ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetmedin 5 mg capsules for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

Active substance:
Pimobendan: 5 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Citric acid anhydrous	
Silica, colloidal anhydrous	
Cellulose microcrystalline	
Povidone	
Magnesium stearate	
Gelatine	
Titanium dioxide (E171)	*1.2320 mg*
Sunset yellow FCF (E110)	*0.3080 mg*

Oblong hard gelatine capsule with an orange opaque cap and a white opaque body.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use, specifying the target species

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

3.3 Contraindications

Do not use in cases of hypertrophic cardiomyopathies or clinical conditions where an increase of cardiac output is not possible for functional or anatomical reasons (e.g. aortic stenosis).
Do not use in dogs with severe hepatic insufficiency since pimobendan is metabolised mainly in the liver.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

Absorption of this veterinary medicinal product is modified when administered with food. Therefore, the optimum efficacy is obtained when the stomach is empty. The veterinary medicinal product should be given one hour before feeding.

3.5 Special precautions for use

Special precautions for safe use in the target species:
In diabetic animals, glucose levels have to be strictly controlled.

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

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

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	- Gastrointestinal adverse reactions (e.g., vomiting and diarrhoea) - Systemic reactions (e.g., lethargy and anorexia) - Cardiovascular system disorders (e.g., moderate positive chronotropic effects)
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	- Signs of effects on primary haemostasis (e.g., petechiae on mucous membranes, subcutaneous haemorrhages)[1]

[1] 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

Pregnancy and lactation:
Laboratory studies in rats and rabbits have not produced any effect on fertility. 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. Therefore, 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 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 ß-antagonist propranolol.

3.9 Administration routes and dosage

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

The veterinary medicinal product 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 daily dose should be divided into two administrations (0.25 mg/kg each), 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.

Body weight (kg)	Pimobendan daily dose (mg)	Vetmedin 1.25 mg No. capsules/adm		Vetmedin 2.5 mg No. capsules/adm		Vetmedin 5 mg No. capsules/adm	
		Morning	Afternoon	Morning	Afternoon	Morning	Afternoon
< 8	2,5	1	1	-	-	-	-
8 – 20	5	-	-	1	1	-	-
21 – 40	10	-	-	-	-	1	1
41 – 60	20	-	-	-	-	2	2
> 60	30	-	-	-	-	3	3

The veterinary medicinal product may be combined with a diuretic treatment such as furosemide or torasemide.

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

The administration of twice the therapeutic dose (1 mg pimobendan/kg body weight) may produce moderate positive chronotropic effects and vomiting. In such situations, treatment should be interrupted until symptoms disappear and then the veterinary medicinal product should be used at the recommended dose.

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 ATCvet code:

QC01CE90

4.2 Pharmacodynamics

Pimobendan, a benzimidazole-pyridazinone derivative, is a non-sympathomimetic, non-glycoside inotropic substance with potent vasodilatative properties.
Pimobendan is a racemic mixture of two stereoisomers. The (-)-enantiomer is the active compound of the mixture.
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). However, the mechanism of action of calcium sensitivity is not totally clear.
It also exhibits a vasodilating action through an inhibitory action on phosphodiesterase III activity and exerts an antithrombotic effect through the inhibition of the plaquetary aggregation.

Pimobendan improves the cardiac relaxation exerting a lusotropic positive effect.

4.3 Pharmacokinetics

Absorption:
Following oral administration of Vetmedin capsules the absolute biovailability of the active ingredient 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.

Distribution:
The volume of distribution in the steady state is 2.6 l/kg after intravenous administration, indicating that pimobendan is distributed readily into the tissues. The mean plasma protein binding in vitro is 93 %.

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

Elimination:
The plasma elimination half-life of pimobendan is 0.4 ± 0.1 hours, consistent with the high clearance of 90 ± 19 ml/min/kg and a short mean residence time of 0.5 ± 0.1 hours.
The main active metabolite is eliminated with a plasma elimination half-life of 2.0 ± 0.3 hours.

After oral administration, the plasma elimination half-life of pimobendan and its major active metabolite is 0.7 ± 0.1 and 1.9 ± 0.4 hours, respectively.
The compound is excreted principally with faeces and in less proportion with urine.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 50 days.

5.3 Special precautions for storage

Do not store above 25ºC.
Keep the bottle tightly closed.

5.4 Nature and composition of immediate packaging

White high-density polyethylene bottles. Each bottle is closed with a child-resistant closure of polypropylene.

Package size:

A folding carton containing 1 bottle of 100 capsules.

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

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

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 III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetmedin 5 mg capsules for dogs

2. STATEMENT OF ACTIVE SUBSTANCES

Each capsule contains:
Pimobendan: 5 mg

3. PACKAGE SIZE

100 capsules

4. TARGET SPECIES

Dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached use by 50 days.

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 ºC.
Keep the bottle tightly closed.

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
Polyethylene bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Vetmedin 5 mg capsules for dogs

2. STATEMENT OF ACTIVE SUBSTANCES

Each capsule contains:
Pimobendan: 5 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 broached use by 50 days.

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25 ºC.
Keep the bottle tightly closed.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Vetmedin 2.5 mg capsules for dogs

2. Composition

Active substance:
Pimobendan: 5 mg

Excipients:
Titanium dioxide (E171): 1.2320 mg
Sunset yellow FCF (E110): 0.3080 mg

Oblong hard gelatine capsule with an orange opaque cap and a white opaque body.

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 regurgitation).

5. Contraindications

Do not use in cases of hypertrophic cardiomyopathies or clinical conditions where an increase of cardiac output is not possible for functional or anatomical reasons (e.g. aortic stenosis).
Do not use in dogs with severe hepatic insufficiency since pimobendan is metabolised in the liver.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Absorption of this veterinary medicinal product is modified when administered with food. Therefore, the optimum efficacy is obtained when the stomach is empty. The veterinary medicinal product should be given one hour before feeding.

Special precautions for safe use in the target species:
In diabetic animals, glucose levels have to be controlled strictly.

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

Pregnancy and lactation:
Laboratory studies in rats and rabbits have not produced any effect on fertility. 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. Therefore, 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 ß-antagonist propranolol.

Overdose:
The administration of twice the therapeutic dose (1 mg pimobendan/kg body weight) may produce moderate positive chronotropic effects and vomiting. In such situations, treatment should be interrupted until symptoms disappear and then the veterinary medicinal product should be used at the recommended dose.

7. Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):
- Gastrointestinal adverse reactions, (e.g., vomiting and diarrhoea) - Systemic reactions (e.g., lethargy and anorexia) - Cardiovascular system disorders (e.g., moderate positive chronotropic effects)
Very rare (<1 animal / 10,000 animals treated, including isolated reports):
- Signs of effects on primary haemostasis (e.g., petechiae on mucous membranes, subcutaneous haemorrhages)[1]

[1] 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 the local representative of the marketing authorisation holder 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 veterinary medicinal product 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 daily dose should be divided into two administrations (0.25 mg/kg each), 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.

Body weight (kg)	Pimoben-dan Daily dose (mg)	Vetmedin 1.25 mg No.capsules/ administration		Vetmedin 2.5 mg No.capsules/ administration		Vetmedin 5 mg No.capsules/ administration	
		Morning	Afternoon	Morning	Afternoon	Morning	Afternoon
<8	2,5	1	1			-	-
8-20	5	-	-	1	1	-	-
21-40	10	-	-	-	-	1	1
41-60	20	-	-	-	-	2	2
>60	30	-	-	-	-	3	3

The veterinary medicinal product may be combined with a diuretic treatment such as furosemide or torasemide.

9. Advice on correct administration

To ensure a correct dosage, body weight should be determined as accurately as possible.
Each dose should be administered approximately one hour before feeding.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 25ºC.
Keep the bottle tightly closed.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton and bottle after Exp. The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: 50 days.

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

Package size:
A folding carton containing 1 bottle of 100 capsules.

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 contact details to report suspected adverse reactions:

Manufacturer responsible for batch release:
Klocke Pharma Service GmbH
Strassburger Strasse 77
D-77767 Appenweier
Germany

Local representatives and contact details to report suspected adverse reactions: