

PART 1B-1

SUMMARY OF PRODUCT CHARACTERISTICS

CARDISURE TABLETS

(5 mg tablets)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cardisure flavoured 5 mg Tablets For dogs
(Austria, Germany, Greece, Ireland, Italy, Poland, Portugal, Spain, United Kingdom(Northern Ireland))

Cardisure flavoured vet. 5 mg Tablets for Dogs
(Denmark)

Cardisure 5 mg flavoured tablets for dogs
(Belgium, Luxembourg, Netherlands)

Cardisure vet. 5 mg Tablets for Dogs
(Finland, Sweden, Norway)

Cardisure 5 mg Tablets for Dogs
(France)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains:

Active substance:

Pimobendan 5 mg

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

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

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

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

4.3 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 4.7.

4.4 Special warnings

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

4.5 Special precautions for use

Special precautions for use in animals

The 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 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 product to dogs with severe hepatic insufficiency.

Monitoring of cardiac function and morphology is recommended in animals treated with pimobendan. (See also section 4.6).

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.

Advice to doctors: accidental ingestion, especially by a child, may lead to the occurrence of tachycardia, orthostatic hypotension, flushing of the face and headaches.

4.6 Adverse reactions (frequency and seriousness)

A moderate positive chronotropic effect and vomiting may occur in rare cases. However, these effects are dose-dependent and may be avoided by reducing the dose in these cases. In rare cases transient diarrhoea, anorexia or lethargy have been observed.

Although a relationship with pimobendan has not been clearly established, in very rare cases, signs of effects on primary haemostasis (petechiae on mucous membranes, subcutaneous haemorrhages) may be observed during treatment. These signs disappear when the treatment is withdrawn.

In rare cases, an increase in mitral valve regurgitation has been observed during chronic pimobendan treatment in dogs with mitral valve disease.

The frequency of adverse reactions is defined using the following convention:

-very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)

-common (more than 1 but less than 10 animals in 100 animals)

-uncommon (more than 1 but less than 10 animals in 1,000 animals)

-rare (more than 1 but less than 10 animals in 10,000 animals)

-very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

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. The safety of the product has not been assessed in pregnant or nursing bitches. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 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.

4.9 Amounts to be administered and administration route

Do not exceed the recommended dosage.

Determine the body weight accurately before treatment to ensure correct dosage.

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 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.

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

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.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Cardiac stimulant (phosphodiesterase inhibitor).

ATCvet code: QC01CE90

5.1 Pharmacodynamic properties

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 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 product has been shown to improve the quality of life and to extend life expectancy in treated dogs.

5.2 Pharmacokinetic particulars

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, microcrystalline
Croscarmellose sodium
Magnesium stearate
Natural meat flavour

6.2 Incompatibilities

Not applicable.

6.3 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.

6.4. Special precautions for storage

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

6.5 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:
5 tablets per blister: 4, 10, 20 or 50 blisters per carton.

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eurovet Animal Health BV
Handelsweg 25
5531 AE Bladel
The Netherlands

BE, DK, EL, LU, NL:

Dechra Regulatory BV
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

To be completed in accordance with national requirements

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

To be completed in accordance with national requirements.

10. DATE OF REVISION OF THE TEXT

To be completed in accordance with national requirements

LABELLING AND PACKAGE LEAFLET

CARDISURE TABLETS

(5 mg tablets)

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cardisure flavoured 5 mg Tablets For dogs
Pimobendan

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 tablet contains:
Active substance:
Pimobendan 5 mg

3. PHARMACEUTICAL FORM

Tablets [Already included in the product name]

4. PACKAGE SIZE

20/50/100/250 tablets

5. TARGET SPECIES

Dogs [Already included in the product name]

6. INDICATIONS

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

7. METHOD AND ROUTE OF ADMINISTRATION

For oral administration.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP: {month/year}

11. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.

Return any divided tablet to the opened blister and use within 3 days.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: Read package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eurovet Animal Health BV
Handelsweg 25, 5531 AE Bladel, The Netherlands

BE, DK, EL, LU, NL:
Dechra Regulatory BV
Handelsweg 25, 5531 AE Bladel, The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

MA number/0/00/000/000

17. MANUFACTURER’S BATCH NUMBER

Lot: {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cardisure flavoured 5 mg Tablets For dogs
Pimobendan

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Eurovet Animal Health BV

BE, DK, EL, LU, NL: Dechra Regulatory BV

3. EXPIRY DATE

EXP: {month/year}

4. BATCH NUMBER

Lot: {number}

5. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

PACKAGE LEAFLET FOR:
Cardisure flavoured 1.25/2.5/5/10 mg
Tablets for dogs

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT:

Marketing authorisation holder:

Eurovet Animal Health BV
Handelsweg 25, 5531 AE Bladel
The Netherlands

BE, DK, EL, LU, NL:

Dechra Regulatory BV
Handelsweg 25, 5531 AE Bladel
The Netherlands

Manufacturer responsible for batch release:

Eurovet Animal Health BV
Handelsweg 25, 5531 AE Bladel
The Netherlands

Genera Inc.

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

Only the site testing and releasing the batches will be mentioned on the printed leaflet.

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

The active substance is pimobendan.

1.25 mg: 1 tablet contains 1.25 mg pimobendan

2.5 mg: 1 tablet contains 2.5 mg pimobendan

5 mg: 1 tablet contains 5 mg pimobendan

10 mg: 1 tablet contains 10 mg pimobendan

Light brown round tablets, scored on one side and plain on the other side.

4. INDICATIONS

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. ADVERSE REACTIONS

A moderate positive chronotropic effect and vomiting may occur in rare cases. However, these effects are dose-dependent and may be avoided by reducing the dose in these cases. In rare cases transient diarrhoea, anorexia or lethargy have been observed.

Although a relationship with pimobendan has not been clearly established, in very rare cases, effects on primary haemostasis (petechia on mucous membranes, subcutaneous haemorrhage) may be observed during treatment. These signs disappear when the treatment is withdrawn.

In rare cases, an increase in mitral valve regurgitation has been observed during chronic pimobendan treatment in dogs with mitral valve disease.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs.

8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION

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 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 product should be used only in dogs with cardiac insufficiency.
Do not exceed the recommended dosage.
Determine the bodyweight accurately before treatment to ensure correct dosage.

10. WITHDRAWAL PERIOD

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 WARNINGS

Special warnings for each target species:

The 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 use in animals:

The 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 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 product to dogs with severe hepatic insufficiency.

Monitoring of cardiac function and morphology is recommended in animals treated with pimobendan. (See also section 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.

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

Use during pregnancy or lactation:

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 they have shown that pimobendan is excreted into milk. The safety of the product has not been assessed in pregnant or nursing bitches. Use only according to the benefit/risk assessment by the responsible veterinarian.

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 (symptoms, emergency procedures, 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.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

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

Package 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.