ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zelys 5 mg chewable tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance:
Pimobendan 5.00 mg

Excipients:

Qualitative composition of excipients and other constituents
Silica colloidal anhydrous
Stearic acid
Copovidone
Croscarmellose sodium
Malic acid
Maize starch
Cellulose microcrystalline
Lactose monohydrate
Dried Yeast (from *Saccharomyces cerevisiae*)
Pig liver powder

Round in shape beige to light brown tablet, with single score line on one side.
The tablets can be divided into two 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 valve regurgitation) or dilated cardiomyopathy.
(See also section 3.9).

3.3 Contraindications

Do not use pimobendan in hypertrophic cardiomyopathies or in diseases in which an improvement in cardiac output cannot be achieved for functional or anatomical reasons (e.g. aortic stenosis).Do not use in dogs with severe impairment of liver function since pimobendan is metabolised mainly via the liver.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
(See also section 3.7).

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.

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 the animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Accidental ingestion, especially by a child, may lead to the occurrence of tachycardia, orthostatic hypotension, flushing of the face and headaches.

Unused part-tablets should be returned to the open blister space, or to the bottle and inserted back into the outer packaging. Keep in a safe place out of the sight and reach of children.

Close bottle tightly with cap directly after removal of the required number of tablets or part-tablets.

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[1], Heart valve disorder[3]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Mucosa petechiae[4], Haemorrhage[4,5]

[1] Dose-dependent and can be avoided by reducing the dose.
[2] Transient
[3] Mitral valve regurgitation has been observed during chronic pimobendan treatment in dogs with mitral valve disease.
[4] Although a relationship with pimobendan has not been clearly established, these signs of effects on primary haemostasis disappear when the treatment is withdrawn.
[5] Subcutaneous

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

Pregnancy and lactation:

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

3.8 Interaction with other medicinal products and other forms of interaction

In pharmacological studies no interaction between the cardiac glycosides strophanthin and pimobendan was observed. The pimobendan-induced increase in cardiac contractility is attenuated by the calcium antagonists verapamil and diltiazem and by 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 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), using a suitable combination of whole, or half of tablets. One half of the dose in the morning and the other half approximately 12 hours later.
Each dose should be given approximately one hour before feeding. Spontaneous intake by the animal or place the tablet directly in the mouth. This corresponds to:
One 5 mg chewable tablet in the morning and one 5 mg chewable tablet in the evening for a body weight of 20 kg.

Tablets (1.25, 5 and 10 mg tablet) are divisible in two equal parts.The veterinary medicinal product may be combined with a diuretic treatment such as furosemide.

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 periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATC vet 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 mechanism of action: increase in calcium sensitivity of cardiac myofilaments and inhibition of phosphodiesterase (type III). It also exhibits a vasodilating action through an inhibitory action on phosphodiesterase III activity. Thus the positive

inotropism is triggered neither by an action similar to that of the cardiac glycosides nor sympathomimetically.

When used in cases of symptomatic 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 symptomatic 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

Following oral administration of pimobendan, the absolute bioavailability of the active principle is 60 - 63 %. Since this bioavailability is considerably reduced when pimobendan is administered with food or shortly thereafter, it is recommended to treat animals approximately 1 hour before feeding.
After oral administration of 0.25 mg/kg b.w of pimobendan, the maximal plasma concentration was 17.4 µg/L (mean C_{max}) and AUC was 20.9 h*µg/L (mean AUC_{0-t}).

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 sulfates.

The plasma elimination half-life of pimobendan is 0.4 hours, consistent with the high clearance of 90 ml/min/kg and a short mean residence time of 0.5 hours.
The main active metabolite is eliminated with a plasma elimination half-life of 2.0 hours. Almost the entire dose is eliminated via faeces.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

For blisters: Shelf life of the veterinary medicinal product as packaged for sale: 3 years

For bottle: Shelf life of the veterinary medicinal product as packaged for sale: 18 months
Shelf life after first opening the immediate packaging: 4 months

5.3 Special precautions for storage

For blisters: Any unused tablet portion should be returned to the blister and be used for the next administration.
Do not store above 30°C.

For bottle: Keep the bottle tightly closed in order to protect from moisture.
Any unused tablet portion should be returned to the bottle and be used for the next administration.
Do not store above 25°C.

5.4 Nature and composition of immediate packaging

For blisters: Polyamide-Aluminium-Polyvinyl chloride / aluminium heat sealed blisters.

Cardboard box with 5 or 16 blisters of 6 tablets

For bottle: High density polyethylene screw bottles with a polypropylene child-resistant closure –twist off cap.
150 ml bottle contains 60 tablets

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

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

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE 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. (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box containing 1 bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zelys 5 mg chewable tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Pimobendan 5.00 mg

3. PACKAGE SIZE

60 tablets

4. TARGET SPECIES

Dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp.{mm/yyyy}
Once opened use within 4 months.
Once opened, use by:…

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C.
Keep the bottle tightly closed in order to protect from moisture.
Any unused tablet portion should be returned to the bottle and be used for the next administration.

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 NUMBER(S)

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zelys 5 mg chewable tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Pimobendan 5.00 mg

3. TARGET SPECIES

Dogs

4. ROUTES OF ADMINISTRATION

Oral use
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

6. EXPIRY DATE

Exp.{mm/yyyy}
Once opened use within 4 months.

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C.
Keep the bottle tightly closed in order to protect from moisture.
Any unused tablet portion should be returned to the bottle and be used for the next administration.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

9. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box containing 30 or 96 tablets

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zelys 5 mg chewable tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Pimobendan 5.00 mg

3. PACKAGE SIZE

30 tablets
96 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.
Any unused tablet portion should be returned to the blister and be used for the next administration.

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 NUMBER(S)

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zelys 

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE

5 mg of pimobendan

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

1. Name of the veterinary medicinal product

Zelys 5 mg chewable tablets for dogs

2. Composition

Each tablet contains:
Active substance:
Pimobendan 5.00 mg
Round in shape beige to light brown tablet, with single score line on one side.
The tablets can be divided into two 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 valve regurgitation) or dilated cardiomyopathy. (See also section "Administration routes and dosage**"**).

5. Contraindications

Do not use pimobendan in hypertrophic cardiomyopathies or in diseases in which an improvement in cardiac output cannot be achieved for functional or anatomical reasons (e.g. aortic stenosis).
Do not use in dogs with severe impairment of liver function since pimobendan is metabolised mainly via the liver.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

(See also section "Pregnancy and lactation").

6. Special warnings

Special warnings:
None.

Special precautions for safe use in the target species:
The chewable tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the animals.
For veterinarians only
The blood glucose should be tested regularly during treatment in dogs with existing diabetes mellitus.
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:
Accidental ingestion, especially by a child, may lead to the occurrence of tachycardia, orthostatic hypotension, flushing of the face and headaches.
Unused part-tablets should be returned to the open blister space, or to the bottle and inserted back into the outer packaging. Keep in a safe place out of the sight and reach of children.
Close bottle tightly with cap directly after removal of the required number of tablets or part-tablets.
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 and lactation:
Laboratory studies in rats and rabbits have not produced any evidence of teratogenic or foetotoxic effects. Laboratory studies in rats and rabbits have shown evidence of maternotoxic and embryotoxic effects at high doses. Pimobendan is excreted into milk. The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only according to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
For veterinarians only
In pharmacological studies no interaction between the cardiac glycosides strophanthin and pimobendan was observed. The pimobendan-induced increase in cardiac contractility is attenuated by the calcium antagonists verapamil and diltiazem and by the β-antagonist propranolol.

Overdose:
In case of overdose, please contact your veterinarian.

For veterinarians only
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[1], Heart valve disorder[3]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Mucosa petechiae[4,5], Haemorrhage[4,6]

[1] Dose-dependent and can be avoided by reducing the dose.
[2] Transient
[3] Mitral valve regurgitation has been observed during chronic pimobendan treatment in dogs with mitral valve disease.

[4] Although a relationship with pimobendan has not been clearly established, these signs of effects on primary haemostasis disappear when the treatment is withdrawn.
[5] Pinpoint discolouration of mucosae due to bleeding
[6] Subcutaneous

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 shown below in his leaflet, or via your national reporting system {national system details}.

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

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 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), using a suitable combination of whole, or half of tablets. One half of the dose in the morning and the other half approximately 12 hours later.
Each dose should be given approximately one hour before feeding.
This corresponds to:
One 5 mg chewable tablet in the morning and one 5 mg chewable tablet in the evening for a body weight of 20 kg.
Tablets (1.25, 5 and 10 mg tablet) are divisible in two equal parts.The veterinary medicinal product may be combined with a diuretic treatment such as furosemide.

9. Advice on correct administration

Spontaneous intake by the animal or place the tablet directly in the mouth.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

For blisters: Any unused tablet portion should be returned to the blister and be used for the next administration.
Do not store above 30°C.

For bottle: Shelf life after first opening the immediate packaging: 4 months
Keep the bottle tightly closed in order to protect from moisture.
Any unused tablet portion should be returned to the bottle and be used for the next administration.
Do not store above 25°C.

Do not use this veterinary medicinal product after the expiry date which is stated on the blister or bottle and carton 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

(MA)

Pack sizes:

For blisters: Cardboard box with 5 or 16 blisters of 6 tablets.
For bottle: 150 ml bottle containing 60 tablets

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{mm/yyyy}
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 contact details to report suspected adverse reactions:
(Name and address to be completed nationally)
Tel: +800 35 22 11 51
Email: pharmacovigilance@ceva.com

Manufacturer responsible for batch release:
Ceva Santé Animale
Boulevard de la Communication
Zone Autoroutière
53950 Louverné
France

15. Other information