Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Benakor 2.5 mg, film-coated tablets for cats.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains:

Active substance:

Benazepril	2.3 mg
(equivalent to 2.5 mg benazepril hydrochloride)	

Excipients:

Titanium dioxide (E-171)	0.53 mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.
White oval divisible tablets scored on both sides.
The tablets can be divided into equal halves.

4 CLINICAL PARTICULARS

4.1 Target Species

Cats.

4.2 Indications for use, specifying the target species

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 (see 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 cats during clinical trials, however, as is routine in cases of chronic kidney disease, it is recommended to monitor plasma creatinine, urea and erythocyte counts during therapy.

The efficacy and safety of the product has not been established in dogs and cats below 2.5 kg body weight.

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 cats with chronic kidney disease, benazepril hydrochloride 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.
Benazepril hydrochloride may increase food consumption and body weight in cats.

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

4.7 Use during pregnancy, lactation or lay

Do not use during pregnancy or lactation. The safety of the product has not been established in breeding, pregnant or lactating 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 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 benazepril hydrochloride 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 Benazepril hydrochloride in combination with a potassium sparing diuretic because of the risk of hyperkalaemia.

4.9 Amounts to be administered and administration route

The product 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)	Benakor 2.5 mg film-coated tablets
2.5 – 5 >5 – 10	1 tablet 2 tablets

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

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

4.11 Withdrawal Period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL 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 degenerative renal changes).

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

In cats with experimental renal insufficiency, benazepril hydrochloride 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 benazepril hydrochloride 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 benazepril hydrochloride on survival in cats with CKD has been shown, but benazepril hydrochloride increased the appetite of the cats, particulary in mor advanced cases.

5.2 Pharmacokinetic properties

After oral administration of benazepril hydrochloride, peak levels of benazepril are attained rapidly (T_{max} 0.43 hours in cats) and decline quickly as the active substance is partially metabolised by liver enzymes to benazeprilat. The systemic bioavailability is incomplete due to incomplete absorption (<30% in cats) and first pass metabolism.

In cats, peak benazeprilat concentrations (C_{max} of 479.2 ng/ml after a dose of 0.95 mg/kg benazepril hydrochloride) are achieved with a Tmax of 1.91 hours.

Benazeprilat concentrations decline biphasically: the initial fast phase ($t_{1/2}$=2.4 hours in cats) represents elimination of free drug, while the terminal phase ($t_{1/2}$ = 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 the product leads to slight bioaccumulation of benazeprilat (R=1.36 in cats with 0.5 mg/kg), steady state being achieved within a few days.
Benazeprilat is excreted 85% via the biliary and 15% via the urinary route in cats. The clearance of benazeprilat is not affected in cats with impaired renal function and therefore no adjustment of benazepril hydrochloride dose is required in cats in cases of renal insufficiency.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Lactose monohydrate
Cellulose microcrystalline
Maize Starch, pregelatinised
Castor oil hydrogenated
Crospovidone
Silica colloidal anhydrous

Tablet coating:
Macrogol poly(vinyl alcohol) grafted copolymer
Poly(vinyl alcohol)
Talc
Macrogol 6000
Titanium dioxide
Silica colloidal anhydrous

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Tablet halves should be used within 2 days.

6.4 Special precautions for storage

Store below 25°C in original blister. 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.

6.5 Nature and composition of immediate packaging

PVC/PCTFE – aluminium blister containing 14 film-coated tablets.
Cardboard box with

- 1 blister (14 tablets);
- 2 blisters (28 tablets);
- 7 blisters (98 tablets);
- 10 blisters (140 tablets).

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

7 MARKETING AUTHORISATION HOLDER

Le Vet Beheer B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands

8 MARKETING AUTHORISATION NUMBER(S)

VPA: 10475/001/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24th September 2012

10 DATE OF REVISION OF THE TEXT