



## FOR VETERINARY USE ONLY

### For dogs and cats

#### Description:

The active ingredient in FORTEKOR is benazepril hydrochloride which is a second generation non-sulphydryl angiotensin converting enzyme (ACE) inhibitor. Following oral administration, benazepril hydrochloride is absorbed and converted by the liver to its active metabolite, benazeprilat.

Benazeprilat acts by inhibiting angiotensin converting enzyme (ACE). This enzyme is part of the renin-angiotensin cascade system and converts inactive Angiotensin I into biologically-active Angiotensin II, the hormone controlling vasoconstriction and release of aldosterone. Thus, ACE inhibitors prevent constriction of the blood vessels, thereby facilitating blood flow and reducing hypertension.

#### Indications:

FORTEKOR is indicated for:

- (1) The treatment of heart failure in dogs caused by mitral regurgitation or dilated cardiomyopathy, in combination with standard therapy.
- (2) As an aid in the management of chronic renal insufficiency associated with proteinuria in cats.

#### Dosage and Administration:

##### Heart Failure in Dogs:

The minimum recommended dose is 0.25 mg/kg body weight, to be given once daily orally according to the following regime:

Dog Weight (kg)	FORTEKOR (2.5 mg)	FORTEKOR (5 mg)	FORTEKOR (20 mg)
2.5 – 5	0.5 tablet	–	–
> 5 – 10	1 tablet	0.5 tablet	–
> 10 – 20	–	1 tablet	–
> 20 – 40	–	2 tablets	0.5 tablet
> 40 – 80	–	–	1 tablet

FORTEKOR can be given with or without food. The duration of treatment is unlimited. The dose can be doubled, still administered once daily, if judged clinically necessary and advised by the veterinarian. FORTEKOR may be given in combination with digoxin, diuretics and anti-arrhythmic drugs as necessary.

##### Chronic Renal Insufficiency in Cats:

The recommended dose is 0.5 mg benazepril hydrochloride / kg body weight, to be given orally once daily according to the following regime:

Cat Weight (kg)	FORTEKOR (2.5mg)	FORTEKOR (5 mg)
2.5 – 5	1 tablet	0.5 tablet
> 5 – 10	2 tablets	1 tablet

FORTEKOR can be given with or without food. The duration of treatment is unlimited.

#### Pharmacology:

1. **Pharmacodynamic Properties:** FORTEKOR contains benazepril hydrochloride, a prodrug hydrolysed *in vivo* to benazeprilat which inhibits angiotensin converting enzyme (ACE), thus preventing the conversion of inactive angiotensin I into active angiotensin II. FORTEKOR reduces all effects mediated by angiotensin II, including vasoconstriction of both arteries and veins and retention of sodium and water by the kidney. FORTEKOR causes long-lasting inhibition of plasma ACE in dogs and cats, with significant inhibition persisting for 24 hours after a single dose. FORTEKOR reduces the pressure and volume load on the heart in dogs with heart failure, and leads to improvements in the quality of life and clinical signs, notably coughing. FORTEKOR also produces a significant reduction in the frequency of mortality as compared to conventional therapy, consistent with an extension in life span. In cats with chronic renal insufficiency, FORTEKOR reduces the protein loss in urine and lowers the systemic and intraglomerular blood pressure.

2. **Pharmacokinetic Properties:** Benazepril is rapidly but incompletely absorbed from the gastrointestinal tract following oral administration. Absorbed benazepril is partially hydrolyzed by hepatic enzymes to the active substance, benazeprilat; unchanged benazepril and hydrophilic metabolites account for the remainder. Peak plasma benazeprilat concentrations are attained within about two hours both in fasting and fed situations. Benazepril and benazeprilat are bound to plasma proteins, and in tissues are found mainly in the liver and kidney. The major part of benazeprilat is rapidly eliminated, although there is in addition a slow terminal elimination phase. Benazeprilat is excreted approximately equally via both biliary and urinary routes in dogs and primarily via the biliary route in cats. Repeated administration of FORTEKOR leads to slight accumulation of benazeprilat in plasma; steady state is attained within four days. Because of its biliary excretion route, there is little risk of bioaccumulation of benazeprilat in dogs with impaired renal function. For this reason, no dose adjustment of FORTEKOR is necessary in cases of renal insufficiency.

#### Safety:

##### Dogs:

FORTEKOR is well-tolerated by the target species. In normal dogs overdosage up to 200 fold was asymptomatic. Transient reversible hypotension may occur in cases of accidental overdosage. Therapy should consist of intravenous infusion of warm isotonic saline solution.

FORTEKOR has been given in combination with digoxin, diuretics and/or anti-arrhythmic drugs without demonstrable adverse interactions.

##### Cats:

FORTEKOR is well tolerated in the target species. In normal cats treated with 10 and 20 mg/kg/day for one year, the only clinically relevant findings were increased urine volume and pH in male cats at 10 and 20 mg/kg, increased urine volume in females at 20 mg/kg/day, and decreased urine specific gravity in both male and female cats at 10 and 20 mg/kg/day, as compared to control animals. Trace to mild hypertrophy/hyperplasia of the juxtaglomerular cells was noted on histopathology in cats receiving 10 and 20 mg/kg/day. The clinical relevance of these changes is unknown.

Transient reversible hypotension may occur in cases of accidental overdosage. Therapy should consist of intravenous infusion of warm isotonic saline.

##### Caution:

##### Dogs:

No evidence of renal toxicity to FORTEKOR has been observed in dogs during clinical trials. Because of the biliary excretion of benazeprilat, there is little risk of bioaccumulation in dogs with impaired renal function. For this reason, no dose adjustment of FORTEKOR is necessary in cases of renal insufficiency. However, as is routine, in cases of renal insufficiency, it is recommended to monitor plasma urea and creatinine levels.

Signs of hypotension such as tiredness or dizziness may appear in rare cases. Reduce the dose of the diuretic, if necessary.

The safety of FORTEKOR has not been tested in breeding dogs. FORTEKOR is therefore not recommended for use in pregnant bitches unless justified by the risk/benefit ratio. No data are available in lactating bitches. FORTEKOR should therefore be used only if justified clinically.

##### Cats:

FORTEKOR may increase plasma creatinine concentrations at the start of therapy. This effect is related to the therapeutic effect of the product in reducing blood pressure, and therefore is not necessarily a reason to stop therapy in the absence of other signs. As is routine in cases of chronic renal insufficiency, it is recommended to monitor plasma creatinine during therapy.

Although not demonstrated in cats, benazepril may cause hyperkalemia in some human patients with chronic renal failure. Periodic monitoring of serum potassium levels during therapy is therefore recommended. FORTEKOR reduced erythrocyte counts in normal cats at high doses, but this effect was not observed at the recommended dose during clinical trials in cats with chronic renal insufficiency. As is routine in cases of chronic renal insufficiency it is recommended to monitor erythrocyte counts during therapy.

The safety of FORTEKOR has not been evaluated in cats with acute renal failure, acute exacerbation of chronic renal failure, hypovolemia, dehydration, or concurrent cardiac or hepatic disease. During the clinical trial, benazepril was administered to cats with elevated ALT levels, without specific adverse events being observed.

The safety of FORTEKOR has not been tested in breeding cats, or pregnant or lactating queens. FORTEKOR should therefore be used only if justified clinically, considering the risk/benefit ratio. ACE inhibitors can cause injury or even death of the developing fetus when used in pregnancy during the second and third trimesters in some species.

There are no known interactions between FORTEKOR and other medications in cats. The combination of ACE inhibitors and other antihypertensive agents (e.g. calcium channel blockers,  $\beta$ -blockers or diuretics) may lead to additive hypotensive effects. In man, the combination of ACE inhibitors and NSAIDs can lead to reduced efficacy of the ACE inhibitor or impaired renal function.

##### Adverse Effects:

In rare cases, fatigue or dizziness may be observed. In double-blind clinical trials, FORTEKOR was well tolerated with an incidence of adverse effects statistically lower than observed in placebo-treated dogs.

##### Warning:

Keep this and all drugs out of the reach of children.

##### Presentations:

Fortekor (2.5 mg) – palatable beige, ovaloid tablets which are scored on both sides, and contain 2.5 mg benazepril hydrochloride. Packaged in plastic blister packs each containing 14 tablets, 2 or 4 blisters to a pack.

Fortekor (5 mg) and (20 mg) – palatable beige to light brown tablets which are scored on both sides, and contain either 5 mg benazepril hydrochloride (Fortekor 5 mg) or 20 mg benazepril hydrochloride (Fortekor 20 mg). Packaged in aluminum blister packs each containing 14 tablets. Packs of 1, 2, 4 or 10 blisters.

##### Storage Conditions:

Store at or below 25° C, in a dry place. Unused half tablets should be returned to the open blister space and replaced within the cardboard box, and used within 2 days. Protect 2.5 mg tablets from light.

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