ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cardisan 1.25 mg chewable tablets for dogs (AT, BE, BG, CY, CZ, DE, EE, EL, ES, FR, HR, HU, IE, IT, LV, LT, LU, MT, NL, PL, PT, RO, SI, SK, UK(NI))
Cardisan Vet 1.25 mg chewable tablets for dogs (DK, FI, IS, NO, SE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Pimobendan 1.25 mg

Excipients:

Qualitative composition of excipients and other constituents
Citric acid Povidone Lactose monohydrate Cellulose, microcrystalline Croscarmellose sodium Chicken flavour Yeast (dried) Silica, colloidal hydrated Magnesium stearate

Chewable tablet.
Light brown with brown spots, round and convex 8 mm tablet with a cross-shaped break line on one side. Tablets can be divided into 2 or 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 dilated cardiomyopathy or valvular insufficiency (mitral and/or tricuspid valve regurgitation).

3.3 Contraindications

Do not use pimobendan in cases of hypertrophic cardiomyopathies or in clinical conditions where an improvement in cardiac output is not possible for functional or anatomical reasons (e.g. aortic stenosis).
Do not use in cases of known hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:
The blood glucose should be tested regularly during treatment in dogs with existing diabetes mellitus.
Since pimobendan is metabolised mainly via the liver, it should not be used in dogs with severe impairment of liver function.
Monitoring of cardiac function and morphology is recommended in animals treated with pimobendan. (See also section 3.6).
The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This product may cause tachycardia, orthostatic hypotension, flushing of the face and headaches.
To avoid accidental ingestion, especially by a child, unused tablet parts should be placed back into the blister and carton and carefully kept away from children. Part used tablets should be used at the time of the next dose.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.

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

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Vomiting*[1] Diarrhoea*[2] Anorexia*[2] Lethargy*[2] Increased heart rate (slightly positive chronotropic effect)*[1] Increase in mitral valve regurgitation*[3]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Signs of effects on primary haemostasis: mucosa petechiae, subcutaneous haemorrhage*[4]

*[1] Effects are dose-dependent (can be avoided by reducing the dose).
*[2] Transient effect.
*[3] Observed during chronic pimobendan treatment in dogs with mitral valve disease.
*[4] 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 also the last section of the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

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

Lactation:
Laboratory studies in rats have also shown that pimobendan is excreted into milk.

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

3.8 Interactions with other medicinal products and other forms of interaction

In pharmacological studies no interaction between the cardiac glycoside strophanthin and pimobendan was observed. The pimobendan-induced increase in cardiac contractility is attenuated by calcium antagonists and by beta-antagonists.

3.9 Administration routes and dosage

For oral use.
Do not exceed the recommended dosage.
Determine the bodyweight accurately before treatment to ensure correct dosage.
The dose should be orally administered and within the dose range of 0.2 mg to 0.6 mg pimobendan/kg bodyweight, divided into two daily doses. The preferable daily dose is 0.5 mg/kg bodyweight, divided into two daily doses (0.25 mg/kg bodyweight each). Each dose should be given approximately 1 hour before feeding.

This corresponds to:
One 1.25 mg chewable tablet in the morning and one 1.25 mg chewable tablet in the evening for a body weight of 5 kg.

Chewable tablets can be divided into four equal parts, for dosage accuracy, according to the bodyweight.
The product may be combined with a diuretic treatment, e.g. furosemide.

In case of congestive heart failure a life-long treatment is recommended. The maintenance dose should be individually adjusted according to the severity of the disease.

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

In the case of overdose, a positive chronotropic effect, vomiting, apathy, ataxia, heart murmurs or hypotension 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. These changes are of pharmacodynamic origin.

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

Not applicable.

3.12 Withdrawal period(s)

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QC01CE90

4.2 Pharmacodynamics

Pimobendan, a benzimadazole-pyridazinone derivative, has a positive inotropic action and possesses pronounced vasodilator properties.

The positive inotropic effect of pimobendan is mediated by two mechanisms of action: increase in calcium sensitivity of cardiac myofilaments and inhibition of phosphodiesterase III. Thus the positive inotropism is triggered neither by an action similar to that of the cardiac glycosides nor sympathomimetics. The vasodilator effect arises from inhibition of phosphodiesterase III.

When used in cases of symptomatic 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 symptomatic 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.

4.3 Pharmacokinetics

Following oral administration of the veterinary medicinal product the absolute bio-availability of the active principle is 60 – 63%. The bio-availability is considerably reduced when pimobendan is administered with food or shortly thereafter. After oral administration of a single dose of 0.2 – 0.4 mg pimobendan/kg bodyweight to dogs fasted overnight, the plasma concentrations increased fast. The peak concentration (C_{max}) of ~ 24 ng/mL was reached after a median of 0.75 hours (T_{max} ranged from 0.25 to 2.5 hours).

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%.

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.

The plasma elimination half-life of pimobendan is ~ 1 hour. Almost the entire dose is eliminated in the 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: 5 years.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

5.4 Nature and composition of immediate packaging

Aluminium-OPA/Aluminium/PVC blisters containing 10 tablets.
Cardboard box of 30, 60, 90, 100 or 120 tablets.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

Alfasan Nederland B.V.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

{MM/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.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cardisan 1.25 mg chewable tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Active substance:
Pimobendan 1.25 mg

3. PACKAGE SIZE

30 tablets
60 tablets
90 tablets
100 tablets
120 tablets

4. TARGET SPECIES

Dogs

5. INDICATION(S)

6. ROUTES OF ADMINISTRATION

For oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

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

Alfasan Nederland B.V.

14. MARKETING AUTHORISATION NUMBER(S)

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Aluminium blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cardisan 1.25 mg chewable tablets

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

pimobendan 1.25 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Cardisan 1.25 mg chewable tablets for dogs
Cardisan 2.5 mg chewable tablets for dogs
Cardisan 5 mg chewable tablets for dogs
Cardisan 10 mg chewable tablets for dogs
Cardisan 15 mg chewable tablets for dogs

2. Composition

Each tablet contains:

Active substance:
Pimobendan 1.25 mg / 2.5 mg / 5 mg / 10 mg / 15 mg

Chewable tablet.
Light brown with brown spots, round and convex 8 / 10 / 13 / 18 / 20 mm flavoured tablet with a cross-shaped break line on one side. Tablets can be divided into 2 or 4 equal parts.

3. Target species

Dogs

4. Indications for use

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

5. Contraindications

Do not use pimobendan in cases of hypertrophic cardiomyopathies or in clinical conditions where an improvement in cardiac output is not possible for functional or anatomical reasons (e.g. aortic stenosis).
Do not use in cases of known hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special precautions for safe use in target species:
The blood glucose should be tested regularly during treatment in dogs with existing diabetes mellitus.
Since pimobendan is metabolised mainly via the liver, it should not be used in dogs with severe impairment of liver function.
Monitoring of cardiac function and morphology is recommended in animals treated with pimobendan. (See also section “Adverse events”).
The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This product may cause tachycardia, orthostatic hypotension, flushing of the face and headaches.
To avoid accidental ingestion, especially by a child, unused tablet parts should be placed back into the blister and carton and carefully kept away from children. Part used tablets should be used at the time of the next dose.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

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

Lactation:
Laboratory studies in rats have also shown that pimobendan is excreted into milk.
The safety of the product has not been assessed in nursing bitches.
Use only according to the benefit/risk assessment by the responsible veterinarian.

Interactions with other medicinal products and other forms of interaction:
In pharmacological studies no interaction between the cardiac glycoside strophanthin and pimobendan was observed. The pimobendan-induced increase in cardiac contractility is attenuated by calcium antagonists and by beta-antagonists.

Overdose:
In the case of overdose, a positive chronotropic effect, vomiting, apathy, ataxia, heart murmurs or hypotension 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. These changes are of pharmacodynamic origin.

Major incompatibilities:
Not applicable.

7. Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Vomiting*[1] Diarrhoea*[2] Anorexia*[2] Lethargy*[2] Increased heart rate (slightly positive chronotropic effect)*[1] Increase in mitral valve regurgitation*[3]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Signs of effects on primary haemostasis: mucosa petechiae, subcutaneous haemorrhage*[4]

*[1] Effects are dose-dependent (can be avoided by reducing the dose).
*[2] Transient effect.
*[3] Observed during chronic pimobendan treatment in dogs with mitral valve disease.
*[4] 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 local representative of> the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

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

For oral use.
Do not exceed the recommended dosage.
Determine the bodyweight accurately before treatment to ensure correct dosage.
The dose should be orally administered and within the dose range of 0.2 mg to 0.6 mg pimobendan/kg bodyweight, divided into two daily doses.
The preferable daily dose is 0.5 mg/kg bodyweight, divided into two daily doses (0.25 mg/kg bodyweight each).
Each dose should be given approximately 1 hour before feeding.

This corresponds to:
One 1.25 mg chewable tablet in the morning and one 1.25 mg chewable tablet in the evening for a body weight of 5 kg.
One 2.5 mg chewable tablet in the morning and one 2.5 mg chewable tablet in the evening for a body weight of 10 kg.
One 5 mg chewable tablet in the morning and one 5 mg chewable tablet in the evening for a body weight of 20 kg.
One 10 mg chewable tablet in the morning and one 10 mg chewable tablet in the evening for a body weight of 40 kg.
One 15 mg chewable tablet in the morning and one 15 mg chewable tablet in the evening for a body weight of 60 kg.

In case of congestive heart failure a life-long treatment is recommended. The maintenance dose should be individually adjusted according to the severity of the disease.

9. Advice on correct administration

Chewable tablets can be divided into four equal parts, for dosage accuracy, according to the bodyweight.
The product may be combined with a diuretic treatment, e.g. furosemide.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
This veterinary medicinal product does not require any special storage conditions.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton and blister after Exp. The expiry date refers to the last day of that month.

12. Special precautions for the 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

Cardisan 1.25 mg / 2.5 mg / 5 mg / 10 mg chewable tablets for dogs
Aluminium-OPA/Aluminium/PVC blisters containing 10 tablets

Cardisan 15 mg chewable tablets for dogs
Aluminium-OPA/Aluminium/PVC blisters containing 5 tablets.

Cardboard box of 30, 60, 90, 100 or 120 tablets.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{DD/MM/YYYY}
Detailed information on this veterinary medicinal product is available in the Union Product Database.

16. Contact details

Marketing authorisation holder <and manufacturer responsible for batch release> <and contact details to report suspected adverse reactions>:
Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

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

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

17. Other information

<to be completed nationally>