# PARTICULARS TO APPEAR ON THE OUTER PACKAGE

## CARTON

### 1 container with 28 tablets, 3 containers each containing 28 tablets or 6 containers each containing 28 tablets

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vasotop 1.25 mg tablets
Ramipril

## 2. STATEMENT OF ACTIVE SUBSTANCES

Each flavoured tablet contains 1.25 mg ramipril.

## 3. PHARMACEUTICAL FORM

Tablet

## 4. PACKAGE SIZE

28 flavoured tablets
3 x 28 flavoured tablets
6 x 28 flavoured tablets

## 5. TARGET SPECIES

Dogs.

## 6. INDICATION(S)

See enclosed leaflet for indications, administration and warnings.

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral

## 8. WITHDRAWAL PERIOD

Not applicable.

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

See package leaflet for full user safety and disposal warnings.

## 10. EXPIRY DATE

EXP {month/year}

## 11. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.
Store in a dry place.
After each opening, please replace the cap tightly.
Do not remove the desiccant capsule.
Keep container in outer carton.

## 12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

See package leaflet for full user safety and disposal warnings.

## 13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IF APPLICABLE

*[Distribution category]*
For animal treatment only.
POM-V
To be supplied only on veterinary prescription.

## 14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of sight and reach of children.

## 15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MSD Animal Health UK Ltd.
Walton Manor, Walton
Milton Keynes
MK7 7AJ

## 16. MARKETING AUTHORISATION NUMBER

Vm 01708/4403

## 17. MANUFACTURER'S BATCH NUMBER

# MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

## CONTAINER LABEL

### 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vasotop 1.25 mg tablets
Ramipril

### 2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Each flavoured tablet contains 1.25 mg ramipril

### 3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

28 flavoured tablets

### 4. ROUTE(S) OF ADMINISTRATION

For oral administration to dogs.
See package leaflet for further information.

### 5. WITHDRAWAL PERIOD

Not applicable.

### 6. BATCH NUMBER

LOT:

### 7. EXPIRY DATE

EXP{month/year}

### 8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.
Vm 01708/4403

# PACKAGE LEAFLET FOR:

# Vasotop Tablets

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

Marketing authorisation holder:
MSD Animal Health UK Ltd.
Walton Manor,Walton
Milton Keynes
Buckinghamshire
MK7 7AJ

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

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vasotop 1.25 mg tablets
Vasotop 2.5 mg tablets
Vasotop 5 mg tablets
Ramipril

## 3. STATEMENT OF THE ACTIVE SUBSTANCE (S) AND OTHER INGREDIENTS

Vasotop 1.25 mg: beige oblong flavoured tablets with dark spots. Half-scored on both sides.
Each tablet contains 1.25 mg ramipril.
Vasotop 2.5 mg: brownish yellow oblong flavoured tablets with dark spots. Half-scored on both sides.
Each tablet contains 2.5 mg ramipril and 0.5 mg yellow ferric oxide (E172).
Vasotop 5 mg: brownish pink oblong flavoured tablets with dark spots. Half-scored on both sides.
Each tablet contains 5 mg ramipril and 0.25 mg red ferric oxide (E172).

## 4. INDICATION(S)

For the treatment of congestive heart failure (NYHA decompensation grades IIIV) in dogs. Vasotop can be used in combination with diuretics, and the cardiac glycosides, digoxin or methyl-digoxin.

## 5. CONTRAINDICATIONS

Not to be used in clinical cases of vascular stenosis (e.g. aortic stenosis) or obstructive hypertrophic cardiomyopathy.

## 6. ADVERSE REACTIONS

No undesirable effects have been noted to date which might be linked with the use of the product. If you observe side-effects in your animal during treatment consult your veterinary surgeon.

## 7. TARGET SPECIES

Dogs

## 8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

The therapeutic dose in the dog is 0.125 mg ramipril per kg bw per day. Depending on the severity of pulmonary congestion the dose may be increased after 2 weeks to 0.25 mg ramipril per kg per day. Treatment is once daily by mouth. Suggested dosage schedule for standard dose (0.125 mg/kg/day).

| Bodyweight (kg) | Vasotop Standard Dose | | |
|---|---|---|---|
| | 1.25 mg | 2.5 mg | 5 mg |
| 6 - 10 | 1 | | |
| 11 - 20 | | 1 | |
| 21 - 40 | | | 1 |
| 41- 50 | 1 | | 1 |
| 51 - 60 | | 1 | 1 |

## 9. ADVICE ON CORRECT ADMINISTRATION

To ensure accurate dosing, each individual should be carefully weighed before calculating the dose.
The product may also be used in combination with the diuretic furosemide and/or the cardiac glycosides digoxin or methyl-digoxin.

## 10. WITHDRAWAL PERIOD(S)

Not applicable

## 11. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C
Store in a dry place.
After each opening, please replace the cap tightly.
Do not remove the desiccant capsule. Keep container in outer carton.
Keep out of sight and reach of children.

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

## 12. SPECIAL WARNING(S)

The use of ACE inhibitors in dogs with hypovolaemia/dehydration (e.g. due to large doses of a diuretic, vomiting or diarrhoea) can lead to acute hypotension. In such cases the fluid and electrolyte status should first be balanced and treatment suspended until it is stabilised.
This also applies if clinical signs of apathy or ataxia occur during treatment with the product (potential signs of hypotension). After these symptoms have subsided, the treatment should be continued at 50% of the original dose.
Substances that deplete blood volume, such as diuretics, or which vasodilate, such as angiotensin-converting enzyme (ACE) inhibitors, may contribute to lowering systemic blood pressure. This may result in pre-renal uraemia (azotaemia). Renal function should be monitored both before and seven days after commencement of treatment with ACE inhibitors. This also applies when the dosage of ACE inhibitor or of a concurrently administered diuretic is increased. It is advisable to periodically monitor renal function throughout treatment.
Ramipril is a pro-drug and is metabolized in the liver to its active form. This conversion may be reduced in dogs with impaired liver function.
In patients at risk of hypovolaemia it is advisable to introduce the product gradually over one week (starting with half the therapeutic dose).
As well as monitoring the hydration status the patient’s renal function should be checked before and seven days after commencement of treatment with ACE inhibitors. This also applies when the dosage of the product or of a concurrently administered diuretic is increased.
It is advisable to periodically monitor renal function throughout treatment. In patients treated with the product and furosemide the dose of the diuretic can be reduced to achieve the same diuretic effect as with furosemide alone.
*Operator warnings*

Pregnant women should take special care to avoid accidental exposure, because ACE inhibitors have been found to affect the unborn child during pregnancy in humans.
Wash hands after use. In case of accidental ingestion by children seek medical advice immediately and show the label to the doctor.
*Use during pregnancy or lactation*
Fertility disorders in male and female rats were not observed. In animal experiments ramipril passes into maternal milk.
No studies have been carried out to assess the use of the drug in pregnancy or lactation in bitches. ACE inhibitors have been found to be teratogenic in the second and third trimesters in other species. An angiotensin converting enzyme is known to be critical to the development of the neonatal kidney, this product should not be used in pregnancy or lactation.
*Interaction*
Diuretics and a low-sodium diet both potentiate the effect of ACE inhibitors by activating the renin-angiotensin-aldosterone (RAAS). High doses of diuretics and a low-sodium diet should therefore be avoided during treatment with ACE inhibitors in order to prevent hypotension (with clinical signs such as apathy, ataxia, rarely syncope or acute renal failure).
Do not administer potassium-sparing diuretics.
The concomitant administration of ACE inhibitors with non-steroidal anti-inflammatory drugs (NSAIDs) leads to poor autoregulation of the glomerular blood pressure and can therefore trigger acute renal failure.
*Adverse reactions*
No undesirable effects have been noted to date which might be linked with the use of the product. If you observe side-effects in your animal during treatment consult your veterinary surgeon.
*Overdose*
Overdoses of up to 2.5 mg ramipril/kg bw (10 times the recommended highest dose) have been well tolerated in healthy young dogs.

## 13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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

## 14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

February 2022

## 15. OTHER INFORMATION

Ramipril is hydrolysed in the liver by esterases to its active metabolite ramiprilat. Ramiprilat inhibits the enzyme dipeptidylcarboxypeptidase I, also referred to as angiotensin-converting enzyme (ACE). This enzyme catalyses the conversion of angiotensin I to angiotensin II in blood plasma and in vascular endothelial tissues and degrades bradykinin. As on the one hand angiotensin II acts as a strong vasoconstrictor, bradykinin on the other hand acts as a vasodilator, the reduced formation of angiotensin II and the inhibition of bradykinin degradation resulting in systemic vasodilation.
Angiotensin II also causes the release of aldosterone (within the renin-angiotensinaldosterone-system – RAAS). Consequently, ramiprilat reduces aldosteronesecretion. This in turn leads to an increase in the serum potassium concentration.
Inhibition of tissue ACE in the heart results in locally reduced levels of angiotensin II and in potentiation of bradykinin effects. Angiotensin II induces cell proliferation in smooth muscle, while bradykinin leads to increases in local prostacyclin (PGI2) and nitric oxide (NO), both inhibiting smooth muscle cell proliferation. The two effects of local ACE inhibition act synergistically in reducing myotropic factors and result in distinct reduction of cardiac and vascular smooth muscle cell proliferation. In this way ramipril prevents or reduces, with lasting effect, myogenous hypertrophy in patients with congestive heart failure (CHF) and results in reduction of peripheral vascular resistance.
The plasma ACE-activity was measured as the principal criterion of the pharmacodynamic effect. After oral administration of ramipril a significant inhibition of this activity occurs quickly and gradually increases again during the dosage interval, reaching 50% of the initial value by 24 hours post administration.
Administration of ramipril in patients with congestive heart failure improves the haemodynamics, the related symptomatology and the prognosis. Ramipril has also been shown to reduce the mortality rate among patients with persistent or transient heart failure following an acute myocardial infarction (man, dog).

**Pharmacokinetic particulars**
Ramipril is rapidly and completely absorbed in the gastrointestinal tract after oral administration and is hydrolysed to the active metabolite ramiprilat in the liver. Metabolism studies in rats, mice and dogs with 14C-labelled ramipril show that the active ingredient is quickly and extensively distributed in the various tissues. In the rat the highest concentrations are measured in the liver, the kidney and the lungs. Following oral administration of 0.125 mg/kg BW ramipril (aqueous solution) to dogs, the maximum ramiprilat concentration of 12.1 ng/ml (day 1) and 17.7 ng/ ml (day 8) respectively appear on average after one hour. The concentrations then decline in a biphasic pattern with biological half-lives of 0.5 and 8.9 hours (day 1) and 0.7 and 10.5 hours (day 8) on average, respectively.

Following oral administration of 0.25 mg/kg BW ramipril (aqueous solution) to dogs, maximum ramiprilat concentrations are reached on average after 1.2 hours (tablet) and 1 hour (aqueous solution) respectively. The mean of these peak concentrations is 18.1 ng/ml (tablet) and 23.0ng/ml (aqueous solution), respectively.
Following oral administration of 0.5 mg/kg BW ramipril (aqueous solution) to dogs, maximum ramiprilat concentration) of 95.5ng/m; appear after 0.8 hours (day 1) and 81.5 ng/ml after 0.9 hours (day 8) on average respectively. The half lives are 13.7 hours (day 1) and 15.7 hours (day 8) respectively.
It would appear from the AUC (area under the plasma concentration versus time curve) that the kinetics in the tested dosage range are linearly related to the dose rate. Cumulative effects were not observed.

## LEGAL CATEGORY

POM-V
To be supplied only on a veterinary prescription
For animal treatment only

1.25 mg tablets Vm 01708/4403
2.5 mg tablets Vm 01708/4404
5 mg tablets Vm 01708/4400

## PACKAGE QUANTITIES

1 x 28 tablets in 15 ml HD polyethylene container per box.
3 x 28 tablets in 15 ml HD polyethylene container per box.
6 x 28 tablets in 15 ml HD polyethylene container per box.
Not all pack sizes may be marketed.

Approved 11 February 2022