SUMMARY OF PRODUCT CHARACHTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nelio 20 mg Tablet for Dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains
Active substance:
Benazepril hydrochloride.....20 mg

Excipient(s):

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

Dogs

4.2 Indications for use, specifying the target species

Dogs:
- Treatment of congestive heart failure

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

No evidence of renal toxicity of the veterinary medicinal product 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 safety and efficacy of the product has not been examined in dogs weighing less than 2.5 kg.

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 double-blind clinical trials in dogs with congestive heart failure, the product was well tolerated with an incidence of adverse reactions lower than 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

Do not use during pregnancy or lactation. The safety of the product has not been established in breeding, pregnant or lactating dogs. In cats benazepril reduced the weight of the ovaries and the ovarian ducts when given at a daily dose of 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 dogs with congestive heart failure, this product has been given in combination with digoxin, diuretics, pimobendan and anti-arrhythmic veterinary medicinal products without demonstrable adverse interactions.

In humans, the association of ACE inhibitors and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) can lead to reduced anti-hypertensive efficacy or impaired renal function. The combination of this 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 this 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.

Dogs:
The product should be administered orally at a minimum dose of 0.25 mg (range 0.25-0.5) benazepril hydrochloride/kg body weight once daily, according to the following table:

Weight of dog (kg)	Standard dose	Double dose
>20-40	0.5 tablet	1 tablet
>40-60	0.75 tablet	1 ½ tablets
>60-80	1 tablet	2 tablet

The dose may be doubled, still administered once daily, to a minimum dose of 0.5 mg/kg (range 0.5-1.0), if judged clinically necessary and advised by the veterinary surgeon.
In case of use of quarters or half tablets: Put the remaining quantity of the tablet back into the blister pocket and use for the next administration.

The tablets are flavoured and may be taken spontaneously by dogs, but can also be administered directly into the dog's mouth or be given with food if necessary.
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 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 case 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 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 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 remodelling effects (including pathological cardiac hypertrophy and degenerative renal changes).
The product causes long-lasting inhibition of plasma ACE activity in dogs, with more than 95% inhibition at peak effect and significant activity (>80%) persisting 24 hours after dosing.
The 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) and decline quickly as the active substance is partially metabolised by liver enzymes to benazeprilat. The systemic bioavailability is incomplete (~13%) due to incomplete absorption (38%) and first pass metabolism.
Peak benazeprilat concentrations (Cmax of 30 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 fast phase (t1/2=1.7 hours) represents elimination of free drug, while the terminal phase (t1/2=19 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.
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 54% via the biliary and 46% via the urinary route. 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

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

6.2 Major incompatibilities

None known

6.3 Shelf life

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

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

[PA-Al-PVC] / Aluminium heat sealed blister strip of 10 tablets

Cardboard box with 1 blister strip of 10 tablets
Cardboard box with 5 blister strips of 10 tablets
Cardboard box with 10 blister strips of 10 tablets
Cardboard box with 14 blister strips of 10 tablets
Cardboard box with 18 blister strips of 10 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product 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 15052/4108

9. DATE OF FIRST AUTHORISATION

07 September 2009

10. DATE OF REVISION OF THE TEXT

October 2021

Approved 06 October 2021