Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

NorOtic Ear Drops, Suspension for Dogs

Date Created: September 2015

PuAR correct as of 27/02/19 when RMS was transferred to IE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0494/001/DC
Name, strength and pharmaceutical form	NorOtic Ear Drops, Suspension for Dogs
Applicant	Norbrook Laboratories Limited, Station Works, Camlough Road, Newry, Co. Down, BT35 6JP, Northern Ireland
Active substance(s)	Marbofloxacin Clotrimazole Dexamethasone (equivalent to dexamethasone acetate)
ATC Vetcode	QS02CA06
Target species	Dogs
Indication for use	Treatment of otitis externa of both bacterial and fungal origin respectively due to bacteria sensitive to marbofloxacin, and fungi especially *Malassezia pachydermatis* sensitive to clotrimazole. The product should be used based on susceptibility testing of isolated bacteria.

MODULE 2

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

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

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 decentralised procedure	17th June 2015
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Netherlands, Poland, Portugal, Slovakia, Spain and Sweden

I. SCIENTIFIC OVERVIEW

NorOtic Ear Drops, Suspension for Dogs has been developed as a generic of Aurizon Ear Drop Suspension. The reference product has been authorised in the UK since July 2001. The application was submitted in accordance with Article 13 (1) of Directive 2001/82/EC as amended; however, as the product is topically applied and acts locally, the conduct of in vivo bioequivalence studies was not considered to be appropriate. The applicant provided a justification for exemption from in vivo studies, on the basis of data and studies assessed in Part II to support equivalence between the test and reference products. This was considered to be in line with the principles of the CVMP bioequivalence guideline (EMA/CVMP/016.00-Rev.2) and was therefore considered acceptable.

The product is a suspension containing 10.0 mg/ml clotrimazole, 3.0 mg/ml marbofloxacin and 0.9 mg/ml dexamethasone and is indicated for the treatment of otitis externa of both bacterial and fungal origin respectively due to bacteria sensitive to marbofloxacin, and fungi especially *Malassezia pachydermatis* sensitive to clotrimazole.

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

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

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 CONSTIUENTS

II.A. Composition

The product contains 3.0 mg/ml marbofloxacin, 10.0 mg/ml clotrimazole and 0.9 mg /ml dexamethasone (equivalent to 1.0 mg/ml dexamethasone acetate) as the active substances. The excipients are propyl gallate (E310), sorbitan oleate, silica colloidal hydrophobic and triglycerides, medium-chain.

The container/closure system consists of low-density polyethylene bottles (LDPE) and LDPE dropper inserts, sealed with an HDPE cap in volumes of 10, 20 and 30 ml. Each bottle will be provided with two PVC cannulae. 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 using conventional manufacturing techniques. Process validation for full-scale batches will be performed post-authorisation.

II.C. Control of Starting Materials

The active substances are marbofloxacin, clotrimazole and dexamethasone, established active substances described in the European Pharmacopoeia (Ph. Eur.), with appropriate data provided in Ph. Eur. Certificates of Suitability and Active Substance Master Files (ASMF). The active substances are 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.

The excipients are commonly used in veterinary medicines and are manufactured in accordance with the relevant Ph. Eur. monographs.

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.

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 substances, viscosity and microbial quality.

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 substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances 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.

Data were provided for batches stored at 30°C/65% RH for 9 months and 40°C/75% RH for 6 months. In-use data were supplied when broached for two and three months stored at 30°C/65% RH. The data support a shelf-life of 2 years and an in-use shelf-life of 3 months.

G. Other Information

- Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
- Shelf life after first opening the immediate packaging: 3 months.
- Do not store above 30°C.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

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

Toxicological Studies

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

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the main routes of indirect exposure are dermal, ocular or oral contact. The risk to the user is low due to the minimal quantities involved. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

- Wash hands carefully after applying the product.
- Avoid contact with eyes. In the event of accidental eye contact, rinse with clean water.
- People with known hypersensitivity to fluoro(quinolones) and other compounds in the product should avoid contact with the veterinary medicinal product.

Environmental Safety

The applicant provided a Phase I environmental risk assessment in accordance with the relevant guidelines which showed that no further assessment was required. As the product is to be used in a non-food species on an individual basis it is not expected to pose a risk for the environment when used as recommended in the SPC.

IV CLINICAL DOCUMENTATION

As this is a generic application submitted according to Article 13 (1), and equivalence with the reference product has been established, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.I. Pre-Clinical Studies

As this is a generic application submitted according to Article 13 (1), and equivalence with the reference product has been established, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

Resistance

The applicant supplied data on the mechanisms of resistance to the active substances and relevant warnings are included on the SPC and product literature.

IV.II. Clinical Documentation

As this is a generic application submitted according to Article 13 (1), and equivalence with the reference product has been established, 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 product is used in accordance with the Summary of Product Characteristics, the benefit/risk profile of the product(s) is favourable

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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 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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