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Nelio 5 mg and 20 mg Tablets for Dogs

Species:	Dogs
Therapeutic indication:	**Pharmaceuticals:** Cardiovascular and respiratory preparations
Active ingredient:	Benazepril Hydrochloride
Product:	Nelio 5 mg and 20 mg Tablets for Dogs
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Qualitative and quantitative composition

Each Nelio 5 mg Tablet contains: benazepril hydrochloride 5 mg

Each Nelio 20 mg Tablet contains: benazepril hydrochloride 20 mg

Pharmaceutical form

Clover shaped scored beige tablets, divisible into halves or quarters.

Clinical particulars

Target species

Dogs

Indications for use

Treatment of congestive heart failure

Contra-indications

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

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 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.

Adverse reactions

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.

Use during pregnancy or lactation

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.

Interactions

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.

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 5 mg tablet	Double dose 5 mg tablet
2.5 - 5	1/4 x 5 mg tablet	1/2 x 5 mg tablet
>5 - 10	1/2 x 5 mg tablet	1 x 5 mg tablet
>10 - 15	3/4 x 5 mg tablet	1 ½ x 5 mg tablets
>15 - 20	1 x 5 mg tablet	2 x 5 mg tablets
Weight of dog (kg)	Standard dose 20 mg tablet	Double dose 20 mg tablet
>20 - 40	1/2	1
>40 - 60	3/4	1 ½
>60 - 80	1	2

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.

Overdose

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.

Withdrawal periods

Not Applicable

Pharmacological particulars

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.

Pharmacokinetic properties

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.

Pharmaceutical particulars

Excipients

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

Major incompatibilities

None known

Shelf life

Nelio 5 mg and Nelio 20 mg: 2 years.

Shelf-life of divisions of the tablets: 72 hours.

Special precautions for storage

Do not store above 30 °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 3 days.

Immediate packaging

Nelio 5 mg Tablets: [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 25 blister strips of 10 tablets.

Nelio 20 mg Tablets: [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.

Disposal

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

Marketing Authorisation Number

Nelio 5 mg Tablets for Dogs: Vm 15052/4110

Nelio 20 mg Tablets for Dogs: Vm 15052/4108

Significant changes

Date of the first authorisation or date of renewal

Nelio 5 mg and 20 mg tablets for Dogs: 7 September 2009

Date of revision of the text

Nelio 5 mg and 20 mg tablets for Dogs: June 2016

Any other information

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Pregnant women should take special care to avoid accidental oral exposure, because ACE inhibitors have been found to affect the unborn child during pregnancy in humans.

Wash hands after use. In case of accidental ingestion by children, seek medical advice immediately and show this label or the package leaflet to the doctor.

Legal category

Legal category: POM-V

GTIN

GTIN description: Nelio 5mg Tablets

GTIN: 03411112273508

GTIN description: Nelio 20mg Tablets

GTIN: 03411112280049