SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

MiPet Benazapet 2.5 mg Tablets for cats and dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance: Benazepril hydrochloride 2.5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.
Beige, ovaloid, divisible, palatable tablet scored on both sides.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs and cats.

4.2 Indications for use, specifying the target species

Dogs:
Treatment of congestive heart failure.

Cats:
Reduction of proteinuria associated with chronic kidney disease.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not use in cases of hypotension, hypovolaemia, hyponatraemia or acute renal failure.
Do not use in cases of cardiac output failure due to aortic or pulmonary stenosis.
Do not use during pregnancy or lactation (section 4.7).

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i. Special precautions for use in animals

No evidence of renal toxicity of the veterinary medicinal product has been observed (in dogs or cats) during clinical trials, however, as is routine in cases of chronic kidney disease, it is recommended to monitor plasma creatinine, urea and erythrocyte counts during therapy.

The efficacy and safety of MiPet Benazapet has not been established in dogs and cats below 2.5 kg bodyweight.

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

Wash hands after use.
In case of accidental oral ingestion, seek medical advice immediately and show the label or the package leaflet to the physician.
Pregnant women should take special care to avoid accidental oral exposure because angiotensin converting enzyme (ACE) inhibitors have been found to affect the unborn child during pregnancy in humans.

4.6 Adverse reactions (frequency and seriousness)

In double-blind clinical trials in dogs with congestive heart failure, MiPet Benazapet was well tolerated with an incidence of adverse reactions lower than observed in placebo-treated dogs.

A small number of dogs may exhibit transient vomiting, incoordination or signs of fatigue.

In cats and dogs with chronic kidney disease, MiPet Benazapet may increase plasma creatinine concentrations at the start of therapy. A moderate increase in plasma creatinine concentrations following administration of ACE inhibitors is compatible with the reduction in glomerular hypertension induced by these agents, and is therefore not necessarily a reason to stop therapy in the absence of other signs.

MiPet Benazapet may increase food consumption and body weight in cats.

Emesis, anorexia, dehydration, lethargy and diarrhoea have been reported in rare occasions in cats.
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).

4.7 Use during pregnancy, lactation or lay

Do not use during pregnancy or lactation. The safety of MiPet Benazapet has not been established in breeding, pregnant or lactating dogs and cats. Benazepril reduced ovary/oviduct weights in cats when administered daily at 10 mg/kg body weight for 52 weeks. Embryotoxic effects (foetal urinary tract malformation) were seen in trials with laboratory animals (rats) at maternally non-toxic doses.

4.8 Interaction with other medicinal products and other forms of interaction

In dogs with congestive heart failure, MiPet Benazapet has been given in combination with digoxin, diuretics, pimobendan and anti-arrhythmic veterinary medicinal products without demonstrable adverse interactions.

In humans, the combination of ACE inhibitors and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) can lead to reduced anti-hypertensive efficacy or impaired renal function. The combination of MiPet Benazapet and other anti-hypertensive agents (e.g. calcium channel blockers, β-blockers or diuretics), anaesthetics or sedatives may lead to additive hypotensive effects. Therefore, concurrent use of NSAIDs or other medications with a hypotensive effect should be considered with care. Renal function and signs of hypotension (lethargy, weakness etc) should be monitored closely and treated as necessary. Interactions with potassium preserving diuretics like spironolactone, triamterene or amiloride cannot be ruled out. It is recommended to monitor plasma potassium levels when using MiPet Benazapet in combination with a potassium sparing diuretic because of the risk of hyperkalaemia.

4.9 Amounts to be administered and administration route

MiPet Benazapet should be given orally once daily, with or without food. The duration of treatment is unlimited.

MiPet Benazapet 2.5 mg tablets are flavoured and are taken voluntarily by most dogs and cats.

Dogs:
MiPet Benazapet should be administered orally at a minimum dose of 0.25 mg (range 0.25-0.5) benazepril hydrochloride/kg body weight once daily, according to the following table:

Weight of dog (kg)	MiPet Benazapet® 2.5 mg	
	Standard Dose	Double Dose
2.5 – 5	0.5 tablet	1 tablet
>5 – 10	1 tablet	2 tablets

The dose may be doubled, still administered once daily, to a minimum dose of 0.5 mg/kg (range 0.5-1.0), if judged clinically necessary and advised by the veterinary surgeon.

Cats:
MiPet Benazapet should be administered orally at a minimum dose of 0.5 mg (range 0.5-1.0) benazepril hydrochloride/kg body weight once daily according to the following table:

Weight of Cat (kg)	MiPet Benazapet® 2.5 mg
2.5 – 5	1 tablet
>5 – 10	2 tablets

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

MiPet Benazapet reduced erythrocyte counts in normal cats when dosed at 10 mg/kg body weight once daily for 12 months and in normal dogs when dosed at 150 mg/kg body weight once daily for 12 months, but this effect was not observed at the recommended dose during clinical trials in cats or dogs.
Transient reversible hypotension may occur in cases of accidental overdose. Therapy should consist of intravenous infusion of warm isotonic saline.

4.11 Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: ACE Inhibitors, plain.
ATCvet code: QC09AA07

5.1 Pharmacodynamic properties

Benazepril hydrochloride is a prodrug hydrolysed *in vivo* to its active metabolite, benazeprilat. Benazeprilat is a highly potent and selective inhibitor of ACE, thus preventing the conversion of inactive angiotensin I to active angiotensin II and thereby also reducing synthesis of aldosterone. Therefore, it blocks effects mediated by angiotensin II and aldosterone, including vasoconstriction of both arteries and veins, retention of sodium and water by the kidney and remodelling effects (including pathological cardiac hypertrophy and degenerative renal changes).

MiPet Benazapet causes long-lasting inhibition of plasma ACE activity in dogs and cats, with more than 95% inhibition at peak effect and significant activity (>80% in dogs and >90% in cats) persisting 24 hours after dosing.

MiPet Benazapet reduces the blood pressure and volume load on the heart in dogs with congestive heart failure.

In cats with experimental renal insufficiency, MiPet Benazapet normalized the elevated glomerular capillary pressure and reduced the systemic blood pressure.

Reduction in glomerular hypertension may retard the progression of kidney disease by inhibition of further damage to the kidneys. Placebo controlled clinical field studies in cats with chronic kidney disease (CKD) have demonstrated that MiPet Benazapet

significantly reduced levels of urine protein and urine protein to creatinine ratio (UPC); this effect is probably mediated via reduced glomerular hypertension and beneficial effects on the glomerular basement membrane.

No effect of MiPet Benazapet on survival in cats with CKD has been shown, but MiPet Benazapet increased the appetite of the cats, particularly in more advanced cases.

5.2 Pharmacokinetic particulars

After oral administration of benazepril hydrochloride, peak levels of benazepril are attained rapidly (T_{max} 0.5 hour in dogs and within 2 hours in cats) and decline quickly as the active substance is partially metabolised by liver enzymes to benazeprilat. The systemic bioavailability is incomplete (~13% in dogs) due to incomplete absorption (38% in dogs, <30% in cats) and first pass metabolism.

In dogs, peak benazeprilat concentrations (C_{max} of 37.6 ng/ml after a dose of 0.5 mg/kg benazepril hydrochloride) are achieved with a T_{max} of 1.25 hours.
In cats, peak benazeprilat concentrations (C_{max} of 77.0 ng/ml after a dose of 0.5 mg/kg benazepril hydrochloride) are achieved with a T_{max} of 2 hours.
Benazeprilat concentrations decline biphasically: the initial fast phase ($t_{1/2}$=1.7 hours in dogs and $t_{1/2}$=2.4 hours in cats) represents elimination of free drug, while the terminal phase ($t_{1/2}$=19 hours in dogs and $t_{1/2}$=29 hours in cats) reflects the release of benazeprilat that was bound to ACE, mainly in the tissues.
Benazepril and benazeprilat are extensively bound to plasma proteins (85-90%), and in tissues are found mainly in the liver and kidney.

There is no significant difference in the pharmacokinetics of benazeprilat when benazepril hydrochloride is administered to fed or fasted dogs. Repeated administration of MiPet Benazapet leads to slight bioaccumulation of benazeprilat (R=1.47 in dogs and R=1.36 in cats with 0.5 mg/kg), steady state being achieved within a few days (4 days in dogs).

Benazeprilat is excreted 54% via the biliary and 46% via the urinary route in dogs and 85% via the biliary and 15% via the urinary route in cats. The clearance of benazeprilat is not affected in dogs or cats with impaired renal function and therefore no adjustment of MiPet Benazapet dose is required in either species in cases of renal insufficiency.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose microcrystalline
Crospovidone
Povidone
Basic butylated methacrylate copolymer
Silicon dioxide anhydrous
Silica colloidal anhydrous
Sodium laurilsulphate
Dibutyl sebacate

Castor oil hydrogenated
Yeast powder
Vanillin

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 30 months.

6.4 Special precautions for storage

Do not store above 25 °C.
Store in a dry place.
Each time an unused half tablet is stored, it should be returned to the open blister space inserted back into the cardboard box and kept in a safe place out of the reach of children.

6.5 Nature and composition of immediate packaging

PVC/PE/PVdC-aluminium blisters with 14 tablets/blister. Cardboard box with 4 blisters.

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 local requirements.

7. MARKETING AUTHORISATION HOLDER

Elanco Europe Ltd.
Form 2, Bartley Way
Bartley Wood Business Park
Hook
RG27 9XA
United Kingdom

8. MARKETING AUTHORISATION NUMBER

Vm 00879/4000

9. DATE OF FIRST AUTHORISATION

16 September 2015

10. DATE OF REVISION OF THE TEXT

January 2021

Approved: 12/01/21