SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NELIO 5 mg TABLET FOR CATS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains
Active substance:
Benazepril hydrochloride .....5 mg

Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet
Clover shaped scored beige tablet, divisible into halves or quarters.

4. CLINICAL PARTICULARS

4.1 Target species

Cats.

4.2 Indications for use, specifying the target species

Cats:
Reduction of proteinuria associated with chronic kidney disease.

4.3 Contraindications

Do not use in case 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 (section 4.7).

4.4 Special warnings for each target species

None

4.5 Special precautions for use

Special precautions for use in animals
Efficacy and safety of benazepril have not been established in cats of weight less than 2.5 kg.

No evidence of renal toxicity to the veterinary medicinal product has been observed in cats 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
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.

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.

4.6 Adverse reactions (frequency and seriousness)

In cats 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 therefore is not necessarily a reason to stop therapy in the absence of other signs.
The product may increase food consumption and body weight.
Emesis, anorexia, dehydration, lethargy and diarrhoea have been reported in rare occasions.

4.7 Use during pregnancy, lactation or lay

Do not use during pregnancy or lactation. The safety of the product has not been established in breeding, pregnant or lactating cats Benazepril reduced ovary / oviduct weights in cats when administered daily at 10 mg / kg for 52 weeks. Embryotoxic effects (foetal urinary tract malformation) were seen in trials with laboratory animals (rats) at maternally nontoxic doses.

4.8 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 product and other anti-hypertensive agents (e.g. calcium channel blockers, ß-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 product in combination with a potassium sparing diuretic because of the risk of hyperkalaemia.

4.9 Amounts to be administered and administration route

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

Cats:
The product should be administered orally at a minimum dose of 0.5 mg (range 0.5-1.0) benazepril hydrochloride/kg body weight once daily according to the following table:

Cat weight (kg)	Number of tablets
2.5 – 5.0	0.5
>5. – 10.0	1

In case of use of half tablets: Put the remaining half of the tablet back into the blister pocket and use for the next administration.
Instruction on how to divide the tablet: Put the tablet on an even surface, with its scored side facing down (convex face up). With the tip of the forefinger, exert slight vertical pressure on the middle of the tablet to break it along its width into halves. Then, in order to obtain quarters, exert slight pressure on the middle of one half with the forefinger to break it into two parts.

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

The product 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 with warm isotonic saline.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Cardiovascular system, ACE Inhibitor, 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 ACE, thus preventing the conversion of inactive angiotensin I to active angiotensin II and thereby also reducing svnthesis 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 product causes long-lasting inhibition of plasma ACE activity in cats, with more than 95% inhibition at peak effect and significant activity (>90%) persisting 24 hours after dosing.
In cats with experimental renal insufficiency, the product normalized 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 the product significantly reduced levels of urine protein and urine protein to creatinine ratio (UPC); this effect is probably mediated via reduced glomerular hypertension and beneficial effects on the glomerular basement membrane.
No effect of the product on survival in cats with CKD has been shown, but the product increased the appetite of the cats, particularly in more advanced cases.

5.2 Pharmacokinetic particulars

After oral administration of benazepril hydrochloride, peak levels of benazepril are attained rapidly (Tmax 2 hours) and decline quickly as the active substance is partially metabolised by liver enzymes to benazeprilat. The systemic bioavailability is incomplete due to incomplete absorption (<30%) and first pass metabolism.
Peak benazeprilat concentrations (Cmax of 110.0 ng/ml after a dose of 0.65 mg/kg benazepril hydrochloride) are achieved with a Tmax of 1 hour and half.
Benazeprilat concentrations decline biphasically: the initial fast phase (t1/2=2.4 hours) represents elimination of free drug, while the terminal phase (1/2=29 hours) 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.
Repeated administration of the product leads to slight bioaccumulation of benazeprilat (R=1.36 with 0.5 mg/kg), steady state being achieved within a few days.
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 product dose is required in cases of renal insufficiency.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pig liver flavour
Yeast
Lactose monohydrate
Croscarmellose sodium
Anhydrous colloidal silica
Hydrogenated castor oil
Microcrystalline cellulose

6.2 Major incompatibilities

Not known.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 1 year.
Shelf-life of divisions of the tablets: 72 hours.

6.4 Special precautions for storage

Do not store above 25°C
Store in original package in order to protect from moisture.
Any part-used tablet should be returned to the opened blister and used within 72 hours.

6.5 Nature and composition of immediate packaging

Aluminium/Aluminium heat-sealed blister pack 10 tablets per strip.
Box with 1 strip of 10 tablets
Box with 2 strips of 10 tablets
Box with 3 strips of 10 tablets
Box with 5 strips of 10 tablets
Box with 10 strips of 10 tablets
Box with 20 strips of 10 tablets
Box with 50 strips of 10 tablets

Not all pack sizes 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

Ceva Animal Health Ltd
Unit 3, Anglo Office Park
White Lion Road
Amersham
Buckinghamshire
HP7 9FB

8. MARKETING AUTHORISATION NUMBER

Vm 15052/4109

9. DATE OF FIRST AUTHORISATION

27 February 2009

10. DATE OF REVISION OF THE TEXT

October 2021

Approved 06 October 2021