College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
3531 AH Utrecht
The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Cardisan (Vet) 1.25 mg chewable tablets for dogs

Cardisan (Vet) 2.5 mg chewable tablets for dogs

Cardisan (Vet) 5 mg chewable tablets for dogs

Cardisan (Vet) 10 mg chewable tablets for dogs

Cardisan (Vet) 15 mg chewable tablets for dogs

Date: November 2022

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0380/001-005/DC
Name, strength and pharmaceutical form	Cardisan (Vet) 1.25 mg, 2.5 mg, 5 mg, 10 mg, 15 mg chewable tablets for dogs
Applicant	Alfasan Nederland BV Kuipersweg 9 3449 JA Woerden The Netherlands
Active substance(s)	pimobendan
ATC Vetcode	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).

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MODULE 2

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

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	2.5 mg: application in accordance with Article 13(1) of Directive 2001/82/EC as amended. 1.25 mg, 5 mg, 10 mg, 15 mg: application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	21 September 2022
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LV, LT, LU, MT, NO, PL, PT, RO, SE, SI, SK, UK(NI)

I. SCIENTIFIC OVERVIEW

Cardisan 1.25 mg, 2.5 mg, 5 mg, 10 mg, 15 mg chewable tablets for dogs 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 slight reactions observed are indicated in the SPC.
Cardisan 1.25 mg, 2.5 mg, 5 mg, 10 mg, 15 mg chewable tablets for dogs 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 risk/benefit analysis is in favour of granting a marketing authorisation.

The quality, safety and efficacy aspects of Cardisan 1.25 mg, 2.5 mg, 5 mg, 10 mg, 15 mg chewable tablets for dogs is based on bioequivalence with the Reference Product Vetmedin 2.5 mg Kapseln für Hunde, with marketing authorisation number DE 400150.00.00, authorized in Germany on 15 April 1999.
Warnings statements and precautions are adopted from the (EU) Reference Product.
Additional statements have been added, based on increased knowledge and the current state of science. Adverse events and contraindications are indicated in the SPC.

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II. QUALITY ASPECTS

A. QUALITATIVE AND QUANTITATIVE PARTICULARS

The tablets contain 1.25 mg, 2.5 mg, 5 mg 10 mg or 15 mg pimobendan and the following excipients:

Citric acid anhydrous, povidone K25, lactose monohydrate, cellulose microcrystalline, croscarmellose sodium, chicken flavour, yeast (dried), silica colloidal hydrated and magnesium stearate.

The tablets are cross scored and meant to be broken in halves or quarters.

The tablets are packed in OPA/AL/PVC-AL blisters.

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

For the generic 2.5 mg tablet strength in-vivo bioequivalence has been demonstrated. According to the comparative dissolution profiles, a biowaiver can be granted for the 1.25 mg, 5 mg, 10 mg and 15 mg tablet strengths.

B. DESCRIPTION OF THE MANUFACTURING METHOD

The products are manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

The products are manufactured using conventional manufacturing techniques. Suitable pre-approval validation results on two common blend validation batches divided into two batches of each strength of pimobendan chewable tablets, resulting in 10 sub-batches have been provided.

The tests performed during production are described.

C. CONTROL OF STARTING MATERIALS

The active substance pimobendan is an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice. The CEP procedure has been employed for the drug substance.

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.

The in-house monographs and additional information in regard to the flavouring agents are acceptable. All other excipients are in conformity with the Ph.Eur. requirements.

None of the starting materials used are affected by the Note for Guidance on TSE/BSE.

D. CONTROL TESTS DURING THE MANUFACTURING PROCESS

The in process controls performed during the manufacturing process of the final drug product are appearance of granulation solution, loss on drying of granulate, characteristic of powder blend, characteristics of the tablets, average tablet mass, friability, disintegration time, resistance to crushing and blister seal integrity.

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The manufacturing process is a standard process and has been adequately described. The IPCs ensure that the process is adequately controlled.

E. CONTROL TESTS ON THE FINISHED PRODUCT

The finished product specification controls the relevant parameters for the pharmaceutical form.
All tests in the release specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product.

The dissolution method has been adequately described and the parameters are justified. The method is discriminatory and has been adequately validated. The proposed method and dissolution limit is in line with the Reflection paper on dissolution

Satisfactory validation data for the analytical methods have been provided.

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

F. STABILITY

The retest period for pimobendan is stated on the CEP.

Stability data on the finished product has been provided in accordance with applicable VICH guidelines.

According to the 60 months stability results provided, the claimed shelf life of 5 years can be granted for all tablet strength.
An in-use shelf life of 3 days after first use (divided tablets), without special storage restrictions can be granted.

G. OTHER INFORMATION

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological and pharmacological tests are not required.

The toxicological and pharmaceutical aspects of these products are identical to the reference product.

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

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline.

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Combined with increased knowledge and the current state of science, warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

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

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

V . OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the products are 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 products 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.

None

Summary of change (Application number)	**Section updated**	**Approval date**