SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ENCARD Tablets for Dogs 10 mg

2. QUALITATIVE AND QUANTITAVIVE COMPOSITION

Per tablet:

Enalapril maleate	10.0 mg
Yellow iron oxide E172	0.5 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet. Round non-scored biconvex uncoated yellow tablets.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

Treatment of mild, moderate and severe congestive heart failure in dogs caused by mitral regurgitation or dilated cardiomyopathy as an adjunctive therapy with diuretics. For improved exercise tolerance and increased survival in dogs with mild, moderate and severe heart failure.

4.3 Contra-indications

Do not use in any dog that has evidence of cardiac output failure e.g. aortic stenosis.
The product is not recommended for use in pregnant bitches. Safety in breeding dogs has not been established.
Do not use with potassium-sparing diuretics.

4.4 Special warnings for each target species

See other sections.

4.5 Special precautions for use

i. Special precautions for use in animals

None known but see other sections.

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

In case of accidental ingestion, seek urgent medical attention showing the product label to the doctor or nurse. Physicians should contact a Poison Control Centre for advice concerning cases of human consumption.

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

The product has been demonstrated to be generally well tolerated. In clinical studies, the overall incidence of side effects was not significantly greater with the product than with vehicle tablets. For the most part side effects have been mild and transient in nature and have not required discontinuation of therapy.

The following side effects have been reported:

Azotemia
In clinical trials, no significant difference in the incidence of azotemia was reported between dogs receiving standard therapy and vehicle tablets (8.3%) and dogs receiving standard therapy and the product (9.4%).

General
No significant difference in the incidence of clinical signs that included dizziness, drowsiness, hypotension, disorientation and in coordination were reported between dogs receiving standard therapy and vehicle tablets (0.8%) and dogs receiving standard therapy and the product (3.0%).

4.7 Use during pregnancy, lactation or lay

The product is not recommended for use in pregnant bitches. Safety in breeding dogs has not been established.

4.8 Interaction with other medicinal products and other forms of interaction

Whilst all clinical data were generated in conjunction with frusemide, the product may be administered to dogs being treated with thiazide diuretics. Do not use the product with potassium-sparing diuretics.

4.9 Amounts to be administered and administration route

The product should be administered orally at a recommended dose rate of 0.5 mg/kg once daily. Individual dosages should be administered on the basis of bodyweight using the appropriate tablet or combination of tablet sizes:

Tablet Size	Colour
1.0 mg	green
2.5 mg	blue

5.0 mg	pink
10.0 mg	yellow
20.0 mg	white

In the absence of a clinical response within 2 weeks following initiation of therapy with the product, the dose should be increased, depending on the patient's response, up to a maximum of 0.5 mg/kg bodyweight administered twice daily. This dose titration may be performed over a two to four week period, or more rapidly if indicated by the presence of continuing signs of congestive heart failure. Dogs should be observed closely for 48 hours following initial dosing or an increase in dose.

Therapy with diuretics should be initiated at least one day prior to starting treatment with the product. Evaluation of the patient should include assessment of renal function prior to initiation of therapy and for 2 to 7 days after treatment with the product.

Renal function impairment in the target species
Pre-renal azotemia is usually a result of hypotension induced by impaired cardio-vascular performance. On occasion substances that deplete blood volume, such as diuretics, or which vasodilate, such as angiotensin-converting enzyme (ACE) inhibitors may contribute to lowering systemic blood pressure. This may create a hypotensive state or exacerbate an existing hypotensive situation and result in pre-renal azotemia.

Dogs with no detectable renal disease may develop minor and transient increases in blood urea nitrogen or serum creatinine when the product is administered concomitantly with a diuretic. Renal function should be monitored both before and 2 to 7 days after starting the treatment with the product.

The dose of the diuretic and/or the product should be reduced or their use should be discontinued if signs of hypotension or azotemia develop or if the concentrations of blood urea nitrogen and/or serum creatinine increase significantly over pre-treatment levels. Periodic monitoring of renal function should be continued. Should clinical signs of overdosage occur (e.g. azotemia) after the dose is increased from once daily to twice daily, the dose should be decreased to once daily.

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

The product at the recommended dose level has been shown to have an adequate margin of safety in dogs with heart failure. The safety of the product has been thoroughly investigated in several animals including mice, rats, monkeys and in man to assess its general toxicity. Normal dogs given 15 mg/kg/day for up to one year showed no adverse effects or changes.

4.11 Withdrawal periods

Not applicable: the product is indicated for use in companion animals.

5. PHARMACOLOGICAL PROPERTIES

Summary presentation of the active principle
ENACARD is the maleate salt of enalapril, a derivative of two amino acids, L-alanine and L-proline. Enalapril is the ethyl ester of the parent diacid, enalaprilat. Following oral administration, enalapril is readily absorbed and then hydrolysed to enalaprilat, which is a highly specific, long-acting, non-sulphydryl angiotensin converting enzyme (ACE) inhibitor.

ATC Vet Code: QC09AA02

5.1 Pharmacodynamic properties

Enalapril is hydrolyzed in dogs, humans and rats to enalaprilat, which inhibits the angiotensin-converting enzyme (ACE). This enzyme a peptidyl dipeptidase catalyses the conversion of angiotensin I to the vasoconstrictor substance angiotensin II. Angiotensin II also stimulates aldosterone secretion by the adrenal cortex. The beneficial effects of enalapril in hypertension and heart failure appear to result primarily from suppression of the renin-angiotensin-aldosterone system. Inhibition of ACE results in decreased plasma angiotensin II, which leads to decreased vasopressor activity and to decreased aldosterone secretion. Although the latter decrease is small, it results in small increases in serum potassium.

Pharmacology studies show that enalapril lowers blood pressure and has utility in heart failure as a consequence of peripheral inhibition of the formation of angiotensin II from angiotensin I via the angiotensin- converting enzyme (ACE). The effect of enalapril on electrolyte excretion and renal function may be a contributing factor in its therapeutic efficacy. Enalapril increases renal blood flow and glomerular filtration rates and promotes saline excretion. The mechanism of action of the natriuresis and a slight increase in serum potassium seen with enalapril is believed to be related to decreased aldosterone, secondary to inhibition of angiotensin II formation by ACE.

5.2 Pharmacokinetic properties

Since the active metabolite of enalapril, enalaprilat, is poorly absorbed orally, it is administered as the prodrug enalapril. Complete hydrolysis of enalapril, an ester, to the active diacid angiotensin-converting enzyme inhibitor occurs in the liver in dogs (similar to man). In dogs the peak plasma levels (radioactivity) occurred at about 2 hours after a 1 mg/kg oral dose. At 24 hours total radioactivity levels were low but still present due to the tight binding to converting enzyme. Despite this long terminal plasma half-life, there appeared to be no significant accumulation since doses as great as 15 mg/kg/day for 1 year did not produce signs of toxicity. Oral absorption at 1 mg/kg was estimated from plasma levels to be about 64%. An average of 40% of the oral dose radioactivity was excreted in the urine and 36% in the faeces in 72 hours. Following i.v. administration of 1 mg/kg enalaprilat, 69% was in the urine and 14% in the faeces. These data suggest biliary excretion of the prodrug and/or enalaprilat occurred. About 22% of a 1 mg/kg i.v. dose of ^{14}C-

enalaprilat was excreted in the bile. Plasma levels and urinary excretion of radioactivity was proportional over the dose range of 0.1 to 3.0 mg/kg orally.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate
Sodium Bicarbonate
Maize Starch
Maize Starch Pregelatinised
Magnesium Stearate
Ferric Oxide Yellow (E172)

6.2 Major incompatibilities

No major incompatibility has been identified.

6.3 Shelf-life, when necessary after reconstitution of the medicinal product or when the immediate packaging is opened for the first time

2 years (HDPE bottle) and 3 years (Blister Pack).

6.4 Special precautions for storage

HDPE Bottle
Do not store above 25°C. Store in a dry place.
When not in use keep container tightly closed. Do not remove desiccant from the container. Subdivision of the product package is not recommended, as the product should be stored in a tightly closed original container.

Blister Pack
Do not store above 25°C. Avoid transient temperatures above 50°C.

6.5 Nature and composition of immediate packaging

The product is packaged in high-density polyethylene (HDPE) bottles with polyethylene (PE) closure. The product is supplied in bottles with desiccant containing 30 tablets.
Alternatively, the tablets may be presented in a “cold form” aluminium blister containing seven tablets, and presented in cartons of four blisters.
Not all pack sizes are marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products, if appropriate

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

Boehringer Ingelheim Animal Health UK Ltd
Ellesfield Avenue
Bracknell
Berkshire
RG12 8YS

8. MARKETING AUTHORISATION NUMBER

Vm 08327/4197

9. DATE OF FIRST AUTHORISATION

17 March 1999

10. DATE OF REVISION OF THE TEXT

November 2018

ANY OTHER INFORMATION REQUIRED BY THE SECRETARY OF STATE

Not applicable.

Approved 01 November 2018