipril. Following oral administration of the drug a rapid and significant inhibition of this activity occurs, which then gradually rises again during the interval between doses, eventually returning to 50 % of the baseline value at 24 hours post administration.

Treatment with ramipril improves the haemodynamic status of patients with congestive heart failure, the associated symptoms and the prognosis. In addition, ramipril reduces the mortality rate in patients with persistent or transient heart failure following an acute myocardial infarction (man, dog).

4.3 Pharmacokinetics

Ramipril is rapidly absorbed in the gastrointestinal tract after oral administration and hydrolysed in the liver to the active metabolite ramiprilat. The relative bioavailability of the different tablets was documented and ranged from 87.9 to 97.7%.

Metabolism studies in dogs with ^{14}C-labelled ramipril show that the active substance is distributed rapidly and extensively into the various tissues.

Following oral administration of 0.25 mg/kg bodyweight ramipril to dogs, maximum ramiprilat concentrations occur on average after 1.2 hours (tablet). The mean of these peak concentrations is 18.1 ng/ml (tablet).

No cumulative effects were observed.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

5.3 Special precautions for storage

Do not store above 30 °C.

Store in a dry place.

After each opening, replace the cap tightly.

Do not remove the desiccant capsule.

5.4 Nature and composition of immediate packaging

15 mL HD polyethylene containers containing 28 tablets closed by LD polypropylene tamper-evident child resistant screw cap. A desiccant capsule is inserted in the cap.

Box of 1, 3 or 6 containers.
Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products 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

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

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

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

{DD/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.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON BOX Vasotop P 0.625 mg tablets

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vasotop P 0.625 mg tablets for dogs

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains 0.625 mg ramipril.

3. PACKAGE SIZE

1 x 28 tablets
3 x 28 tablets
6 x 28 tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C.
Store in a dry place.
After each opening, replace the cap tightly.
Do not remove the desiccant capsule.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

CONTAINER LABEL
Vasotop P 0.625 mg tablets

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vasotop P 0.625 mg tablets for dogs

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

0.625 mg/tablet

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Vasotop P 0.625 mg tablets for dogs

2. Composition

Each tablet contains:

Active substance:
Ramipril 0.625 mg

Excipients:
Brown ferric oxide (E172) 1.0 mg

Brownish orange flavoured oblong tablet with dark spots with a score line on both sides.
Embossing: One side: V on both sides of the score line.
The tablets can be divided into two equal parts.

3. Target species

Dogs.

4. Indications for use

For treatment of chronic heart disease (congestive heart failure, according to New York Heart Association (NYHA) classification grade II, III & IV) caused by valvular insufficiency due to chronic degenerative valvular heart disease (endocardiosis) or cardiomyopathy, with or without adjunct therapy with the diuretic furosemide and/or the cardiac glycosides digoxin or methyldigoxin.

Class	Clinical signs
II	Fatigue, shortness of breath, coughing etc. become evident when ordinary exercise is exceeded. Ascites may appear at this stage.
III	Comfortable at rest, but exercise capacity is minimal.
IV	No capacity for exercise. Disabling clinical signs are present even at rest.

In patients treated concurrently with the veterinary medicinal product and furosemide, the dose of the diuretic can be reduced to achieve the same diuretic effect as treatment with furosemide alone.

5. Contraindications

Do not use in any dog with haemodynamically relevant stenosis (e.g. aortic stenosis, mitral valve stenosis) or obstructive hypertrophic cardiomyopathy.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special precautions for safe use in the target species:

If signs of apathy or ataxia (potential signs of hypotension) occur during treatment with the veterinary medicinal product , the drug should be discontinued and treatment resumed at 50% of the original dose once symptoms have subsided.

The use of veterinary medicinal product in dogs with low blood pressure (hypovolaemia)/dehydration (e.g. as a result of diuretic treatment, vomiting or diarrhoea) can lead to low blood pressure (acute hypotension). In such cases the fluid and electrolyte balance should be restored immediately and treatment with veterinary medicinal product suspended until it has been stabilised.

In animals at risk of hypovolaemia, the veterinary medicinal product should be introduced gradually over one week (starting with half the normal dose).

1-2 days before and after commencement of treatment with veterinary medicinal product , the patient's hydration status and renal function should be checked. This is also necessary after the veterinary medicinal product dose has been increased or if a diuretic is given concurrently.

Use according to the benefit/risk assessment in dogs with renal and hepatic failures. In those dogs, renal and/or hepatic function should be monitored during treatment with veterinary medicinal product.

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

Wash hands after use. In case of accidental ingestion seek immediately medical advice and show the package leaflet or the label to the physician.

Pregnancy and lactation:

As no data are available on the use of the veterinary medicinal product during pregnancy and lactation, the veterinary medicinal product should not be used in pregnant or lactating bitches.

Interaction with other medicinal products and other forms of interaction:

As with other substances lowering the blood pressure, the concomitant use of hypotensive medicinal products (e.g. diuretics) or anaesthetics with a hypotensive effect may add to the anti-hypertensive effect of ramipril. In dogs treated concurrently with the veterinary medicinal product and a diuretic, the dose of the diuretic can be reduced to achieve the same diuretic effect as treatment with the diuretic alone.

Interactions with potassium preserving drugs (e.g. spironolactone) cannot be ruled out. It is recommended to monitor plasma potassium levels when using ramipril in combination with a potassium sparing diuretic.

Overdose:

Oral doses of up to 2.5 mg ramipril per kg bodyweight (10-times the recommended highest dose) have been well tolerated in healthy young dogs.

Hypotension may occur as a symptom of overdose with signs of apathy and ataxia.

Major incompatibilities:

Not applicable.

7. Adverse events

Dogs:

Rare	Low blood pressure[1] (visible as fatigue, lethargy or ataxia)

(1 to 10 animals / 10,000 animals treated):	

[1] At the start of treatment with ACE inhibitors or after a dosage increase. In such cases treatment should be discontinued until the patient's condition has returned to normal and then resumed with 50% of the original dose. As high doses of diuretics can also lead to a fall in blood pressure, the concurrent administration of diuretics in the early phase of treatment with ACE inhibitors should be avoided in these patients.

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: <{national system details}

8. Dosage for each species, routes and method of administration

For oral use.

The therapeutic dose in the dog is a single daily oral administration of 0.125 mg ramipril per kg body weight (1 tablet of veterinary medicinal product 0.625 mg per 5 kg bodyweight).

To ensure accurate dosing, each individual should be carefully weighed before calculating the dose.

Treatment should always be started with this lowest recommended dose. The dose should only be increased if the animal does not respond to the recommended initial dosage of 0.125 mg ramipril per kg bodyweight.

Depending on the severity of the clinical signs, the dose may be increased after 2 weeks to 0.25 mg ramipril per kg BW and day.

9. Advice on correct administration

The veterinary medicinal product tablets are flavoured. Offer the tablet to the dog in the hand or in its food dish. If the dog refuses it, give the tablet by placing it in its mouth.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 30 °C.

Store in a dry place.

After each opening, replace the cap tightly.

Do not remove the desiccant capsule.

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

12. Special precautions for disposal

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 or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

15 mL HD polyethylene containers containing 28 tablets closed by LD polypropylene tamper-evident child resistant screw cap. A desiccant capsule is inserted in the cap.

Pack sizes: Box of 1, 3 or 6 containers.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Manufacturer responsible for batch release:
Intervet GesmbH
Siemensstrasse 107
1210 Vienna
Austria

Local representatives <and contact details to report suspected adverse reactions:
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.