Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Vetmedin 1.5 mg/ml Oral Solution for Dogs

Date Created: March 2025

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Vetmedin 1.5 mg/ml Oral Solution for Dogs, Oral solution
Applicant	Boehringer Ingelheim Animal Health UK Ltd, Ellesfield Avenue, Bracknell, Berkshire, RG12 8YS
Active substance	Pimobendan
ATC Vet code	QC01CE90
Target species	Dogs
Indication 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.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Full application in accordance with Article 8 of VMRs 2013 (Schedule 1, Part 1) as amended.
Date of conclusion of the procedure	03/03/2025

I. SCIENTIFIC OVERVIEW

The product was submitted for a full application in accordance with Article 8 of VMRs 2013 (Schedule 1, Part 1) as amended. The application is to extend the Vetmedin product range to include the new pharmaceutical form of oral solution. To support the applicant bioequivalence to the reference product, Vetmedin 5 mg Hard Capsules for Dogs (Vm 08327/4316) was demonstrated.

Vetmedin 1.5 mg/ml oral solution for dogs is an oral solution containing 1.5 mg/ml pimobendan. The product is indicated for the treatment of canine congestive heart failure originating from cardiomyopathy or valvular insufficiency, for the treatment of dilated cardiomyopathy in the preclinical stage, and treatment of dogs with myxomatous mitral valve disease in the pre-clinical stage. The dose is 0.25 mg pimobendan/kg bodyweight twice daily (equivalent to 0.17 ml of the product twice daily).

The product is classified as POM-V, a veterinary medicinal product subject to prescription.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released on the market. It has been shown that the product can be safely used in the target species, any reactions observed are indicated in the SPC[1]. The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy[2] of the product was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains pimobendan and the excipients sorbic acid, hydroxypropyl-ß-Cyclodextrin, hydroxypropyl methylcellulose, ascorbic acid, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) and purified water.

The container/closure system consists of 60 ml amber glass bottle containing 50 ml oral solution and fitted with a child resistant cap. A second child-resistant cap with integrated plug-in adapter is also provided and should be used after the bottle is first opened. Each bottle is packed in a cardboard box and is equipped with a measuring syringe. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the presence of preservative are justified.

The product is an established pharmaceutical form, and its development is adequately described in accordance with the relevant regulatory guidelines.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of two main steps:

- Compounding
- Filling

Process validation data on the product have been presented in accordance with the relevant regulatory guidelines.

II.C. Control of Starting Materials

The active substance is pimobendan, an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice and has a valid Certificate of Suitability.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

All excipients comply with their European Pharmacopoeia monographs and are not new to veterinary medicinal products in Great Britain.

Pimobendan is packed in a polyethylene bag in a triple layered laminated bag placed in a fibre drum.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. Satisfactory validation data for the analytical methods have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

II.F. Stability

Stability data on the active substance has been provided in accordance with applicable regulatory guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on the finished product have been provided in accordance with applicable regulatory guidelines, demonstrating the stability of the product throughout its shelf life, when stored under the approved conditions.

G. Other Information

The shelf life of the product as packaged for sale is 2 years. The shelf life of the product after first opening the immediate packaging is 8 weeks. The product should be stored below 30°C.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

Due to the legal basis of the application, no pharmacological or toxicological data are required, except to support the user risk assessment. The applicant has claimed bioequivalence with Vetmedin capsules, meaning the user risk assessment is based on the Vetmedin capsules safety assessment.

Warnings and precautions listed on the product literature are adequate to ensure safety of the product to users and the environment.

III.A Safety Documentation

Pharmacological Studies

As this application is to extend the Vetmedin range, bioequivalence to the approved reference product, Vetmedin capsules, was demonstrated.

Studies have been conducted that show that pimobendan has a positively inotropic action, increasing the strength of cardiac contractions, and possesses pronounced vasodilator properties. When used in cases of symptomatic valvular insufficiency, in conjunction with furosemide, pimobendan 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, pimobendan has been shown to improve the quality of life and to extend life expectancy in treated dogs.

In dogs with preclinical myxomatous mitral valve disease, administration of pimobendan has been associated with an increased time to onset of clinical signs of heart failure or cardiac death/euthanasia. Overall survival time was prolonged by approximately 170 days in all dogs receiving pimobendan. In dogs with preclinical dilated cardiomyopathy, it has been shown that the time to onset of congestive heart failure or sudden death is extended and survival time is prolonged in dogs given pimobendan.

Studies have also been conducted regarding the pharmacokinetics of pimobendan. After oral administration the bioavailability is 60-63%. It has been shown that food intake reduces the bioavailability, so pimobendan should be administered about 1 hour before feeding. Upon absorption, pimobendan is distributed readily into the tissues and the mean plasma protein binding is 93%. The major active metabolite is UD-CG 212. 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. The most significant active metabolite is eliminated with a plasma elimination half-life of 2.0 ± 0.3 hours and almost the entire dose is eliminated in the faeces.

Toxicological Studies

This was not required for the product due to the legal basis of the application. Based on data for the reference product, pimobendan is not considered to be genotoxic, mutagenic, or carcinogenic in the quantities used in the product.

The excipients are all used in medicines (human and/or veterinary) or food and are not considered to pose a risk to the user, except for mild skin or eye irritation.

Observations in Humans

Pimobendan may cause eye or skin irritation and the excipients used may cause mild skin or eye irritation.

User Safety

A user risk assessment was provided in compliance with the relevant guideline.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore, the following applicant's user recommendations are appropriate:

- Accidental ingestion, especially by a child, may lead to the occurrence of tachycardia, orthostatic hypotension, flushing of the face and headaches.
- Do not leave a filled syringe unattended.
- This product may cause eye or skin irritation. Avoid skin and eye contact.
- In case of accidental eye or skin contact, immediately rinse thoroughly with water.
- In case irritation develops or if accidental ingestion occurs, seek medical advice immediately and show the package leaflet or the label to the physician.
- People with known hypersensitivity to pimobendan should avoid contact with the product.
- Do not eat, drink, or smoke while handling the product.
- Wash hands after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:
The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required.

IV. CLINICAL DOCUMENTATION

Due to the application being an extension of the current Vetmedin range, clinical information was supplied to demonstrate bioequivalence to the reference product.

IV.I. Pre-Clinical Studies

Pharmacology

To support target species safety and efficacy, the product was compared during a comparative bioavailability study with the reference product, Vetmedin capsules. This study was a randomised, cross-over bioequivalence study, consistent with the regulatory requirements and VICH guidance. It was concluded that bioequivalence was successful demonstrated.

Tolerance in the Target Species

Tolerance studies were not required because this is an extension of the Vetmedin range and data on the reference product could be used to demonstrate safety in dogs.

IV.II. Clinical Documentation

To support efficacy of the product, information was provided on the reference product. Since bioequivalence between the products was shown, the reference data are supportive of the target species effectiveness of the product for the indications given in dogs.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics the benefit/risk profile of the product is favourable.

MODULE 4

POST- AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Product Information Database of the Veterinary Medicines Directorate website.

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The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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