ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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(Reference Member State)

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Malaseb Shampoo

PuAR correct as of 01/08/2018 when RMS was transferred to IE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0333/001/MR
Name, strength and pharmaceutical form	Malaseb Shampoo
Applicant	Dechra Veterinary Products A/S Mekuvej 9 Uldum 7171 Denmark
Active substances	Chlorhexidine gluconate Miconazole nitrate
ATC Vetcode	QD08 and AC52
Target species	Dogs and Cats
Indication for use	Dogs: For the treatment and control of seborrhoeic dermatitis associated with *Malassezia pachydermatis* and *Staphylococcus intermedius.* Cats: As an aid in the control and treatment of ringworm due to *Microsporum canis* in conjunction with griseofulvin

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (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.
Date of completion of the original mutual recognition procedure	29 October 2008
Date product first authorised in the Reference Member State (MRP only)	14 November 2007
Concerned Member States for original procedure	Austria Denmark Finland Iceland Ireland The Netherlands Sweden
Concerned Member States added subsequent to Renewal Procedure 05/03/10:-	Belgium Cyprus Czech Republic Estonia France Germany Greece Hungary Italy Latvia Lithuania Poland Portugal

	Romania Slovakia Slovenia Spain

I. SCIENTIFIC OVERVIEW

Malaseb Shampoo contains the active substances chlorhexidine gluconate 2 % w/v and miconazole nitrate 2 % w/v. The product is indicated in dogs for the treatment and control of seborrhoeic dermatitis associated with *Malassezia pachydermatitis* and *Staphylococcus intermedius*. It is also indicated in cats as an aid in the control and treatment of ringworm due to *Microsporum canis* in conjunction with griseofulvin.

This application is submitted under Article 13 (1) of the Directive 2001/82/EC as amended by Directive 2004/28/EC. The applicant has confirmed that the formulation of Malaseb Shampoo is a generic of an approved product, Sebolyse shampoo which was authorised in the UK since 1996 and Dechra Veterinary Products A/S is the Marketing Authorisation Holder for both products.

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 slight 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 over all risk/benefit analysis is in favour of granting a marketing authorisation. The product is produced and controlled using validated methods and tests which ensure the consistency of the product released on the market.

II. QUALITY ASPECTS

A. Composition

The product contains chlorhexidine digluconate (as chlorhexidine digluconate 20% w/v solution), miconazole nitrate 2% w/v and excipients, methylchloroisothiazolinone, methylisothiazolinone, macrogol lauryl ether, cocamidopropyl betaine, sodium benzoate, disodium cocoamphodiacetate, cetrimonium chloride, PEG-120 methyl glucose dioleate, citric acid monohydrate, hydrochloric acid and purified water.

The container is a 250 ml polyethylene bottle with a screw top. The particulars of the containers and controls performed are provided and conform to current guidelines.

The choice of the formulation and presence of preservatives 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

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

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

Active substances

The first active substance is chlorhexidine digluconate solution, an established substance described in the European Pharmacopoeia and a copy of the Certificate of Suitability for this material has been provided. A certificate of analysis also indicates that the material meets additional requirements relating to the control of residual solvents. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The second active substance, miconazole nitrate solution, is also the subject of a monograph in the European Pharmacopoeia and a copy of the Certificate of Suitability for this material has been provided. A certificate of analysis also indicates that the material meets additional requirements relating to the control of residual solvents and impurities. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specifications are considered adequate to control the quality of the materials.

Other Substances
There are four non-pharmacopoeial excipients in the product, disodium cocoamphodiacetate solution, cetrimonium chloride solution, preservative mixture (containing methylchloro-isothiazolinone and methylisothiazolinone) and PEG-120 methyl glucose dioleate. The disodium cocoamphodiacetate, cetrimonium chloride and the isothiazolinones are listed in the CTFA Handbook. Copies of the listings have been provided, together with acceptable specifications and certificates of analysis.

The remaining substances are the subject of a monograph in the European Pharmacopoeia and copies of the Certificates of analysis have been provided.

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

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

E. Control on intermediate products

Not applicable.

F. 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.

G. Stability

Stability data on the active substances have 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 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.

The claim of a 3 month stability after broaching is based on the demonstration of stability for a batch broached and stored for 13 weeks at 25°C/60% RH.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

The application is supported with respect to quality.

Pharmaceutical Warnings:
Do not store above 30°C
Do not refrigerate or freeze

Shelf life
Unopened – 2 years
Opened – 3 months after first opening.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, data on pharmacodynamics and pharmacokinetics are not required.

Toxicological Studies

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

Observations in Humans

Not applicable.

User Safety

The user risk assessment submitted makes reference to the assessment for the reference product and has concluded that as the product is identical to the reference product, the same user warnings are proposed as given below, which are satisfactory:

- If known hypersensitivity to chlorhexidine exists, handle product with care.
- This product can cause eye irritation. Avoid contact with the eyes. In case of accidental contact with eyes, rinse with plenty of water. If irritation persists consult your doctor.
- Avoid excessive handling and stroking of treated animals immediately following treatment.
- Ringworm in the cat is infectious to human beings and so it is advisable to wear gloves and have arms covered when shampooing cats. To avoid prolonged contact with the shampoo, wash and dry hands gently after shampooing the animal. Do not scrub.

The assessment includes a summary of adverse reactions to similar products since the launch of the reference product. There have been a number of reports of irritation and allergic reactions but the overall incidence is very low.

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.

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 that since use of the product is limited to individual domestic animals for short periods only, assessment can stop at Phase I according to the decision tree in the Phase I Guideline VICH GL6. No additional warnings are therefore required.

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 the environment.

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies
Pharmacology

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.

Tolerance in the Target Species of Animals

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

Resistance

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, resistance data are not required.

IV.B Clinical Studies

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

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.

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.

(www.gov.uk/check-animal-medicine-licensed)

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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