

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AT, BE, BG, CY, CZ, EE, EL, ES, FR, HU, IE, LI, LU, LV, NL, PL, PT, RO, SI, SK, UK(NI):
Vetmedin 10 mg chewable tablets for dogs

IT:

Vetmedin vet. 10 mg chewable tablets for dogs

LT:

Pimobendan "Boehringer" 10 mg chewable tablets for dogs

IS, NO, SE:

Pimobendan Boehringer Ingelheim Vetmedica 10 mg chewable tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

Active substance:

Pimobendan 10 mg

Excipients:

Qualitative composition of excipients and other constituents
<i>Povidone</i>
<i>Lactose monohydrate</i>
<i>Maize starch</i>
<i>Croscarmellose sodium</i>
<i>Citric acid, anhydrous</i>
<i>Artificial powdered beef flavour</i>
<i>Silica, colloidal anhydrous</i>
<i>Magnesium stearate</i>

Oblong, scored, mottled brown tablets with fine white spots, embossed with Boehringer Ingelheim logo and P04.

The tablets can be divided into 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).

For the treatment of dilated cardiomyopathy in the preclinical stage (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter) in Doberman Pinschers following echocardiographic diagnosis of cardiac disease.

For the treatment of dogs with myxomatous mitral valve disease (MMVD) in the preclinical stage (asymptomatic with a systolic mitral murmur and evidence of increased heart size) to delay the onset of clinical symptoms of heart failure.

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). Since pimobendan is metabolised mainly via the liver, it should not be used in dogs with severe impairment of liver function.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

The veterinary medicinal product has not been tested in cases of asymptomatic DCM in Dobermans with atrial fibrillation or sustained ventricular tachycardia.

The veterinary medicinal product has not been tested in cases of asymptomatic myxomatous mitral valve disease in dogs with significant supraventricular and/or ventricular tachyarrhythmia.

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. For use in the preclinical stage of dilated cardiomyopathy (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter), a diagnosis should be made by means of a comprehensive cardiac examination (incl. echocardiographic examination and possibly Holter monitoring).

For use in the preclinical stage of myxomatous mitral valve disease (stage B2, according to ACVIM consensus: asymptomatic with mitral murmur $\geq 3/6$ and cardiomegaly due to myxomatous mitral valve disease), a diagnosis should be made by means of a comprehensive physical and cardiac examination which should include echocardiography or radiography where appropriate.

Monitoring of cardiac function and morphology is recommended in animals treated with pimobendan.

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:

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):	- Vomiting ¹ , diarrhoea ² - Anorexia ² , lethargy ² - Increased heart rate ^{1,3} , increase in mitral valve regurgitation ⁴
Very rare (< 1 animal / 10,000 animals treated, including isolated reports):	- Mucosa petechiae ⁵ , haemorrhage (subcutaneous) ⁵

¹ These effects are dose-dependent and can be avoided by reducing the dose.

² Transient

³ Due to a slight positively chronotropic effect.

⁴ Observed during chronic pimobendan treatment in dogs with mitral valve disease.

⁵ A relationship with pimobendan has not been clearly established, 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 https://www.ema.europa.eu/documents/template-form/qrd-appendix-i-adverse-event-phv-mss-reporting-details_en.docx. 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. 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.

3.8 Interaction 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 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.

Determine the bodyweight accurately before treatment to ensure correct dosage.

The dose should be 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) approximately 12 hours apart. Each dose should be given approximately 1 hour before feeding.

This corresponds to:

One 10 mg chewable tablet in the morning and one 10 mg chewable tablet in the evening for a bodyweight of 40 kg.

Chewable tablets can be halved at the score line provided, for dosage accuracy, according to the bodyweight.

Use any divided tablet at the next administration time.

The veterinary medicinal product may be combined with a diuretic, e.g., 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 ATCvet code:

QC01CE90

4.2 Pharmacodynamics

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.

In a randomized and placebo controlled study in 363 dogs with preclinical myxomatous mitral valve disease, all dogs met the following inclusion criteria: age ≥ 6 years, bodyweight ≥ 4.1 and ≤ 15 kg, characteristic systolic heart murmur of moderate to high intensity (\geq grade 3/6) with maximal intensity over the mitral area; echocardiographic evidence of advanced myxomatous mitral valve disease (MMVD) defined as characteristic valvular lesions of the mitral valve apparatus, echocardiographic evidence of left atrial and left ventricular dilatation and radiographic evidence of cardiomegaly (vertebral heart sum (VHS) > 10.5). The median time to onset of clinical signs of heart failure or cardiac death/euthanasia was extended in these dogs by approximately 15 months. Additionally, there was a reduction in the heart size of dogs treated with pimobendan in the preclinical stage of myxomatous mitral valve disease. Furthermore, overall survival time was prolonged by approximately 170 days in all dogs receiving pimobendan independent of their cause of death (cardiac death/euthanasia and non-cardiac death/euthanasia). Cardiac related death or euthanasia occurred in 15 dogs in the pimobendan group and 12 dogs in the placebo group prior to the onset of CHF. Dogs in the pimobendan group spent a longer time in the study (347.4 patient years) than those in the placebo group (267.7 patient years) resulting in a lower rate of occurrence.

In a randomized and placebo-controlled study including Doberman Pinschers with preclinical dilated cardiomyopathy (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter following echocardiographic diagnosis), the time to onset of congestive heart failure or sudden death was extended and survival time was prolonged among dogs administered pimobendan.

Additionally, there was a reduction in the heart size of dogs treated with pimobendan in the preclinical stage of dilated cardiomyopathy. Efficacy evaluation is based on data from 19 (of 39) and 25 (of 37) dogs that reached the primary efficacy endpoint in the pimobendan and the placebo group, respectively.

Pimobendan, a benzimidazole-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.

4.3 Pharmacokinetics

Absorption:

After oral administration of the veterinary medicinal product the absolute bioavailability is 60 - 63%. Since simultaneous or previous food intake reduces the bioavailability, pimobendan should be administered about 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 demethylated by oxidation to the major active metabolite (UD-CG 212). Further metabolic steps are phase II conjugates of UD-CG 212, such as glucuronides and sulphates.

Elimination:

The plasma elimination half-life of pimobendan is 0.4 ± 0.1 hours, which corresponds to the high clearance of 90 ± 19 ml/min/kg and the short mean residence time of 0.5 ± 0.1 hours.

The most significant active metabolite is eliminated with a plasma elimination half-life of 2.0 ± 0.3 hours. 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: 30 months.

Shelf life after first opening the immediate packaging: 100 days.

5.3 Special precautions for storage

Keep the bottle tightly closed in order to protect from moisture.

5.4 Nature and composition of immediate packaging

Cardboard box containing 50 tablets in a polyethylene bottle, closed with a polypropylene child-resistant screw cap.

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 \(https://medicines.health.europa.eu/veterinary\)](https://medicines.health.europa.eu/veterinary).

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

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Pimobendan "Boehringer" 10 mg chewable tablets

IS, NO, SE:

Pimobendan Boehringer Ingelheim Vetmedica 10 mg chewable tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Each chewable tablet contains:

Pimobendan 10 mg

3. PACKAGE SIZE

50 tablets

4. TARGET SPECIES

Dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

Shelf life after first opening the bottle: 100 days.

9. SPECIAL STORAGE PRECAUTIONS

Keep the bottle tightly closed in order to protect from moisture.

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}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Polyethylene bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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2. STATEMENT OF ACTIVE SUBSTANCES

Each chewable tablet contains:
Pimobendan 10 mg

3. TARGET SPECIES

Dogs

4. ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Oral use.

5. WITHDRAWAL PERIODS

6. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use by

7. SPECIAL STORAGE PRECAUTIONS

Keep the bottle tightly closed in order to protect from moisture.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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2. Composition

Each chewable tablet contains:

Pimobendan 10 mg

Oblong, scored, mottled brown tablets with fine white spots, embossed with Boehringer Ingelheim logo and P04.

The tablet can be divided into 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).

For the treatment of dilated cardiomyopathy in the preclinical stage (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter) in Doberman Pinschers following echocardiographic diagnosis of cardiac disease.

For the treatment of dogs with myxomatous mitral valve disease (MMVD) in the preclinical stage (asymptomatic with a systolic mitral murmur and evidence of increased heart size) to delay the onset of clinical symptoms of heart failure.

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). Since pimobendan is metabolised mainly via the liver, it should not be used in dogs with severe impairment of liver function.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

The veterinary medicinal product has not been tested in cases of asymptomatic DCM in Dobermans with atrial fibrillation or sustained ventricular tachycardia.

The veterinary medicinal product has not been tested in cases of asymptomatic myxomatous mitral valve disease in dogs with significant supraventricular and/or ventricular tachyarrhythmia.

Special precautions for safe use in the target species:

The blood glucose should be tested regularly during treatment in dogs with existing diabetes mellitus. For use in the preclinical stage of dilated cardiomyopathy (asymptomatic with an increase in left ventricular end-systolic and end-diastolic diameter), a diagnosis should be made by means of a comprehensive cardiac examination (incl. echocardiographic examination and possibly Holter monitoring).

For use in the preclinical stage of myxomatous mitral valve disease (stage B2, according to ACVIM consensus: asymptomatic with mitral murmur $\geq 3/6$ and cardiomegaly due to myxomatous mitral valve disease), a diagnosis should be made by means of a comprehensive physical and cardiac examination which should include echocardiography or radiography where appropriate.

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 the animals.

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 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 veterinary medicinal 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 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 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.

7. Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):

<ul style="list-style-type: none"> - Vomiting¹, diarrhoea² - Anorexia (loss of appetite)², lethargy² - Increased heart rate^{1,3}, increase in mitral valve regurgitation⁴
Very rare (<1 animal / 10,000 animals treated, including isolated reports):
<ul style="list-style-type: none"> - Mucosa petechiae (small red spots on mucosa)⁵, haemorrhages (subcutaneous)⁵

¹ These effects are dose-dependent and can be avoided by reducing the dose.

² Transient

³ Due to a slight positively chronotropic effect.

⁴ Observed during chronic pimobendan treatment in dogs with mitral valve disease.

⁵ A relationship with pimobendan has not been clearly established, 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.

Determine the bodyweight accurately before treatment to ensure correct dosage.

The dose should be 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) approximately 12 hours apart. Each dose should be given approximately 1 hour before feeding.

This corresponds to:

One 10 mg chewable tablet in the morning and one 10 mg chewable tablet in the evening for a bodyweight of 40 kg.

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

9. Advice on correct administration

Do not exceed the recommended dosage.

Chewable tablets can be halved at the score line provided, for dosage accuracy, according to the bodyweight. Use any divided tablet at the next administration time.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Keep the bottle tightly closed in order to protect from moisture.

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 bottle: 100 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 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

Bottle of 50 tablets

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the [Union Product Database \(https://medicines.health.europa.eu/veterinary\)](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:

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim/Rhein
Germany

Local representatives and contact details to report suspected adverse reactions:

17. Other information

