Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Actikor 20 mg Film-coated Tablets for Dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Active substance:
Benazepril 18.4 mg (equivalent to 20 mg of benazepril hydrochloride).

Excipient(s):
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets.

Tan coloured, oval, biconvex, film-coated tablets with a breakline on one side and plain on the other side.

The tablets can be divided into two equal parts.

4 CLINICAL PARTICULARS

4.1 Target Species

Dog

4.2 Indications for use, specifying the target species

Dogs weighing more than 20 kg:

Treatment of congestive heart failure associated with, in particular, dilated cardiomyopathy or mitral insufficiency.

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 hypotension, hypovolaemia, hyponatraemia or acute renal failure.
Do not use in cases of cardiac output failure due to aortic stenosis 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 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

- ACE inhibitors have been found to affect the unborn child during pregnancy in humans. Pregnant women should take special care to avoid accidental exposure, including hand-to-mouth contact.
- Wash hands after use.
- Benazepril may cause hypotension after oral ingestion.
- In case of accidental ingestion, particularly by children, seek medical advice immediately and show the package leaflet or the label 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

Studies in laboratory animals (rats) have shown embryotoxic effects of benazepril at non-maternotoxic doses (malformations of the foetal urinary system). Benazepril administered to cats at a daily dose of 10 mg/kg for 52 weeks resulted in the reduction of ovary/oviduct weights. In humans ACE inhibitors have been found to be teratogenic during pregnancy.
Do not use in breeding, pregnant or lactating dogs as the safety of the product in these animals has not been tested.

4.8 Interaction with other medicinal products and other forms of interaction

None known in dogs.

In dogs with heart failure, Benazepril hydrochloride has been given in combination with digoxin, diuretics and anti-arrythmic drugs without demonstrable adverse interactions. In human, the combination of ACE inhibitors and 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 closely monitored 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 as life threatening reactions are a possibility.

4.9 Amounts to be administered and administration route

For oral use.

The therapeutic oral dose is 0.25 mg benazepril hydrochloride/kg body weight once daily, with or without food according to the following dose regime:

Dogs weighing 5-10 kg: ½ Actikor 5 mg tablet.
Dogs weighing 11-20 kg: 1 Actikor 5 mg tablet.
Dogs weighing 21-40 kg: ½ Actikor 20 mg tablet.
Dogs weighing 41-80 kg: 1 Actikor 20 mg tablet.

The dose may be doubled (0.5 mg benazepril hydrochloride/kg body weight) still administered once daily, 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 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 overdosage. Therapy should consist of intravenous infusion of warm isotonic saline.

4.11 Withdrawal Period(s)

Not applicable.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Cardiovascular system, agents acting on the renin- angiotensin system, ACE inhibitors, plain, benazepril.
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 angiotensin converting enzyme (ACE), thus preventing the conversion of inactive angiotensin I to active angiotensin II. Therefore, it blocks effects mediated by angiotensin II, including vasoconstriction of both arteries and veins, retention of sodium and water by the kidney.

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

5.2 Pharmacokinetic properties

After oral administration of benazepril hydrochloride, peak levels of benazepril are attained rapidly (tmax 0.5 h) and decline quickly as the drug is partially metabolised by liver enzymes to benazeprilat. Unchanged benazepril and hydrophilic metabolites account for the remainder. Peak benazeprilat concentrations (Cmax of 26.7 ng/ml after a dose of 0.5 mg/kg benazepril hydrochloride) are achieved with a Tmax of 1.25h. The systemic bioavailability is incomplete (~13 %) due to incomplete absorption (38 %) and first pass metabolism.
Benazeprilat concentrations decline biphasically: the initial fast phase ($t_{1/2}$=1.7h) represents elimination of free drug, while the terminal phase ($t_{1/2}$=19h) reflects the release of benazeprilat that was bound to ACE, mainly in the tissues.
Benazepril and benazeprilat are extensively bound to plasma proteins, 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 leads to slight bioaccumulation of benazeprilat (R=1.47 with 0.5 mg/kg), steady state being achieved within a few days (4 days).
Benazeprilat is excreted via the biliary (54 %) and urinary (46 %) routes. 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

Colloidal anhydrous silica
Cellulose, Microcrystalline
Lactose monohydrate
Pregelatinised maize starch
Crospovidone
Hypromellose
Iron oxide red (E172)
Iron oxide yellow (E172)
Macrogol 8000
Purified Talc
Titanium dioxide (E171)
Zinc Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

Shelf life of veterinary medicinal product as packaged for sale - 3 years

6.4 Special precautions for storage

Do not store above 30 °C.
In case of using halved tablets: Return any remaining half tablet to the opened blister pocket.
Use the remaining half tablet for the next administration.

6.5 Nature and composition of immediate packaging

Tablets are presented in aluminium foil blister packs of 14, 28, 56, 84 and 140 tablets.

Not all pack sizes 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

Ecuphar NV
Legeweg 157-i
8020 Oostkamp
Belgium

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10491/002/002

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17th June 2011

Date of last renewal: 17th June 2016

10 DATE OF REVISION OF THE TEXT

July 2016