SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bexepril 5mg Film-coated tablet for dogs (BE & IE)
Bexepril 5mg Film-coated tablet for dogs (BG, CY, CZ, DK, EL, ES, HU, LU, NL, NO, PT, RO, SI, SK & UK)
Sirdis 5mg Film-coated tablet for dogs (IT)
Bexepril 5mg Film-coated tablets for dogs (PL)
Bexepril 5 Film-coated tablet for dogs (FR)
Bexepril l 5mg Film-coated tablet for dogs, Benazeprilhydochlorid (AT)
Benadog Flavour 5mg Film-coated tablets for dogs, Benzeprilhydochlorid (DE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each tablet contains:
Benazepril 4.6mg
(equivalent to Benazepril Hydrochloride 5mg)

Excipient:
Titanium Dioxide (E171) 0.9348mg
Iron Oxide Yellow (E172) 0.0476mg

Quinoline Yellow Aluminum Lake (E104) 0.0176mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.
A round yellow biconvex tablet with break line on one side. The tablets can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

In dogs weighing more than 10 kg:
Treatment of congestive heart failure associated with, in particular, dilated cardiomyopathy and/or mitral insufficiency.

4.3 Contraindications

Do not use in any dog that has evidence of cardiac output failure due, for example, to aortic stenosis.
Do not use in animals known to be hypersensitive to the active substance or to any of the excipient(s).
See 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 to the product has been observed in dogs during clinical trials. However, as is routine in cases of renal insufficiency, it is recommended to monitor plasma creatinine and urea 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 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.

4.6 Adverse reactions (frequency and seriousness)

On rare occasions transient signs of hypotension, such as lethargy and ataxia may occur.

4.7 Use during pregnancy, lactation or lay

Do not use in pregnant or nursing bitches or in bitches intended for breeding.
Studies in laboratory animals have shown embryotoxic effects of benazepril at non-maternotoxic doses (urinary tract abnormalities in the foetus). The safety of the product has not been assessed during pregnancy and lactation in dogs.
Laboratory studies in rats and observations in humans have produced evidence of teratogenic effects.

4.8 Interaction with other medicinal products and other forms of interaction

In dogs with heart failure, Benazepril has been given in combination with digoxin, diuretics and anti-arrythmic drugs without demonstrable adverse interactions.
In man, the combination of ACE inhibitors and NSAIDs can lead to reduced anti-hypertensive efficacy or impaired renal function. The combination of Benazepril and other anti-hypertensive agents (e.g. calcium channel blockers, P-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 in combination with a potassium sparing diuretic as life-threatening reactions are possible. As with other ACE Inhibitors, the use of hypotensive medicinal products or anaesthetics with a hypotensive effect may add to the anti-hypertensive effect of benazepril.

4.9 Amounts to be administered and administration route

For oral use only.
To ensure correct dosage, body weight should be determined as accurately as possible to avoid underdosing.

The recommended oral dose is 0.23 mg of benazepril per kg bodyweight per day, equivalent to 0.25 mg of benazepril hydrochloride per kg bodyweight per day, as one administration. The dose may be doubled, still administered once daily, if judged clinically necessary and advised by the veterinary surgeon.
Benazepril should be given orally once daily, with or without food. The duration of treatment is unlimited.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary
In normal dogs, overdosage up to 200-fold was asymptomatic. Transient reversible hypotension may occur in cases of accidental overdosage. Therapy should consist of intravenous infusion of warm isotonic saline.

4.11 Withdrawal period(s)
Not applicable

5. PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group:
ACE Inhibitors, Benazepril, ATCvet code: QC09AA07.

5.1 Pharmacodynamic properties
Benazepril hydrochloride is a prodrug hydrolysed *in vivo* to its active metabolite, benazeprilat. Benazeprilat is a selective inhibitor of angiotensin converting enzyme (ACE), thus preventing the conversion of inactive angiotensin I to active angiotensin II Therefore, it blocks effects mediated by angiotensin II, including vasoconstriction of both arteries and veins; retention of sodium and water by the kidney and modelling effects (including pathological cardiac hypertrophy).
The 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. It reduces the blood pressure and volume load on the heart in dogs with heart failure.

5.2 Pharmacokinetic particulars
After oral administration of benazepril hydrochloride, peak levels of benazepril are attained rapidly (t_{max} 1.74 h in dogs) and decline quickly as the drug is partially metabolised by liver enzymes to benazeprilat. In dogs, unchanged benazepril and hydrophilic metabolites account for the remainder. In dogs, peak benazeprilat concentrations (C_{max} of 35.02 ng/ml after a dose of 0.5 mg/kg benazepril hydrochloride) are achieved with a T_{max} of 1.74h. The systemic bioavailability is incomplete (-13% in dogs) due to incomplete absorption (38% in dogs) and first pass metabolism.
Benazeprilat concentrations decline biphasically: the initial fast phase ($t_{l/2}$=1.7h in dogs) represents elimination of free drug, while the terminal phase (t1/2=19h 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, 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 leads to slight bioaccumulation 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 dose is required in cases of renal insufficiency.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core Tablet:
Lactose Monohydrate
Maize Starch
Microcrystalline Cellulose
Colloidal anhydrous silica
Crospovidone
Talc
Magnesium Stearate
Film Coat:
Grilled Meat Flavour
Opadry II Yellow
Consisting of Polyvinyl Alcohol,
Titanium Dioxide (E171),
Macrogol 3350,
Talc (E553b),
Iron Oxide Yellow (E172)
Quinoline Yellow Aluminum Lake (E104)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years
Unused half tablet must be used within 24 hours.

6.4. Special precautions for storage

Do not store above 25ºC. Store in original package in order to protect from light.
Each time an unused half tablet is stored, it should be returned to the open blister space and inserted back into the cardboard box.

6.5 Nature and composition of immediate packaging

Heat-sealed blister packs made up of a PVC/PE/PVDC laminate with aluminium lidding foil with 14 tablets per strip.

Pack sizes:
Carton of : 14, 28, 42, 56, 70, 84, 98, 112, 128, 140, 154, 168, 182, 196, 210, 224, 238, 252, 266, 280, 294, 308, 350, 392, 448, 546, 602, 700, 798, 896, 994 and 1008 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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd.
Loughrea
Co. Galway
Ireland

8. MARKETING AUTHORISATION NUMBER

Vm: 08749/4021

9. DATE OF FIRST AUTHORISATION

Date: 23 April 2010

10. DATE OF REVISION OF THE TEXT

Date: June 2015

PROHIBITION OF SALE, SUPPLY AND/OR USE
To be supplied only on veterinary prescription

Approved: **17/06/2015**