Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Vitofyllin 50 mg
Vitofyllin 100 mg

Date: 06 March 2023

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0198/001 DE/V/0198/002
Name, strength and pharmaceutical form	Vitofyllin 50 mg film-coated tablets Vitofyllin 100 mg film-coated tablets
Applicant	Wirtschaftsgenossenschaft deutscher Tieraerzte eG, Siemensstrasse 14 30827 Garbsen Germany
Active substance(s)	Propentofylline
ATC Vetcode	QC04AD90
Target species	Dogs
Indication for use	For the improvement of peripheral and cerebral vascular blood circulation. For improvement in dullness, lethargy and overall demeanour in dogs.

MODULE 2

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original Decentralised procedure	22nd February 2012
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Austria, Belgium, France, Hungary, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, United Kingdom (Northern Ireland).
Concerned Member States for subsequent recognition procedure	Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Greece, Latvia, Lithuania, Norway, Poland, Romania, Slovakia, Slovenia, Sweden.

I. SCIENTIFIC OVERVIEW

These were generic applications for which the reference products were Vivitonin 50 mg Tablets and Vivitonin 100 mg tablets authorised in the UK since 1991 and 1994 respectively.

Bioequivalence with the reference products have been demonstrated with *in vitro* studies. No animal studies have been presented as the products are exempt in line with the Biopharmaceutics Classification System (BCS) Biowaiver.

The indication for Vitofyllin 50 mg and 100 mg Film-coated Tablets for Dogs is for the improvement of peripheral and cerebral vascular blood circulation, for improvement in dullness, lethargy and overall demeanour in dogs. The products are recommended to be administered at 6-10 mg per kg, divided into two 3-5 mg/kg doses. Tablets can be divided into equal halves and quarters to achieve more accurate dosing. The tablets

are administered orally directly onto the back of the dog's tongue or can be mixed in a small ball of food at least 30 minutes before feeding.

The products are produced and controlled using validated methods and tests which ensure the consistency of the products released on the market.
It has been shown that the products can be safely used in the target species; the slight reactions observed are indicated in the SPC[1]. The products are 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 products was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting marketing authorisations.

II. QUALITY ASPECTS

A. Composition

The tablets contain propentofylline and excipients lactose monohydrate, maize starch, crospovidone, talc, silica colloidal anhydrous, and magnesium stearate. The tablet film coating contains titanium dioxide (E171), ferric oxide yellow (E172), hypromellose, macrogol 6000, and talc.

The containers for these products are polyvinylchloride – polyvinylidene dichloride/aluminium blisters with 14 tablets, contained in a cardboard box. The products come in pack sizes of 56 and 140 tablets. The particulars of the containers and controls performed are provided and conform to the regulation. The absence of preservative is justified.

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

B. Method of Preparation of the Product

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

Process validation data on two batches of the 50mg tablet strength and one batch of the 100mg tablet strength have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

[1] Summary of Product Characteristics.

The active substance is propentofylline. The active substance specification is considered adequate to control the quality of the material. Batch analytical data on three batches demonstrating compliance with this specification have been provided. The active substance is manufactured in accordance with an Active Substance Master File (ASMF). The excipients maize starch, lactose monohydrate, crospovidone, purified talc, silica colloidal anhydrous, magnesium stearate, hypromellose, macrogol 6000, titanium dioxide (E171), and purified water are described in the European Pharmacopoeia. The excipient ferric oxide yellow (E172) is described in the United States Pharmacopoeia and the United States National Formulary (USP-NF).

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

For each tablet strength, a declaration has been provided stating that the finished product complies with the latest version of the Committee for Proprietary Medicinal Products (CPMP)/ Committee for Medicinal Products for Veterinary Use (CVMP) TSE guideline.

The only material of animal origin used in the manufacture of these products is lactose monohydrate. The applicant has provided a declaration from the supplier of lactose monohydrate stating that the milk used is sourced appropriately.

E. Control on intermediate products

Not applicable.

F. Control Tests on the Finished Product

The finished product specification for both product strengths 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. Batch analytical data on two batches from the proposed production site have been provided demonstrating compliance with the specification. Tests include those for appearance, divisibility, uniformity of dosage units, identity of propentofylline, and those for imputities.

G. Stability

Stability data on 3 batches of 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. Tests include those for appearance, solubility, and related substances.

Stability data on 2 batches of the 50mg strength tablets and 100mg strength tablets have been provided in accordance with applicable European guidelines, demonstrating the stability of the product when stored under the approved

conditions. Tests include those for appearance, divisibility, uniformity of dosage units, and uniformity of mass of divided tablets.

J. Other Information

Shelf-life:
Shelf-life of the veterinary medicinal product as packaged for sale: 5 years
Unused divided tablets should be returned to the blister pack and any divided tablet portions remaining after 72 hours should be discarded.

Special precautions for storage:
Store in the original package (blister) and keep the blister packs in the outer carton and store in a dry place. Divided tablets should be stored in the blister pack.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As these are generic applications according to Article 13, and bioequivalence with a reference product has been demonstrated, results of safety tests are not required. The applicant has provided results of a suitable bioequivalence study which is discussed further in Section IV – Clinical Assessment.

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

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the very slight difference in formulations of film coating are not expected to adversely impact on the user safety profile of the products. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the product is not expected to pose a risk to the environment when used as recommended.

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.

In order to demonstrate bioequivalence, the applicant has submitted *in vitro* dissolution studies and supporting literature references to prove that the products are suitable for exemption from *in vivo* studies in line with the BCS Biowaiver. It is concluded that bioequivalence is adequately demonstrated. No animal studies have therefore been presented.

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.

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 in 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.

•	09 November 2021	Change of the name of the API manufacturer and deletion of a non-significant specification parameter DE/V/0198/001-002/IA/008/G
•	19 February 2020	Change of the manufacturer of a starting material and changes in the manufacturing process of the active substance DE/V/198/001-002/IB/007/G
•	21 June 2019	Introduction of a new PV system which has been assessed for another product of the same MAH DE/V/0198/001-002/IB/005
•	14 May 2018	Change of RMS from UK to DE and (purely national variation) MAH transfer to Wirtschaftsgenossenschaft deutscher Tierärzte eG (WDT).
•	08 August 2017	Change in the safety database of an existing pharmacovigilance system as described in the DDPS.
•	28 April 2017	Renewal – UK as RMS.
•	03 June 2015	Change in shelf life of finished product from 3 years to 5 years.
•	26 February 2015	Change in distributor details.
•	31 July 2014	Change to extend the re-test period for the active substance, from 2 years to 5 years.
•	08 August 2013	Change in the address of the Marketing Authorisation Holder. Change to the QPPV contact details.

Other changes

Summary of change **(Application number)**	**Section updated in Module 3**	**Approval date**
Update of the QRD templates in accordance with Regulation (EU) 2019/6 (DE/V/0198/001-002/A/009s)	N/A	22.09.2022