Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Virbakor 20 mg film-coated tablet for dogs
Benazepril hydrochloride.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each divisible tablet contains:
Active substance:
Benazepril Hydrochloride.....20 mg
(equivalent to Benazepril 18.42 mg)
Excipients:
Titanium dioxide (E171)..... 1.929 mg
Iron oxide yellow (E172)..... 0.117 mg
Iron oxide red (E172)..... 0.014 mg
Iron oxide black (E172)..... 0.004 mg

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet.
Beige oblong biconvex film-coated divisible tablets.
The tablets can be divided into equal halves.

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 ingredients in 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 of the veterinary medicinal 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

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.
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.

4.6 Adverse reactions (frequency and seriousness)

In double-blind clinical trials in dogs with congestive heart failure, the incidence of adverse reactions in treated dogs was lower than that 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 non-toxic doses.

4.8 Interaction with other medicinal products and other forms of interaction

In dogs with congestive heart failure, the product 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 the product 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 the product in combination with a potassium sparing diuretic because of the risk of hyperkalaemia.

4.9 Amounts to be administered and administration route

Oral use.

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 bodyweight once daily, according to the following table:

Weight of dog (kg)	VIRBAKOR 20 mg Film-Coated Tablets	
	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.

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

The product reduced erythrocyte counts in clinical healthy dogs when dosed at 150 mg/kg 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.
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).

The product causes long-lasting inhibition of plasma ACE activity, 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 properties

After oral administration of benazepril hydrochloride, peak levels of benazepril are attained rapidly (T_{max} 0.5 hour 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 40.9 ng/ml after a dose of 0.5 mg/kg benazepril hydrochloride) are achieved with a T_{max} of 1.5 hours.

Benazeprilat concentrations decline biphasically: the initial fast phase ($t_{1/2}$= 1.7 hours in dogs) represents elimination of free drug, while the terminal phase ($t_{1/2}$= 12.4 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 the veterinary medicinal product leads to slight bioaccumulation 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 the product dose is required in cases of renal insufficiency.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Iron oxide yellow (E-172)
Iron oxide red (E-172)
Iron oxide black (E-172
Titanium dioxide (E-171)
Cellulose microcrystalline
Lactose monohydrate
Povidone
Maize starch
Silica colloidal anhydrous
Magnesium stearate
Hypromellose
Macrogol 8000

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life of halved tablet: 1 day.

6.4 Special precautions for storage

Do not store above 25°C. Store in a dry place.
Return any halved tablet to the blister pack and use within 1 day.
The blister pack should be inserted back into the cardboard box.

6.5 Nature and composition of immediate packaging

Blister made of clear film of PVC/PE/PVDC and aluminium film containing 14 tablets.
Carton box with:
- 1 blister (14 tablets)
- 10 blisters (140 tablets).

Not all pack size 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 materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

VIRBAC
1ère avenue 2065 m LID
06516 Carros
France

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10988/093/002

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30th January 2015

10 DATE OF REVISION OF THE TEXT