*[Version 9.1,11/2024]*

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cardisure flavoured 2.5 mg Tablets For dogs
(AT, DE, EL, ES, IE, IT, PL, PT, UK (NI))

Cardisure flavoured vet. 2.5 mg Tablets for Dogs
(DK)

Cardisure 2.5 mg flavoured tablets for dogs
(BE, LU, NL)

Cardisure vet. 2.5 mg Tablets for Dogs
(FI, SE, NO)

Cardisure 2.5 mg Tablets for Dogs
(FR)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

**Active substances:**
Pimobendan 2.5 mg

**Excipients:**

| **Qualitative composition of excipients and other constituents** |
|---|
| Cellulose, microcrystalline |
| Croscarmellose sodium |
| Magnesium stearate |
| Natural meat flavour |

Light brown, round tablets, scored on one side and plain on the other side.
The tablets can be divided into 4 equal parts.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Dogs.

### 3.2 Indications for use for each target species

For the treatment of canine congestive heart failure originating from valvular insufficiency (mitral and/or tricuspid regurgitation) or dilated cardiomyopathy.

### 3.3 Contraindications

Do not use in cases of hypertrophic cardiomyopathies or clinical conditions where an augmentation of cardiac output is not possible for functional or anatomical reasons (e.g. aortic stenosis).
See also section 3.7.

## 3.4 Special warnings

The veterinary medicinal product should be administered on an empty stomach at least one hour before meals, as absorption is reduced when given with feed.

## 3.5 Special precautions for use

Special precautions for safe use in the target species:

The veterinary medicinal product is flavoured. To avoid accidental ingestion the tablets should be stored out of reach of dogs.
An *in vitro* study in rat tissue demonstrated that pimobendan increased glucose-induced insulin release from pancreatic β-cells in a dose-dependent manner. If the veterinary medicinal product is administered to diabetic dogs, blood glucose levels should be carefully monitored.
As pimobendan is metabolised in the liver, particular care should be taken when administering the veterinary medicinal product to dogs with severe hepatic insufficiency.
Monitoring of cardiac function and morphology is recommended in animals treated with pimobendan.(See also section 3.6).

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

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

To the physician: Accidental ingestion, especially by a child, may lead to the occurrence of tachycardia, orthostatic hypotension, flushing of the face and headaches.

Special precautions for the protection of the environment:

Not applicable.

## 3.6 Adverse events

Dogs:

| | |
|---|---|
| Rare<br>(1 to 10 animals / 10 000 animals treated): | Increased heart rate[a,b], Increase in mitral valve regurgitation[c]<br>Vomiting[b], Diarrhoea[d]<br>Anorexia[d], Lethargy[d] |
| Very rare<br>(<1 animal / 10 000 animals treated, including isolated reports): | Mucosa petechiae[e], Subcutaneous haemorrhage[e] |

[a] Moderate positive chronotropic effect.

[b] These effects are dose-dependent and may be avoided by reducing the dose in these cases.

[c] Has been observed during chronic pimobendan treatment in dogs with mitral valve disease.

[d] Transient.

[e] Although a relationship with pimobendan has not been clearly established, signs of effects on primary haemostasis may be observed during treatment. These signs disappear when the treatment is withdrawn.

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

The safety of the veterinary medicinal product has not been established during pregnancy or lactation.

Pregnancy and lactation:
Use only according to the benefit-risk assessment by the responsible veterinarian.
Laboratory studies in rats and rabbits have not produced any evidence of teratogenic or foetotoxic effects. However, these studies have shown evidence of maternotoxic and embryotoxic effects at high doses and have also shown that pimobendan is excreted into milk.

### 3.8 Interaction with other medicinal products and other forms of interaction

In pharmacological studies no interaction between the cardiac glycoside ouabain and pimobendan was detected. The pimobendan-induced increase in contractility of the heart is attenuated in the presence of the calcium antagonist verapamil and the β-antagonist propranolol.

### 3.9 Administration routes and dosage

Oral use.

Do not exceed the recommended dosage.

To ensure a correct dosage, body weight should be determined as accurately as possible.

The tablets should be administered orally at a dose range of 0.2 mg to 0.6 mg pimobendan/kg body weight per day. The preferable daily dose is 0.5 mg pimobendan/kg body weight. The dose should be divided into two administrations (0.25 mg/kg body weight each), one half of the dose in the morning and the other half approximately 12 hours later. The maintenance dose should be individually adjusted by the responsible veterinarian according to the severity of the disease.

The veterinary medicinal product may be combined with a diuretic treatment, e.g. furosemide.

To break a double scored tablet into quarters, place the tablet on an even surface with the scored side up and apply pressure on the middle with your thumb.

Each dose should be given approximately one hour before feeding.

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

In the case of overdose, a positive chronotropic effect and vomiting may occur. In this situation, the dosage should be reduced and appropriate symptomatic treatment should be initiated.
In prolonged exposure (6 months) of healthy beagle dogs at 3 and 5 times the recommended dose, mitral valve thickening and left ventricular hypertrophy were observed in some dogs.

### 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 :

QC01CE90

### 4.2 Pharmacodynamics

Pimobendan, a benzimidazole-pyridazinone derivative, is a non-sympathomimetic, non-glycoside inotropic substance with potent vasodilatative properties.

Pimobendan exerts its stimulatory myocardial effect by a dual mode of action: it increases calcium sensitivity of cardiac myofilaments and inhibits phosphodiesterase (type III). It also exhibits a vasodilatory action through inhibition of phosphodiesterase III activity.

When used in cases of valvular insufficiency in conjunction with furosemide, the veterinary medicinal product has been shown to improve the quality of life and extend life expectancy in treated dogs.

When used in a limited number of cases of dilated cardiomyopathy in conjunction with furosemide, enalapril and digoxin the veterinary medicinal product has been shown to improve the quality of life and to extend life expectancy in treated dogs.

### 4.3 Pharmacokinetics

Absorption:
Following oral administration of this veterinary medicinal product the absolute bio-availability of the active principle is 60-63%. Since this bio-availability is considerably reduced when pimobendan is administered with food or shortly thereafter, it is recommended to treat animals approximately 1 hour before feeding.

Distribution:
The volume of distribution is 2.6 l/kg, indicating that pimobendan is distributed readily into the tissues. The mean plasma protein binding is 93%.

Metabolism:
The compound is oxidatively demethylated to its major active metabolite (UD-CG 212). Further metabolic pathways are phase II conjugates of UD-CG-212, in essence glucuronides and sulphates.

Elimination:
The plasma elimination half-life of pimobendan is 1.1 ± 0.7 hours. The main active metabolite is eliminated with a plasma elimination half-life of 1.5 ± 0.2 hours. Almost the entire dose is eliminated via faeces.

## 5. PHARMACEUTICAL PARTICULARS

### 5.1 Major incompatibilities

Not applicable.

### 5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.
Shelf life of divided tablets after first opening the blister: 3 days.

### 5.3 Special precautions for storage

Do not store above 30 °C.
Return any divided tablet to the opened blister and use within 3 days.

### 5.4 Nature and composition of immediate packaging

Aluminium – PVC/PE/PVDC blister:
10 tablets per blister: 2, 5, 10 or 25 blisters per carton.

Aluminium – Aluminium blister:
10 tablets per blister: 2, 5, 10 or 25 blisters per carton.

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

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

## 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 II**

**LABELLING AND PACKAGE LEAFLET**

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**BOX**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cardisure flavoured 2.5 mg Tablets

## 2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Pimobendan 2.5 mg

## 3. PACKAGE SIZE

20/50/100/250 tablets

## 4. TARGET SPECIES

Dogs.

## 5. INDICATIONS

## 6. ROUTES OF ADMINISTRATION

Oral use.

## 7. WITHDRAWAL PERIODS

## 8. EXPIRY DATE

Exp. {mm/yyyy}

## 9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C.
Return any divided tablet to the opened blister and use within 3 days.

## 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

Cardisure flavoured

## 2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Pimobendan 2.5 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

Cardisure flavoured 1.25/2.5/5/10 mg Tablets for Dogs

## 2. Composition

**Active substances:**
Pimobendan

1.25 mg: Each tablet contains 1.25 mg pimobendan
2.5 mg: Each tablet contains 2.5 mg pimobendan
5 mg: Each tablet contains 5 mg pimobendan
10 mg: Each tablet contains 10 mg pimobendan

Light brown round tablets, scored on one side and plain on the other side.
The tablets can be divided into 2 (1.25 mg) or 4 (2.5 mg, 5 mg and 10 mg) equal parts.

## 3. Target species

Dogs.

## 4. Indications for use

For the treatment of canine congestive heart failure originating from valvular insufficiency (mitral and/or tricuspid regurgitation) or dilated cardiomyopathy.

## 5. Contraindications

Do not use in cases of hypertrophic cardiomyopathies or clinical conditions where an augmentation of cardiac output is not possible for functional or anatomical reasons (e.g. aortic stenosis).

## 6. Special warnings

Special warnings:
The veterinary medicinal product should be administered on an empty stomach at least one hour before meals, as absorption is reduced when given with feed.

Special precautions for safe use in the target species:
The veterinary medicinal product is flavoured. To avoid accidental ingestion the tablets should be stored out of reach of dogs.
An *in vitro* study in rat tissue demonstrated that pimobendan increased glucose-induced insulin release from pancreatic β-cells in a dose-dependent manner. If the veterinary medicinal product is administered to diabetic dogs, blood glucose levels should be carefully monitored.
As pimobendan is metabolised in the liver, particular care should be taken when administering the veterinary medicinal product to dogs with severe hepatic insufficiency.
Monitoring of cardiac function and morphology is recommended in animals treated with pimobendan.(See also section Adverse events).

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.
To the physician: Accidental ingestion, especially by a child, may lead to the occurrence of tachycardia, orthostatic hypotension, flushing of the face and headaches.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy or lactation.
Use only according to the benefit-risk assessment by the responsible veterinarian.
Laboratory studies in rats and rabbits have not produced any evidence of teratogenic or foetotoxic effects. However, these studies have shown evidence of maternotoxic and embryotoxic effects at high doses and have also shown that pimobendan is excreted into milk.

Interaction with other medicinal products and other forms of interaction:
In pharmacological studies no interaction between the cardiac glycoside ouabain and pimobendan was detected. The pimobendan-induced increase in contractility of the heart is attenuated in the presence of the calcium antagonist verapamil and the β-antagonist propranolol.

Overdose:
In the case of overdose, a positive chronotropic effect and vomiting may occur. In this situation, the dosage should be reduced and appropriate symptomatic treatment should be initiated.
In prolonged exposure (6 months) of healthy beagle dogs at 3 and 5 times the recommended dose, mitral valve thickening and left ventricular hypertrophy were observed in some dogs.

## 7. Adverse events

Dogs:

| | |
|---|---|
| Rare<br>(1 to 10 animals / 10 000 animals treated): | Increased heart rate[a,b], Increase in mitral valve regurgitation[c]<br>Vomiting[b], Diarrhoea[d]<br>Anorexia (loss of appetite)[d], Lethargy (lack of energy)[d] |
| Very rare<br>(<1 animal / 10 000 animals treated, including isolated reports): | Mucosa petechiae (tiny blood spots under the skin)[e], Subcutaneous haemorrhage (bleeding)[e] |

[a]Moderate positive chronotropic effect.

[b]These effects are dose-dependent and may be avoided by reducing the dose in these cases.

[c]Has been observed during chronic pimobendan treatment in dogs with mitral valve disease.

[d]Transient.

[e]Although a relationship with pimobendan has not been clearly established, signs of effects on primary haemostasis may be observed during treatment. These signs disappear when the treatment is withdrawn.

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 its local representative 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 tablets should be administered orally at a dose range of 0.2 mg to 0.6 mg pimobendan/kg body weight per day. The preferable daily dose is 0.5 mg pimobendan/kg body weight. The dose should be divided into two administrations (0.25 mg/kg body weight each), one half of the dose in the morning and the other half approximately 12 hours later. The maintenance dose should be individually adjusted according to the severity of the disease.

The veterinary medicinal product may be combined with a diuretic treatment, e.g. furosemide.

To break a tablet into two halves, place the tablet on an even surface with the scored side up, hold one half of the tablet and press down on the other half.

To break a double scored tablet into quarters, place the tablet on an even surface with the scored side up and apply pressure on the middle with your thumb.

Each dose should be given approximately one hour before feeding.

## 9. Advice on correct administration

This veterinary medicinal product should be used only in dogs with cardiac insufficiency.
Do not exceed the recommended dosage.
To ensure a correct dosage, body weight should be determined as accurately as possible.

## 10. Withdrawal periods

Not applicable.

## 11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 30 °C.
Return any divided tablet to the opened blister and use within 3 days.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.

## 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

**Pack sizes:**
Aluminium – PVC/PE/PVDC blister:
10 tablets per blister: 2, 5, 10 or 25 blisters per carton.

Aluminium – Aluminium blister:
1.25 and 2.5 mg tablet: 10 tablets per blister: 2, 5, 10 or 25 blisters per carton.
5 and 10 mg tablet: 5 tablets per blister: 4, 10, 20 or 50 blisters per carton.

Not all pack sizes may be marketed.

## 15. Date on which the package leaflet was last revised

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 manufacturer responsible for batch release and contact details to report suspected adverse events:

Manufacturer responsible for batch release:
Eurovet Animal Health B.V.
Handelsweg 25, 5531 AE Bladel
The Netherlands

Genera d.d.
Svetonedeljska cesta 2, Kalinovica
10436 Rakov Potok, Croatia

Additional for XI:
Dales Pharmaceuticals Limited
Snaygill Industrial Estate, Keighley Road, Skipton
North Yorkshire, BD23 2RW, United Kingdom

Local representatives and contact details to report suspected adverse events:

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

## 17. Other information

When used in cases of valvular insufficiency in conjunction with furosemide, the veterinary medicinal product has been shown to improve the quality of life and extend life expectancy in treated dogs.

When used in a limited number of cases of dilated cardiomyopathy in conjunction with furosemide, enalapril and digoxin, the veterinary medicinal product has been shown to improve the quality of life and to extend life expectancy in treated dogs.