

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Benamix 6.25 mg/g premix for medicated feeding stuff for cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:

Benazepril hydrochloride	6.25 mg
equivalent to Benazepril	5.76 mg

Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Butylhydroxyanisole (E320)	0.2 mg
Silica colloidal anhydrous	
Polysorbate 80	
Triglycerides, medium chain	

White to yellow suspension.

3. CLINICAL INFORMATION

In accordance with Regulation 2019/4, the medicated feed label must include in a simple, clear and easily understandable manner all the bolded clinical information listed in sections 3.1 to 3.12.

3.1 Target species

Cats.

3.2 Indications for use for each target species

Reduction of proteinuria associated with chronic kidney disease.

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.

Do not use during pregnancy or lactation (see section 3.7.).

3.4 Special warnings

The uptake of the medicated feed can be altered as a consequence of CKD or other diseases and should be monitored. In case of insufficient feed intake, i.e less than 50% of the prescribed feed intake for more than 7 consecutive days, the efficacy of the treatment cannot be guaranteed and the animal should be presented to a veterinarian in order to investigate the cause of this diminished feed

intake and apply the suitable treatment. Cats suffering from anorexia or inappetence should not be treated via medicated feed.

To ensure a better acceptance of the new feed and to avoid digestive issues, a feed transition may be implemented over some days at the discretion of the veterinarian.

3.5 Special precautions for use

Special precautions for safe use in the target species:

If more than one cat is living in the household, ensure that only the cat for which this treatment is prescribed has access to the medicated feed, and that the cat being treated receives the appropriate dose (i.e., amount of medicated feed)

No evidence of renal toxicity of benazepril has been observed 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 cats below 2.5 kg body weight.

The use of a Renin-Angiotensin-Aldosterone System (RAAS) inhibitor is not recommended in any cat that is clinically dehydrated or is showing signs of hypovolemia. Check and correct dehydration before using these drugs, otherwise glomerular filtration rate may drop precipitously if these drugs are introduced before the patient is adequately hydrated.

Precautions to be taken by the person administering the medicated feed to animals:

The medicated feed may be harmful when ingested by children.

Avoid accidental ingestion.

The medicated feed and the feed bowl should be placed out of the reach and sight of children.

In case of accidental oral ingestion, seek medical advice immediately and show the label of the medicated feed to the physician.

Angiotensin converting enzyme (ACE) inhibitors have shown to affect the foetus.

Pregnant women, and women of childbearing potential, should take special care to avoid any skin exposure with the medicated feed, including oral exposure due to hand-to-mouth contact.

In case of accidental skin exposure or accidental ingestion, wash or rinse thoroughly and immediately with water, seek medical advice and show the label of the medicated feed to the physician.

Angiotensin converting enzyme (ACE) may cause hypersensitivity reactions.

People with known hypersensitivity to benazepril should avoid contact.

In case of hypersensitivity reactions, seek medical advice and show the label of the medicated feed to the physician.

Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cats.

Rare (1 to 10 animals / 10,000 animals treated):	Diarrhoea, Emesis Anorexia, Dehydration, Lethargy
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Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Elevated creatinine¹ Increased appetite, Weight gain
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¹ **In cats 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.**

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 respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during breeding, pregnancy and lactation.

Pregnancy and lactation:

Benazepril reduced ovary/oviduct weights in cats when administered daily at the overdose of 10 mg/kg body weight for 52 weeks. Embryotoxic effects (foetal urinary tract malformation) were seen in trials with laboratory animals (rats) at maternally non toxic doses.

Do not use during pregnancy or lactation.

3.8 Interaction with other medicinal products and other forms of interaction

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 veterinary medicinal 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, telmisartan 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.

3.9 Administration routes and dosage

In-feed use.

Only to be mixed into dry feed by a feed business operator.

The veterinary medicinal product is a premix intended for the manufacture of medicated feeding stuff. Do not administer the veterinary medicinal product other than mixed with feed by an authorized manufacturer of medicated feed.

Mixing

instructions:

The barrel should be shaken about 20 seconds before use.

The incorporation process should consist in the incorporation of the whole barrel through simple mixing steps performed under normal conditions of temperature.

The premix should be incorporated only by a coating process at the coating stage of the kibbles. An appropriate amount of fat and a palatable agent for cats should be incorporated in the external coating of the kibble. The premix should not be incorporated in the feed during the extrusion of the kibbles or by another process than coating.

To ensure the shelf-life of 12 months after incorporation in the feed, it is recommended that the medicated feed be filled into a bag with an aluminized layer and an internal polyethylene PE layer, and stored at a temperature not above 25°C.

The veterinary medicinal product should be administered orally after incorporation in feed in order to achieve a minimum dose of 0.5 mg (range 0.5 - 1.0) benazepril hydrochloride/kg body weight per day. In order to obtain the correct dosage, the concentration of the premix in the medicated feed may need to be adjusted accordingly by the feed business operator, taking into account the metabolizable energy of the feed.

In case the veterinary medicinal product is mixed at an incorporation rate of 72mg of benazepril per kg feed into a feed appropriate for renal patients, with a metabolizable energy of 416 kcal/ 100g, the feeding recommendation table might read as follows:

Body Weight (kg)	Range of daily ration (g/day) depending on the body condition and the activity of the cat*
2.5 - 2.9	25 - 35
3.0 - 3.4	25 - 35
3.5 - 3.9	30 - 45
4.0 - 4.4	35 - 50
4.5 - 4.9	40 - 55
5.0 - 5.4	45 - 60
5.5 - 5.9	50 - 65
6.0 - 6.4	55 - 75
6.5- 6.9	60 - 80
7.0 - 7.4	65 - 85
7.5 - 7.9	70 - 90
8.0 - 8.4	75 - 95
8.5 - 8.9	80 - 105
9.0 - 9.4	80 - 110
9.5 - .9.9	85 - 115
10.0 - 10.4	90 - 120

***for adult neutered indoor cat with optimal BW: recommended ration is 9 g/kg BW/day**

The intake of medicated feed depends on the body weight, the activity and the body condition of the animal.

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

Benazepril reduced erythrocyte counts in normal cats when dosed at 10 mg/kg body weight once daily for 12 months, but this effect was not observed at the recommended dose during clinical trials in cats.

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 the angiotensin converting enzyme (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 remodeling effects (including pathological cardiac hypertrophy and degenerative renal changes).

In cats with experimental renal insufficiency, benazepril normalised the elevated glomerular capillary pressure and reduced the systemic blood pressure. Reduction in glomerular hypertension may retard the progression of kidney disease by inhibition of further damage to the kidneys. Placebo controlled clinical field studies in cats with chronic kidney disease (CKD) have demonstrated that benazepril significantly reduced levels of urine protein and the urine protein to creatinine ratio (UPC); this effect is probably mediated via reduced glomerular hypertension and beneficial effects on the glomerular basement membrane.

4.3 Pharmacokinetics

After oral administration of benazepril hydrochloride (pro-drug) via the feed, peak levels of benazepril are attained between 3 and 5 hours in cats and decline quickly as it is partially metabolised by liver enzymes to benazeprilat.

In the literature, after administration of a tablet at a dose of 1 mg/kg benazepril hydrochloride, 23% of the benazepril dose is absorbed and 13% of this absorbed fraction is metabolised to benazeprilat. The systemic bioavailability of benazeprilat is therefore 3%.

Benazepril and benazeprilat are extensively bound to plasma proteins (>80%), and in tissues are found mainly in the liver and kidney.

Benazeprilat is excreted 85% via the biliary and 15% via the urinary route. The clearance of benazeprilat is not affected in cats with impaired renal function and therefore no adjustment of the dose of the veterinary medicinal product is required in cases of renal insufficiency.

After administration of 0.5 mg/kg benazepril hydrochloride via the feed, peak benazeprilat concentrations (C_{max}) of around 16 ng/ml are achieved with a T_{max} of around 13 hours.

When given via the feed, no effect of speed of feed consumption (less than 30 minutes or within 24 hours) on plasmatic concentrations and pharmacokinetic parameters has been shown.

Benazeprilat concentrations decline biphasically: the initial fast phase ($t_{1/2}$ between 1 and 3 hours) represents elimination of free drug, while the terminal phase ($t_{1/2}$ between 12 and 27 hours) reflects the release of benazeprilat that was bound to ACE, mainly in the tissues.

Repeated administrations of benazepril hydrochloride via the feed leads to slight bioaccumulation of benazeprilat ($R=1.5$ in cats with 0.5 mg/kg/day), steady state being achieved within 2.5 days.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

Shelf life after first opening the immediate packaging: use immediately.

Shelf life of the medicated feed : 12 months.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

5.4 Nature and composition of immediate packaging

Plastic barrel (high density polyethylene) closed by a plastic screw cap (polypropylene cap equipped with an inviolability ring and a polyethylene seal)

Pack size:

Plastic barrel of 5 L containing 4.23 L (or 4.032 kg).

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

VIRBAC S.A.,

7. MARKETING AUTHORISATION NUMBER(S)

VPA10988/119/001

8. DATE OF FIRST AUTHORISATION

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

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 \(https://medicines.health.europa.eu/veterinary\)](https://medicines.health.europa.eu/veterinary).