1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Benefortin Flavour 20 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substances:
Benazepril hydrochloride 20.0 mg (equivalent to 18.40 mg Benazepril)

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate
Cellulose, microcrystalline
Wheat starch
Sodium starch glycolate (Type A)
Glycerol distearate
Dried yeast
Liver powder flavour
Talc

Brownish, oval, divisible, tablet scored on both sides. The tablets can be divided into equal halves.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Dogs:
Treatment of congestive heart failure.

3.3 Contraindications

Do not use in cases 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.
See also section 3.7.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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.
The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.

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 package leaflet or the label 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.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Undetermined frequency (cannot be estimated from the available data):	Vomiting[1], Fatigue, Elevated creatinine[2], Incoordination

[1]Transient

[2]In dogs with chronic kidney disease, 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.
In double-blind clinical trials in dogs with congestive heart failure, the veterinary medicinal product was well tolerated with an incidence of adverse reactions lower than observed in placebo-treated dogs.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for the relevant contact details.

3.7 Use during pregnancy, lactation or lay

The safety of benazepril hydrochloride has not been established in breeding, pregnant or lactating dogs.

Pregnancy and lactation:
Do not use during pregnancy or lactation.
Embryotoxic effects (foetal urinary tract malformation) were seen in trials with laboratory animals (rats) at maternally non-toxic doses.

Fertility:
Do not use in breeding dogs.

3.8 Interaction with other medicinal products and other forms of interaction

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 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 in combination with a potassium-sparing diuretic because of the risk of hyperkalaemia.

3.9 Administration routes and dosage

Oral use. The veterinary medicinal product should be given orally once daily, with or without food. The duration of treatment is unlimited.
The tablets are flavoured and are taken voluntarily by most dogs.

Tablets 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)	Benamax/Benefortin Flavour 20 mg	
	Standard dose	Double dose
>20- 40	0.5 tablet	1 tablet
>40 – 80	1 tablet	2 tablet

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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Benazepril 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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods
Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code : QC09AA07

4.2 Pharmacodynamics

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).

Benazeprilat 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.

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

4.3 Pharmacokinetics

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 37.6 ng/ml after a dose of 0.5 mg/kg benazepril hydrochloride) are achieved with a T_{max} of 1.25 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 ($t_{1/2}$=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 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 dose of the veterinary medicinal product is required in either species in cases of renal insufficiency.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities
Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 18 months.
Shelf life of tablet halves: 2 days.

5.3 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.

5.4 Nature and composition of immediate packaging

PVC/Aluminium/Polyamide blister -forming laminate with aluminium lidding foil with 7 tablets/blister.
Cardboard box with 1 blister strip of 7 tablets (7 tablets)
Cardboard box with 2 blister strips of 7 tablets (14 tablets)
Cardboard box with 4 blister strips of 7 tablets (28 tablets)
Cardboard box with 10 blister strips of 7 tablets (70 tablets)

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Lavet Pharmaceuticals Ltd.

7. MARKETING AUTHORISATION NUMBER(S)

VPA10482/001/003

8. DATE OF FIRST AUTHORISATION

27/01/2012

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

15/10/2026

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).