SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Prilocard 2.5mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Ramipril 2.5 mg

Excipients:
yellow ferric oxide 0.40 mg (E172)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

Light yellow capsule-shaped biconvex tablets scored on one side of the tablet and imprinted with 'B' and '49' on either side of the scoring line. The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

For treatment of congestive heart failure (equivalent to New York Heart Association [NYHA] classes II, III and IV) caused by valvular insufficiency due to endocardiosis or cardiomyopathy. The preparation may if applicable be administered concomitantly with furosemide (diuretic) and/or the cardiac glycosides digoxin or methyl digoxin.

Class	Clinical symptoms
II	Fatigue, dyspnoea, cough etc. seen in normal activity. Ascites may occur at this stage.
III	Comfortable at rest, but capacity for activity minimal.
IV	Incapable of any activity. Clinical symptoms of disablement occur even at rest.

In patients treated concomitantly with ramipril and furosemide, the diuretic dose may be reduced to achieve the same diuretic effect as in treatment with furosemide alone.

4.3 Contraindications

Do not use in haemodynamically-related stenoses (e.g. aortic stenosis, mitral stenosis) nor in cases of obstructive hypertrophic cardiomyopathy.

Do not use in cases of hypersensitivity to the active substance, ACE-inhibitors or to any of the excipient(s).

See Section 4.7 for use in Pregnancy and Lactation

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
If symptoms of apathy and ataxia (potential symptoms of hypotension) occur during treatment with ramipril, administration of the preparation should be stopped and resumed at only 50% of the original dose as soon as the symptoms have diminished.

The use of ACE inhibitors in dogs with hypovolaemia/dehydration (e.g. after diuretic treatment, vomiting or diarrhoea) or in those dogs receiving other vasodilators may cause acute hypotension and pre renal azotaemia. In such cases, the fluid and electrolyte balance should be re-established immediately and treatment with ramipril discontinued until the situation is stabilised.

In dogs at risk of hypovolaemia, the dosage of ramipril should be gradually increased over a week (starting at half the normal dose).

The patient's fluid balance and renal function should be checked 1-2 days before and seven days after the start of treatment with ACE inhibitors. This is also necessary when the dose of ramipril is increased, or if a diuretic is given concomitantly.
Use according to the benefit/risk assessment by the responsible veterinarian in dogs with renal and/or hepatic failure.
In dogs with renal insufficiency, renal function should be checked regularly during treatment with ramipril.

Ramipril is a pro-drug and is metabolised in the liver to its active form. This conversion may be reduced in dogs with impaired liver function.

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.

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

Pregnant women should take special care to avoid accidental oral 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 seek immediately medical advice and show the package leaflet or the label to the physician.

People with known hypersensitivity to the active ingredient should avoid contact with the product.

4.6 Adverse reactions (frequency and seriousness)

In the beginning or after a dose increase, treatment with ACE inhibitors may in rare cases produce a decrease in blood pressure, which shows itself in fatigue, drowsiness, apathy or ataxia. In such cases treatment should be discontinued until the patient's condition has normalised and then resumed at 50% of the original dose. Since high doses of diuretics may also produce a drop in blood pressure, concomitant intake of diuretics in the early phase of treatment with ACE inhibitors should be avoided in these patients.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Pregnancy:
As no data are available on the use of the product during pregnancy and lactation the product should not be used in pregnant and lactating 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.

Lactation:
Do not use in lactating bitches. Ramipril has been shown to pass into maternal milk

4.8 Interaction with other medicinal products and other forms of interaction

Both diuretics and low sodium intake potentiate the effect 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 to avoid hypotension (with symptoms such as apathy, ataxia and more rarely fainting and acute renal insufficiency).

Concomitant intake of potassium and potassium-sparing diuretics should be avoided because of the risk of hyperkalaemia.

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

4.9 Amounts to be administered and administration route

Dogs:
Oral use. 0.125 mg Ramipril per kg body weight once daily. This is equivalent to 1 tablet of 2.5 mg per 20 kg body weight once daily.
To ensure accurate dosing, each individual should be carefully weighed before calculating the dose.

Treatment should always be started at the lowest recommended dose. The dose should be increased only if the animal does not respond to the recommended initial dose of 0.125 mg ramipril per kg. Depending on the degree of pulmonary congestion in patients with cough or pulmonary oedema, the dose may be increased after two weeks to 0.25 mg ramipril per kg body weight once daily.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

An oral dose of up to 2.5 mg ramipril per kg body weight (10 times the maximum recommended dose) was well tolerated by young, healthy dogs.

Hypotension with symptoms of apathy and ataxia may occur as symptoms of overdose.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL AND IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: ACE inhibitors, ramipril..
ATCvet code: QC09AA05.

5.1 Pharmacodynamic properties

Ramipril is hydrolysed in the liver by esterases to the active metabolite ramiprilate. Ramiprilate inhibits the enzyme dipeptidyl carboxypeptidase I, which is also called angiotensin-converting enzyme (ACE). This enzyme catalyses the conversion of angiotensin I to angiotensin II in blood plasma and the endothelium and the breakdown of bradykinin. Since angiotensin II has a powerful vasoconstrictive effect and bradykinin is a vasodilator, the reduced formation of angiotensin II and the inhibition of bradykinin results in vasodilatation.

In addition, plasma angiotensin II causes a release of aldosterone (in the renin-angiotensin-aldosterone system or RAAS). Ramiprilate therefore also reduces the secretion of aldosterone, leading to an increase of serum potassium.

The inhibition of ACE in tissue causes a reduction of local angiotensin II (especially in the heart) and increases the effect of bradykinin. Angiotensin II induces cell division in smooth musculature, while bradykinin causes a local increase in prostacyclins (PG12) and NO2, which conversely inhibits the proliferation of smooth musculature. These two synergistic effects of the local ACE inhibition amount to a reduction of myotropic factors and produce a significant reduction in the proliferation of smooth musculature in the heart muscle and blood vessels. Ramipril therefore hinders or reduces the myogenic hypertrophy significantly in the event of cardiac insufficiency and leads to a reduction in the peripheral resistance.

The ACE activity in plasma was measured as a criterion for a pharmacodynamic effect of ramipril. Following oral intake there is a rapid and significant inhibition of this activity, which then gradually rises between doses and finally returns to 50% of the base value 24 hours after intake.

Ramipril treatment improves the haemodynamic status in patients with cardiac insufficiency, including symptoms and prognosis. Ramipril also reduces mortality in patients with persistent or transient congestive heart failure after acute myocardial infarction (in humans and dogs).

5.2 Pharmacokinetic properties

Ramipril is absorbed rapidly from the gastrointestinal tract after oral intake and hydrolysed in the liver to the active metabolite ramiprilate.

Investigations of the metabolism in dogs with ^{14}C-marked ramipril shows that the active substance is distributed rapidly and extensively to the various tissues.

Following oral administration of ramipril 0.25 mg/kg body weight to dogs, the maximum concentration of ramiprilate is subsequently achieved after an average of 1.2 hours (tablet). The average maximum concentration is 18.1 ng/ml (tablet).

No cumulative effect has been observed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Yellow ferric oxide (E172)
Lactose anhydrous
Glycerol dibehenate
Sodium starch glycolate (Type A)
Sodium stearyl fumarate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

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

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and composition of immediate packaging

Blister packs made of PVDC-coated PVC and aluminium foil.
Pack size(s): 28 tablets (2 x 14 tablets), 140 tablets (10 x 14 tablets).

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

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

7. MARKETING AUTHORISATION HOLDER

aniMedica GmbH
Im Südfeld 9
48308 Senden-Bösensell
Germany.

8. MARKETING AUTHORISATION NUMBER

Vm 24745/4007

9. DATE OF FIRST AUTHORISATION

18 July 2012

10. DATE OF REVISION OF THE TEXT

March 2017

Approved: 09 March 2017