Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Benakor 20 mg tablets for dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Benazepril hydrochloride 20 mg

Excipient:
Colourant: Iron oxides (E172) 8 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets.
Orange oblong divisible tablets, with a break mark on both sides.

4 CLINICAL PARTICULARS

4.1 Target Species

Dogs

4.2 Indications for use, specifying the target species

Treatment of congestive heart failure.

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

Special precautions for use in animals
No evidence of renal toxicity to the product has been observed in dogs 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.

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, benazepril hydrochloride 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 dogs with chronic kidney disease, the product 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.

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 dogs. Embryotoxic effects (foetal urinary tract malformation) were seen in trials with laboratory animals (rats) at maternally nontoxic doses.

4.8 Interaction with other medicinal products and other forms of interactions

In dogs with congestive heart failure, benazepril hydrochloride 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 antihypertensive efficacy or impaired renal function. The combination of benazepril hydrochloride and other antihypertensive 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 given orally once daily, with or without food. The duration of treatment is unlimited.

The product 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)	Benakor 20 mg	
	Standard dose	Double dose
>20-40	0.5 tablet	1 tablet
>40-80	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.

In case of using halved tablets: Put the remaining half of a divided tablet back in the blister pocket and store it in a dry place below 25ºC. Use the remaining tablet half for the next administration.

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

Benazepril hydrochloride reduced erythrocyte counts 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 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(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: ACE inhibitors, plain
ATC-vet code: QC09AA07

5.1 Pharmacodynamic properties

Benazepril hydrochloride is a pro-drug 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).

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

The product reduces the blood pressure and volume load on the heart in dogs with congestive heart failure.

5.2 Pharmacokinetic particulars

After oral administration of benazepril hydrochloride, peak levels of benazepril are attained rapidly (T_{max}1.1 hours in dogs) 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) and first pass metabolism. In dogs, peak benazeprilat concentrations ($C_{max}$of 384.16 ng/ml after a dose of 1.6 mg/kg benazepril hydrochloride) are achieved with a $T_{max}$of 1.1 hours.

Benazeprilat concentrations decline biphasically: the initial fast phase (t1/2=1.7 hours in dogs) represents elimination of free drug, while the terminal phase (t1/2=19 hours in dogs) 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 benazepril hydrochloride leads to slight accumulation of benazeprilat (R=1.47 in dogs 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. The clearance of benazeprilat is not affected in dogs with impaired renal function and therefore no adjustment of benazepril hydrochloride dose is required in cases of renal insufficiency.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silica colloidal anhydrous (E551)
Microcrystalline cellulose (E460)
Lactose anhydrous
Colorcon Pigment Orange 23069 (Iron oxides, E172)
Sodium cyclamate (E952)
Sodium starch glycolate Type A
Magnesium stearate (E470b).

6.2 Major incompatibilities

Not applicable.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale:
PVC/PE/PVDC-Aluminium blister: 12 months.
Aluminium/Aluminium blister: 36 months.
Tablet halves should be used within one day.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package.
Store tablet halves in the original blister in the original package.

6.5 Nature and composition of immediate packaging

1 carton contains:
1, 2, 3, 4, 5, 6 or 7 PVC/PE/PVDC/Alu-foil blisters of 14 tablets each
or
1,2,3,4,5,6,7 Alu/Alu-foil blisters of 14 tablets each.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Le Vet BV
Wilgenweg 7
3421 TV Oudewater
Netherlands

8 MARKETING AUTHORISATION NUMBER(S)

VPA10816/005/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 July 2013

10 DATE OF REVISION OF THE TEXT

December 2021