[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Benazepril hydrochloride 20 mg tablets for dogs (NL)
Benakor 20 mg tablets for dogs (DE, EL, HU)
Benakor vet. 20 mg tablets for dogs (DK, SE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Benazepril hydrochloride 20 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Colorcon Pigment Orange 23069 (Iron oxides, E172)	8 mg
Microcrystalline cellulose (E460)	
Lactose anhydrous	
Silica colloidal anhydrous (E551)	
Sodium cyclamate (E952)	
Sodium starch glycolate Type A	
Magnesium stearate (E470b)	

Orange oblong divisible tablets, with a break mark on both sides.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Treatment of congestive heart failure.

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 (section 3.7).

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:
No evidence of renal toxicity of the veterinary medicinal product has been observed in dogs 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.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Vomiting[a] Fatigue Incoordination
Undetermined frequency (cannot be estimated from the available data)	Elevated creatinine[b]

[a] Transient
[b] In dogs with chronic kidney disease. At the start of therapy, a moderate increase in plasma creatinine concentration after administration of ACE inhibitors is compatible with the reduction of glomerular hypertension induced by these agents. This is therefore, in the absence of other symptoms, not necessarily a reason to discontinue treatment.

In double-blind clinical trials in dogs with congestive heart failure, benazepril hydrochloride was well tolerated with an incidence of adverse reactions lower than observed in placebo-treated dogs.

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

Pregnancy and lactation:
Do not use during pregnancy or lactation. The safety of the veterinary medicinal product has not been established during pregnancy or lactation.
Laboratory studies in rats have shown evidence of embryotoxic effects (foetal urinary tract malformation) at maternally nontoxic doses.

Fertility:
The safety of the veterinary medicinal product has not been established in breeding animals.

3.8 Interaction with other medicinal products and other forms of interaction

In dogs with congestive heart failure, benazepril hydrochloride has been given in combination with digoxin, diuretics, pimobendan and anti-arrhythmic veterinary medicinal products without demonstrable adverse interactions.

In humans, the combination of ACE inhibitors and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) can lead to reduced antihypertensive efficacy or impaired renal function. The combination of benazepril hydrochloride and other antihypertensive 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 benazepril hydrochloride in combination with a potassium sparing diuretic because of the risk of hyperkalaemia.

3.9 Administration routes and dosage

Oral use.
The veterinary medicinal product should be given orally once daily, with or without food. The duration of treatment is unlimited.

The veterinary medicinal 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)	20 mg tablets	
	Standard dose	Double dose
>20-40	0.5 tablet	1 tablet
>40-80	1 tablet	2 tablets

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 using halved tablets: Put the remaining half of a divided tablet back in the blister pocket and store it in a dry place below 25 ºC. Use the remaining tablet half for the next administration.

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

Benazepril hydrochloride 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 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

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:
QC09AA07

4.2 Pharmacodynamics

Benazepril hydrochloride is a pro-drug 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 veterinary medicinal product causes long-lasting inhibition of plasma ACE activity in dogs, with more than 95% inhibition at peak effect and significant activity (>80% in dogs) persisting 24 hours after dosing.

The veterinary medicinal product reduces the blood pressure and volume load on the heart in dogs with congestive heart failure.

4.3 Pharmacokinetics

After oral administration of benazepril hydrochloride, peak levels of benazepril are attained rapidly (T_{max} 1.1 hours in dogs) and decline quickly as the active substance is partially metabolised by liver enzymes to benazeprilat. The systemic bioavailability is incomplete (~13% in dogs) due to incomplete absorption (38% in dogs) and first pass metabolism. In dogs, peak benazeprilat concentrations (C_{max} of 384.16 ng/ml after a dose of 1.6 mg/kg benazepril hydrochloride) are achieved with a T_{max} of 1.1 hours.

Benazeprilat concentrations decline biphasically: the initial fast phase ($t_{1/2}$=1.7 hours in dogs) represents elimination of free drug, while the terminal phase ($t_{1/2}$=19 hours in dogs) 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 benazepril hydrochloride leads to slight accumulation of benazeprilat (R=1.47 in dogs with 0.5 mg/kg), steady state being achieved within a few days (4 days in dogs).

Benazeprilat is excreted 54% via the biliary and 46% via the urinary route in dogs. The clearance of benazeprilat is not affected in dogs with impaired renal function and therefore no adjustment of benazepril hydrochloride dose is required in cases of renal insufficiency.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:
PVC/PE/PVDC-Aluminium blister: 15 months.
Aluminium/Aluminium blister: 3 years.
Tablet halves should be used within one day.

5.3 Special precautions for storage

Do not store above 25 ºC.
Store in the original package.
Store tablet halves in the original blister in the original package.

5.4 Nature and composition of immediate packaging

PVC/PE/PVDC/Alu-foil blister
Cardboard box of
1, 2, 3, 4, 5, 6 or 7 blisters of 14 tablets.
or
Alu/Alu-foil blister
Cardboard box of 1, 2, 3, 4, 5, 6 or 7 blisters of 14 tablets.

Not all pack sizes may be marketed.

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 or household waste.

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

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: <{DD/MM/YYYY}><{DD month YYYY}>.

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

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

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).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Benazepril hydrochloride 20 mg tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:

Benazepril hydrochloride 20 mg

3. PACKAGE SIZE

14 tablets
28 tablets
42 tablets
56 tablets
70 tablets
84 tablets
98 tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Tablet halves should be used within one day.

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 ºC.
Store in the original package.
Store tablet halves in the original blister in the original package.

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Benazepril hydrochloride

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Benazepril hydrochloride: 20 mg/tablet

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Benazepril hydrochloride 20 mg tablets for dogs (NL)
Benakor 20 mg tablets for dogs (DE, EL, HU)
Benakor vet. 20 mg (DK, SE)

2. Composition

Each tablet contains:

Active substance:
Benazepril hydrochloride 20 mg

Excipients:
Colorcon Pigment Orange 23069 (Iron oxides, E172) 8 mg

Orange oblong divisible tablets, with a break mark on both sides.

3. Target species

Dogs.

4. Indications for use

The veterinary medicinal product belongs to a group of medicines called Angiotensin Converting Enzyme (ACE) inhibitors. It is prescribed by the veterinary surgeon for the treatment of congestive heart failure in dogs.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance benazepril hydrochloride or to any of the excipients
Do not use in cases of hypotension (low blood pressure), hypovolemia (low blood volume), hyponatraemia (low blood sodium levels) or acute renal failure.
Do not use in cases of cardiac output failure due to aortic or pulmonary stenosis.
Do not use in pregnant or lactating dogs because the safety of benazepril hydrochloride has not been established during pregnancy or lactation in this species.

6. Special warnings

Special precautions for safe use in the target species:
In cases of chronic kidney disease, your veterinarian will check the hydration status of your pet before starting therapy and may recommend that regular blood tests are carried out during therapy in order to monitor plasma creatinine concentrations and blood erythrocyte counts.

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 ACE inhibitors have been found to affect the unborn child during pregnancy in humans.

Pregnancy and lactation:
Do not use during pregnancy or lactation. The safety of the veterinary medicinal product has not been established in pregnant or lactating dogs.
Laboratory studies in rats have shown evidence of embryotoxic effects (foetal urinary tract malformation) at maternally nontoxic doses.

Fertility:
The safety of the veterinary medicinal product has not been established in breeding animals.

Interaction with other medicinal products and other forms of interaction:
Inform the veterinary surgeon if the animal is taking, or has recently taken, any other medicines.
In dogs with congestive heart failure, benazepril hydrochloride has been given in combination with digoxin, diuretics, pimobendan and anti-arrhythmic veterinary medicinal products without evidence of associated adverse reactions.
In humans, the combination of ACE inhibitors and NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) can lead to reduced anti-hypertensive efficacy or impaired kidney 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 or other medications with a hypotensive effect should be considered with care.
Your veterinary surgeon may recommend to closely monitor kidney function and for signs of hypotension (lethargy, weakness etc) and treat these if necessary.
Interactions with potassium-preserving diuretics like spironolactone, triamterene or amiloride cannot be ruled out. Your veterinary surgeon may recommend monitoring plasma potassium concentrations when using the veterinary medicinal product in combination with a potassium-sparing diuretic because of the risk of hyperkalaemia (high blood potassium).

Overdose:
Benazepril hydrochloride 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 (low blood pressure) may occur in cases of accidental overdose. Therapy should consist of intravenous infusion of warm isotonic saline.

7. Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Vomiting[a] Fatigue Incoordination
Undetermined frequency (cannot be estimated from the available data)	Elevated creatinine[b]

[a] Transient

[b] In dogs with chronic kidney disease. At the start of therapy, a moderate increase in plasma creatinine concentration after administration of ACE inhibitors is compatible with the reduction of glomerular hypertension induced by these agents. This is therefore, in the absence of other symptoms, not necessarily a reason to discontinue treatment.

In double-blind clinical trials in dogs with congestive heart failure, benazepril hydrochloride was well tolerated with an incidence of adverse reactions lower than observed in placebo-treated dogs.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder <or the local representative of the marketing authorisation holder> using the contact details at the end of this leaflet, or via your national reporting system:{national system details}.

8. Dosage for each species, routes and method of administration

Oral use.
The veterinary medicinal product should be given orally once daily, with or without food. The duration of treatment is unlimited.

The veterinary medicinal 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)	20 mg tablets	
	Standard dose	Double dose
>20-40	0.5 tablet	1 tablet
>40-80	1 tablet	2 tablets

In dogs with congestive heart failure, the dose may be doubled, still administered once daily, to a minimum dose of 0.5 mg (range 0.5-1.0) benazepril hydrochloride/kg bodyweight if judged necessary and advised by the veterinary surgeon. Always follow the dosing instructions given by the veterinary surgeon.

In case of using halved tablets: Put the remaining half of a divided tablet back in the blister pocket and store it in a dry place below 25 ºC. Use the remaining tablet half for the next administration.

9. Advice on correct administration

For animal treatment only. For oral use only.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 25 ºC.
Store in the original package

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and the blister after Exp. The expiry date refers to the last day of that month.
Tablet halves should be used within one day.
Store tablet halves in the original blister in the original package.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon <or pharmacist> how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

PVC/PE/PVDC/Alu-foil blister
Cardboard box of 1, 2, 3, 4, 5, 6 or 7 blisters of 14 tablets.
or
Alu/Alu-foil blister
Cardboard box of 1, 2, 3, 4, 5, 6 or 7 blisters of 14 tablets.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder <and contact details to report suspected adverse reactions>:

Manufacturer responsible for batch release:
Lelypharma B.V.
Zuiveringweg 42
8243 PZ Lelystad
The Netherlands

Genera d.d..
Svetonedeljska cesta 2, Kalinovica

10 436 Rakov Potok
Croatia

[1]The printed package leaflet will state the name and address of the manufacturer responsible for the release of the concerned batch only.

<Local representatives <and contact details to report suspected adverse reactions>:>

<For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.>

<17. Other information>