United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Clearium 31.2 mg/ml Shampoo for Dog (AT, BE, BG, CZ, DE, ES, GR, HU, IT, NL, PL, PT, RO, SK, UK)
Clearium Vet 31.2mg/ml Shampoo for dog (DK, FI, NO, SE)
Clearium Shampoo for dog (FR)

Date Created: January 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0677/001/DC
Name, strength and pharmaceutical form	Clearium 31.2 mg/ml Shampoo for dog
Applicant	Virbac 1ère avenue - 2065m – LID 06516 Carros France
Active substance(s)	Chlorhexidine Gluconate
ATC Vetcode	QD08AC02
Target species	Dogs
Indication for use	For the treatment of *Malassezia pachydermatis* surface proliferation and the control of associated clinical signs in dogs.

MODULE 2

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

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic 'hybrid' application in accordance with Article 13 (3) of Directive 2001/82/EC as amended.
Date of conclusion of the decentralised procedure	21st November 2018
Date product first authorised in the Reference Member State	Not applicable
Concerned Member States for original procedure	Austria, Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Italy, The Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Spain, Sweden

I. SCIENTIFIC OVERVIEW

This was an application for a generic 'hybrid' product, Clearium 31.2 mg/ml Shampoo for Dog. This was determined a generic 'hybrid' application because bioequivalence could not be demonstrated or inferred through bioavailability studies/waivers from bioequivalence study requirements. The proposed product was established as being identical to the reference product, also produced by the same marketing authorisation holder. The reference product is Microbex Shampoo, first authorised in the UK in June 2009.

The product is indicated for use in dogs, for the treatment of *Malassezia pachydermatis* surface proliferation and the control of associated clinical signs.

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 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 per ml, 31.2mg chlorhexidine diglucontate solution, (corresponding to 17.5 mg chlorhexidine), and the excipients ponceau 4R (E124), lauryl glucoside, cocamidopropyl betaine, glucono δ-lactone (for pH adjustment), purified water.

The container/closure system consists of a carton box containing one 200 ml white high-density polyethylene bottle, closed by a white polypropylene screw cap. A translucent polypropylene cup is placed on top as an administration device. 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 manufacturing method consists of a simple mixing and filling process.

Manufacture and 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 chlorhexidine diglutonate, an established active substance described in the European Pharmacopoeia. 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. An appropriate Certificate of Suitability was provided.

There is a monograph in the United States Pharmacopoeia for glucono δ-lactone. The remaining excipients are not described in a pharmacopoeia, but are governed by appropriate specifications. Packaging materials are also under appropriate specifications.

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. Appropriate documentation was provided.

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. Control tests on the finished product are those for: appearance, pH, relative density, identity of the active substance and associated products, and microbial purity.

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. A retest period of 3 years was established if stored in HDPE drums with an external metallic cover, at a temperature not exceeding 25ºC. A reduced retest period of 2 years is stated if stored in HDPE drums, without the metallic cover, at a temperature not exceeding 25ºC.

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.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf life after first opening the immediate packaging: 2 months.

Do not refrigerate.

Do not store below 8°C.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Due to the nature of the application no pharmacological or toxicological data were required.

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. The following applicant's user recommendations are appropriate:

- This product may cause hypersensitivity following dermal contact and can be irritating to skin.
- Avoid prolonged contact with the shampoo by gently washing and drying hands immediately after use of the product. If you develop symptoms following exposure such as skin rash or skin irritation, you should seek medical advice and show the physician the label or package leaflet.
- People with known hypersensitivity to chlorhexidine or any of the excipients should avoid contact with the veterinary medicinal product.

- Accidental eye contact with undiluted product may cause serious eye irritation. Avoid contact with eyes.
- In case of accidental eye contact, rinse with plenty of water, seek medical advice and show the physician the label or package leaflet.

- Accidental ingestion may cause adverse reactions, such as stomach irritation and nausea.
- Avoid contact with mouth and hand-to-mouth transfer. In the event of accidental ingestion, seek medical advice and show the package leaflet or the label to the physician

- Keep the product in the original packaging until use and immediately after use, in order to prevent children from getting direct access to the product

- Avoid handling and stroking of treated animals immediately following treatment.
- Do not eat, drink or smoke while handling this product.

Environmental Safety

The applicant has performed and submitted a Phase I ERA in accordance with VICH guidelines. Assessment ends at Phase I based on use in non-food producing animals only. The disposal advice given in the SPC and product literature is acceptable and the product is not expected to pose a risk to the environment when used as recommended.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

The bioequivalence guideline was written for products that are systemically acting. However, an exemption was supported for this product by extrapolation of the principles of section 7.1d of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 2). Therefore, the absence of data in this section was accepted, and the safety and efficacy of the product can be extrapolated from the reference product.

Tolerance in the Target Species

Due to the nature of the application, no additional data were required for this section, other than to update the SPC.

Resistance

Due to the nature of the application, no additional data were required for this section. Adequate warnings and precautions appear on the product literature.

IV.II. Clinical Documentation

Due to the nature of the application, no additional data were required for this section.

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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