IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Pimodine 5 mg/ml Oral Suspension for Dogs

PRODUCT SUMMARY

EU Procedure number	IE/V/0672/001/DC
Name, strength and pharmaceutical form	Pimodine 5 mg/ml Oral Suspension for Dogs
Active substances(s)	Pimobendan
Applicant	Norbrook Laboratories (Ireland) Limited Rossmore Industrial Estate, Monaghan, Ireland.
Target species	Dogs
Indication(s) for use	For the treatment of canine congestive heart failure originating from valvular insufficiency (mitral and/or tricuspid regurgitation) or dilated cardiomyopathy (DCM).
ATCvet code	QC01CE90

Please note that the development of the veterinary medicinal product during its lifecycle is reflected in the section "Post-authorisation procedures" of this report, as well as in the current SPC and product information. Therefore, for products that have been authorised for some time, any other part of this document may include outdated information.

SUMMARY OF ASSESSMENT

Legal basis of original application*	Hybrid application in accordance with Article 19 of Regulation (EU) 2019/6 as amended.
Marketing authorisation holder	Boehringer Ingelheim Vetmedica GmbH
Marketing authorisation number	VPA10454/021/001
EU procedure number	N/A
Date of authorisation	01/10/1999
Date of completion of the original decentralised procedure	10/06/2026
Concerned Member States for original procedure	BE, DE, DK, ES, FR, HU, IT, NL, PL, RO, UK(NI)
Withdrawn CMS during original decentralised procedure	N/A

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in relevant articles of Regulation (EU) 2019/6. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland. The Summary of Product Characteristics (SPC), the labelling and package leaflet for this product are available in the Union Product Database (UPD).

I. SCIENTIFIC OVERVIEW

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; the reactions observed are indicated in the SPC.
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 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.

II. QUALITY ASPECTS

A. Product description

The product contains pimobendan (5 mg) and the excipients sodium benzoate (1.5 mg), hydroxypropylcellulose, macrogol 300, citric acid anhydrous, xanthan gum, glycerol, microcrystalline cellulose and carmellose sodium, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate, roast beef flavour and purified water.

The container/closure system is standard for this dosage form and is described in the SPC.

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

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

B. Method of Preparation of the Product Description of the manufacturing method

The product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

The product is manufactured using conventional manufacturing techniques. Process validation for full-scale batches will be performed post-authorisation.

C. Control of Starting Materials Production and control of starting materials

The active substance is pimobendan, an established active substance. The active substance is manufactured in accordance with the principles of good manufacturing practice.

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

D. Control tests carried out on isolated intermediates during the manufacturing process

Not applicable.

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 has been provided.
Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.

F. Stability tests (pharmaceuticals)

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

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

G. Other Information (pharmaceuticals)

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a hybrid application according to Article 19 of Regulation (EU) 2019/6 and bioequivalence with the reference VMP, Vetmedin 5 mg capsules, has been demonstrated, results of safety and efficacy tests are not required.

III. SAFETY ASSESSMENT

III.A Safety Tests

This application was submitted in accordance with Article 19 of Regulation (EU) 2019/6 (a hybrid veterinary medicinal product). The reference veterinary medicinal product cited is Vetmedin 5 mg capsules (VPA10454/021/001 – Boehringer Ingelheim Vetmedica GmbH), which has been authorised in the EU for greater than ten years.
Warnings and precautions as listed on the product literature include those of the reference product and are adequate to ensure safety of the product to users and the environment.

Pharmacological Studies

The candidate product is quantitatively and qualitatively the same as the reference product in terms of the active substance (pimobendan). However, it differs in excipients and pharmaceutical form, i.e. the candidate product is an oral suspension, and the reference product is a capsule.
In the application dossier, the applicant initially submitted an *in-vivo* bioequivalence study conducted using the Third-Country authorised product, Vetmedin 5 mg Chewable tablets (NADA 141-273), as comparator. For that study, the 90% confidence intervals for the ratio of the means of $AUC_{last,}$ 104% - 115.9%, were entirely contained within the limits 80% - 125%, whilst the 90% confidence intervals for the ratio of the means of $C_{max,}$ 129% – 149% exceeded the widened limits of 70% - 143%. Moreover, numerous deficiencies were identified in the data presented to support similarity with the EU-authorised reference product and the applicant abandoned this approach.
A new *in vivo* bioequivalence study was provided comparing the candidate product, Pimobendan Oral Suspension 5 mg/ml, and Vetmedin® 5 mg Hard Capsules (Vm 61700/3010, Boehringer Ingelheim Vetmedica GmbH formerly Vm08327/4316). As per CMDV guidance regarding "Different scenarios to use a reference product authorised in UK for generic applications", EMA/CMDv/176758/2025, the use of a VMP authorised in the UK before 31/12/2020 as a reference product is considered acceptable in exceptional cases. The use of the UK reference product (authorised while the UK was part of the European Union) can be accepted.
The applicant specified *a-priori* that bioequivalence would be concluded if the 90% confidence interval for the ratio of the means of $AUC_{0\text{-}Last}$ and C_{max} were included within the interval 80 - 125% and 70 – 143% respectively. The results of this study indicate that the 90% confidence intervals for the ratio of the means of $AUC_{0\text{-}Last}$ [106.2-123.4] and C_{max} [109.7 - 136] lie within the pre-specified limits, indicating bioequivalence. Appropriate justification for widening of the acceptance limits for C_{max} was provided. The intra-individual variability for C_{max} was found to exceed 30%, indicating high variability of pimobendan for this parameter.
Based on the totality of the data provided, equivalence between the test and reference item in terms of safety and efficacy profile can be accepted.

Toxicological Studies

Based on the findings from the *in vivo* bioequivalence study and the additional information and data provided, results of toxicological tests were not required. The safety aspects of this product are expected to be the same as those of the reference product. Warnings and precautions as listed on the product literature are broadly in line with those of the reference product.

User Safety

The applicant has provided a user safety risk assessment in compliance with the relevant guideline.
Given that risk for user exposure to an oral suspension (the candidate product) is likely to be greater than the risk of user exposure to a solid pharmaceutical form (the reference product), data obtained from published literature characterising the potential for dermal/ocular irritancy and skin sensitisation were provided. Given that a lack of conclusive data was retrieved for the active substance, and a risk that the excipient sodium benzoate may be associated with skin and eye irritation was identified, a warning indicating the possibility of skin/eye irritation following dermal/ocular exposure to the formulation was included. The remaining user safety statements are broadly in line with those of the reference product.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product, and read as follows:

- People with known hypersensitivity to pimobendan, sodium benzoate, or any other excipients should avoid contact with the veterinary medicinal product.
- This veterinary medicinal product may cause skin or eye irritation. Avoid contact with skin and eyes. In case of contact with the eyes or spillage onto the skin, immediately rinse thoroughly with water.
- Wash hands after use.
- Do not eat, drink, or smoke while handling the product.
- Accidental ingestion, especially by a child, may lead to the occurrence of tachycardia, orthostatic hypotension, flushing of the face and headaches.

- To avoid accidental ingestion, do not leave a filled syringe unattended and store the bottle and used syringe in the original carton to prevent children from getting access to the veterinary medicinal product.
- Close the bottle tightly with the cap directly after removal of the required amount of suspension. The veterinary medicinal product must be used and kept out of sight and reach of children.
- In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Environmental Risk Assessment

Phase I:

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the VMP will only be used in non-food animals.

Conclusion

Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

IV. CLINICAL ASSESSMENT

As this is a hybrid application according to Article 19 of Regulation (EU) 2019/6 and bioequivalence with the reference VMP, Vetmedin 5 mg capsules, has been demonstrated, efficacy studies are not required. The efficacy claims for this VMP are equivalent to those of the reference VMP. In addition, it is considered that the risk to the target species will be similar for both the candidate and the reference products. The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.A Pre-Clinical Studies

Pharmacology

As this is a hybrid application (according to Article 19), and bioequivalence with the reference VMP, Vetmedin 5 mg capsules, has been accepted (see Section III. Pharmacological studies), results of pharmacological tests are not required.

Tolerance in the Target Species of Animals

No proprietary data were submitted. As this is a hybrid application (according to Article 19), and bioequivalence with the reference VMP, Vetmedin 5 mg capsules, has been accepted, results of target animal safety tests are not required.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical Studies

No proprietary data were submitted. As this is a hybrid application (according to Article 19), and bioequivalence with the reference VMP, Vetmedin 5 mg capsules, has been accepted, the results of efficacy tests are not required. The clinical efficacy profile of the candidate product is not expected to differ from that of the reference product.

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 for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

VI. 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 Union Product Database (UPD).
This section 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.

Changes:

None.