Austrian
Federal Office for
Safety in Healthcare
BASG

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Vetmedin 0.75 mg/ml Solution for Injection for Dogs

AT/V/0019/001/DC

(Former: UK/V/0516/001/DC)

Date: 16/10/2014

Last update: 07/03/2024

MODULE 1

PRODUCT SUMMARY

EU Procedure number	AT/V/0019/001/DC
Name, strength and pharmaceutical form	Vetmedin 0.75 mg/ml Solution for Injection for Dogs
Applicant	Boehringer Ingelheim Vetmedica GmbH Binger Strasse 173 55216 Ingelheim an Rhein Germany
Active substance(s)	Pimobendan
ATC Vetcode	QC01CE90
Target species	Dogs
Indication for use	To initiate treatment of canine congestive heart failure originating from valvular insufficiency (mitral and/or tricuspid regurgitation) or dilated cardiomyopathy.

Modules 1-3 reflect the scientific discussion for the approval of Vetmedin 0.75 mg/ml Solution for Injection for Dogs. The procedure was finalised on 23/07/2014. For information on changes after this date please refer to module 4.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Reference medicinal product	Vetmedin 0.75 mg/ml Solution for Injection for Dogs marketed by Boehringer Ingelheim Ltd.
Date of completion of the original decentralised procedure	23rd July 2014
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Austria, Belgium, Cyprus, Czech Republic, Denmark, Finland, Germany, Greece, Hungary, Iceland, Ireland, Italy, Luxembourg, The Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Spain, Sweden.

I. SCIENTIFIC OVERVIEW

Vetmedin 0.75 mg/ml Solution for Injection for Dogs has been developed as a generic of Vetmedin 0.75 mg/ml Solution for Injection for Dogs. The reference product is also marketed by Boehringer Ingelheim Ltd and has been authorised in the UK since September 2012. Vetmedin solution for injection belongs to the same global MA as Vetmedin 2.5 mg Hard Capsules which were first authorised in the UK in July 1999. The formulation of Vetmedin can be considered identical to that of the reference product therefore bioequivalence has been accepted.

The product is indicated for use in dogs to initiate the treatment of congestive heart failure resulting from valvular insufficiency or dilated cardiomyopathy. The proposed dose is 0.15 mg pimobendan/ kg bodyweight administered via intravenous (IV) injection. The product is contraindicated in hypertrophic cardiomyopathies or clinical conditions where augmentation of cardiac output is not possible for functional or anatomical reasons, for example aortic stenosis. The product should also not be used in cases of hypersensitivity to the active substance or any of the excipients.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto 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

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

demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains pimobendan as the active substance and the excipients hydroxypropylbetadex, disodium phosphate dodecahydrate, sodium dihydrogen phosphate dihydrate, sodium hydroxide, hydrochloric acid and water for injection.

The container/closure system consists of single-use 5 ml or 10 ml colourless injection Type I glass vials closed with a butyl rubber stopper and sealed with an aluminium cap. The vials will be packaged singly in a cardboard box. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the absence of preservative are justified. The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European 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 product is manufactured by dissolving the excipients and pimobendan in the water for injections. The final solution is filtered under aseptic conditions and filled into sterilised vials before autoclaving. Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is pimobendan, an established active substance described in the European Pharmacopoeia (Ph. Eur.). A Ph. Eur. Certificate of Suitability has been provided for the active substance manufacturer. 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 have been provided.

All the excipients are manufactured in compliance with their respective Ph. Eur. Monographs. Certificates of analysis have been provided for each excipient.

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. The tests include those for identification and assay of the active substance, identification of impurities, colour and clarity of the solution, appearance, pH and sterility.

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 have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. The certificate of suitability specifies a retest period of 4 years for the active substance.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions. Data were provided for batches stored at 25°C/65% RH and 30°C/65% RH for 36 months and for an accelerated study where batches were stored at 40°C/75% RH for 6 months. A shelf life of 3 years has been established.

II.G. Other Information

Shelf life
Shelf life of the finished product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: use immediately.

Special precautions for storage
This veterinary medicinal product does not require any special storage conditions.
This product does not contain an antimicrobial preservative.
This product is intended for single use only.
Any product remaining in the bottle after withdrawal of the required dose should be discarded.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Pharmacodynamics
Pimobendan is a non-sympathomimetic[3], non-glycoside inotropic[4] substance and has potent vasodilatative[5] properties. Pimobendan exerts a stimulatory effect on the myocardium. This is achieved by increasing the calcium sensitivity of cardiac myofilaments and inhibition of phosphodiesterase. Inhibition of phosphodiesterase III also results in vasodilation.

Pharmacokinetics
Following IV administration the bioavailability of pimobendan is 100% and it is readily distributed to the tissues, demonstrated by the volume of distribution of 2.6 L/kg. The mean plasma protein binding is 93%. Pimobendan is metabolised by oxidative demethylation to form its major metabolite (UD-CG212). Phase II conjugates, glucuronides and sulfates, are also

[3] Sympathomimetic –mimics the effect of the sympathetic nervous system.
[4] Inotropic substance – alters the force of the hearts contractions.
[5] Vasodilatative – widening of blood vessels.

formed. Following IV administration the plasma elimination half-life is 0.4 ±0.1 hours, which is consistent with the high clearance of 90 ±19 ml/min/kg. The plasma elimination half-life of the main active metabolite is 2.0 ±0.3 hours. Almost the entire dose is eliminated via the faeces.

Toxicological Studies

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product has been established, the results of toxicological studies are not required.

User Safety

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product has been established, a user risk assessment was not provided. The user warnings listed on the SPC and product literature are identical to those for the reference product and are adequate to ensure safety to users of the product.

- In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
- Wash hands after use.

Environmental Safety

A Phase I Environmental Risk Assessment (ERA) was submitted in accordance with VICH and CVMP guidelines.

Phase I:
The ERA concluded that the product will only be used in non-food animals and is to be administered as a single dose IV treatment. Due to the nature of this product the environmental exposure will be minimal and a Phase II ERA was not required.

IV. CLINICAL DOCUMENTATION

IV.A. Pre-Clinical Studies

Pharmacology

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product has been established, the results of pharmacological studies are not required. A brief overview of the pharmacology was provided in Section III.

Tolerance in the Target Species

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product has been established, tolerance studies are not required.

IV.B. Clinical Documentation

Laboratory Trials

As this is a generic application submitted according to Article 13 (1) of Directive 2001/82/EC as amended and bioequivalence with the reference product has been established, the results of laboratory trials are not required.

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

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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 Heads of Veterinary Medicines Agencies website (www.HMA.eu).

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.

Significant changes

Summary of change (Application number)	**Approval date**
Change of RMS from UK to AT	19/01/2018
This marketing authorisation was renewed unlimited. (AT/V/0019/R/001)	12/07/2019
*** No significant changes since ***	