SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BENADIL 20 mg, film-coated tablets for dogs (BE, CZ, DE, HU, LU, NL, PL, PT, SK)
BENADIL 20, film-coated tablets for dogs (FR)
KELAPRIL 20 mg, film-coated tablets for dogs (UK)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains:
Active substance:
Benazepril Hydrochloride..... 20 mg
(equivalent to Benazepril 18.4 mg)

Excipients:

Titanium dioxide (E171)	0.52 mg
Iron oxide red (E172)	0.06 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet
Reddish-pink, oval divisible tablets scored on both sides.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Dogs:
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 in 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 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.

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

Wash hands after use.
To avoid accidental ingestion, particularly by a child, unused part-tablets should be returned to the open blister space and inserted back into the carton.
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, the product 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.

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 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.

Dogs:
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)	Kelapril 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.

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

The product reduced erythrocyte counts in normal 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

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).

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 particulars

After oral administration of benazepril hydrochloride, peak levels of benazepril are attained rapidly (Tmax 0.58 hour in dogs) and decline quickly as the drug 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 (Cmax of 39.4 ng/ml after a dose of 0.40 mg/kg benazepril hydrochloride) are achieved with a Tmax of 1.43h.

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 the product the 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

Lactose monohydrate
Cellulose microcrystalline
Starch pregelatinised
Castor oil hydrogenated
Crospovidone
Silica colloidal anhydrous

Coating:
Macrogol poly(vinyl alcohol) grafted copolymer
Poly(vinyl alcohol)
Silica colloidal anhydrous
Talc
Macrogol 6000
Titanium dioxide (E171)
Iron oxide red (E172)

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Tablet halves should be used within 2 days.

6.4 Special precautions for storage

Store below 30°C in the original package.
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 used at the next administration.

6.5 Nature and composition of immediate packaging

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

- 2 blisters (28 tablets);
- 7 blisters (98 tablets).

Not all pack sizes may be marketed.

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

Richter Pharma AG
Feldgasse 19
4600 Wels
Austria

8. MARKETING AUTHORISATION NUMBER

Vm 22080/4019

9. DATE OF FIRST AUTHORISATION

12 February 2013

10. DATE OF REVISION OF THE TEXT

January 2020

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription.

Approved: 31 January 2020