Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

ARIXIL vet 20 mg film-coated tablet for dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated 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 tablets. The tablets can be divided into halves.
Beige oblong biconvex tablets with a score line.

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 cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in cases of cardiac output failure, due to aortic or pulmonary stenosis.
Do not use in cases of hypotension, hypovolaemia, hyponatraemia or acute renal failure.
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

Special precautions for use in animals
No evidence of renal toxicity to 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 efficacy and safety of the veterinary medicinal product has not been established in dogs below 2.5 kg body weight.

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 enzymes (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 veterinary medicinal product was well tolerated with an incidence of adverse reactions in treated dogs 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 veterinary medicinal 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, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Do not use during pregnancy or lactation. The safety of the veterinary medicinal 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. Do not use in breeding dogs.

4.8 Interaction with other medicinal products and other forms of interactions

In dogs with congestive heart failure, the veterinary medicinal product has been given in combination with digoxin, diuretics, pimobendane 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 veterinary medicinal product in combination with a potassium sparing diuretic because of the risk of hyperkalaemia.

4.9 Amounts to be administered and administration route

For oral use.
It should be given orally once daily, with or without food. The dose is 0.23 mg benazepril /kg bw per day, corresponding to 0.25 mg of Benazepril hydrochloride / kg bw per day, according to the following table:

Weight of dog (kg)	Number of tablets
>20 - 40	1/2 tablet
>40 - 80	1 tablet

Dosage may be doubled, still administered once daily, if judged clinically necessary and advised by the veterinary surgeon.

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

The veterinary medicinal product 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 cats or 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, benazepril.
ATC vet code: QC09AA07

5.1 Pharmacodynamic properties

Benazepril hydrochloride is a prodrug hydrolysed in vivo to its active metabolite, benaprezilat.
Benaprezilat is a highly potent and selective inhibitor of angiotensin converting enzyme (ACE), thus preventing the conversion of inactive angiotensin I to its 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 veterinary medicinal 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 veterinary medicinal 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 0.5 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 (Cmax of 40.9 ng/ml after a dose of 0.5 mg/kg benazepril hydrochloride) are achieved with a Tmax of 1.5 hours.
Benazeprilat concentrations decline biphasically: the initial phase (t1/2=1.7 hours in dogs) represents elimination of free drug, while the terminal phase (t1/2=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

Constituents of the tablet core:
Cellulose microcrystalline
Lactose monohydrate
Povidone
Maize starch
Silica colloidal anhydrous
Magnesium stearate
Constituents of the coating:

Iron oxide yellow (E-172)
Iron oxide red (E-172)
Iron oxide black (E-172
Titanium dioxide (E-171)
Hypromellose
Macrogol 8000

6.2 Major incompatibilities

Not applicable.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf-life of half tablets: 24 hours

6.4 Special precautions for storage

Do not store above 25°C.
Store in a dry place.
Store in the outer carton in order to protect from light.
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.
Box with:
- 1 blister (14 tablets)
- 2 blisters (28 tablets)
- 4 blisters (56 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 derived from the use of such products

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

7 MARKETING AUTHORISATION HOLDER

Vetpharma Animal Health, S.L.
Les Corts, 23
08028 Barcelona
Spain

8 MARKETING AUTHORISATION NUMBER(S)

VPA10516/020/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 05 April 2019

10 DATE OF REVISION OF THE TEXT