Veterinary Medicines Directorate

**United Kingdom**
**Veterinary Medicines Directorate**
**Woodham Lane**
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**Surrey KT15 3LS**

**NATIONAL PROCEDURE**

# PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

## Marbotis 3mg/ml + 10mg/ml + 1mg/ml Ear Drops, Suspension for Dogs

**Date Created: December 2024**

# MODULE 1

## PRODUCT SUMMARY

| | |
|---|---|
| Name, strength and pharmaceutical form | Marbotis 3mg/ml + 10mg/ml + 1mg/ml Ear Drops, Suspension for Dogs |
| Applicant | Vet-Agro Multi-Trade Company Sp. z o.o.<br>Gliniana 32<br>Lublin, 20-616<br>Poland |
| Active substance | Clotrimazole<br>Dexamethasone<br>Marbofloxacin |
| ATC Vetcode | QS02CA06 |
| Target species | Dogs |
| Indication for use | Treatment of otitis externa of bacterial and fungal origin – respectively due to bacteria sensitive to marbofloxacin, and fungi (*Malassezia pachydermatis* sensitive to clotrimazole). |

# 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 hybrid application in accordance with Article 8 of VMRs 2013 (Schedule 1, Para 10a) as amended. |
| Date of conclusion of the procedure | 20/09/2024 |

## I. SCIENTIFIC OVERVIEW

This is a generic hybrid application with the reference product being Aurizon Ear Drops, Suspension which has been authorised in the UK since 2001. This is considered a hybrid application as the test and reference products are topically administered so bioequivalence cannot be demonstrated by way of blood level studies.

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, any reactions observed are indicated in the SPC.[1] The product is safe for the user, 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.

## II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

### *II.A. Composition*

The product contains marbofloxacin, clotrimazole and dexamethasone acetate and the excipients propyl gallate, sorbitan oleate, silica colloidal hydrophobic, and triglycerides medium-chain.

The container/closure system consists of a LDPE bottle with a LDPE applicator closed with a HDPE tamper evident cap. 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.

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

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.

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

### *II.C. Control of Starting Materials*

The active substances are marbofloxacin, clotrimazole and dexamethasone acetate, which are established active substances described in the European Pharmacopoeia. 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.

### *II.C.4. Substances of Biological Origin*

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

### *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<s> have been provided demonstrating compliance with the specification. Control tests on the finished product are appropriate for this pharmaceutical form.

### *II.F. Stability*

Stability data on the active substances have been provided in accordance with applicable regulatory 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 regulatory 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: 2 years
Shelf life after first opening the immediate packaging: 6 months
Do not store above 30°C.

## III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

### *III.A Safety Documentation*

### *Pharmacological Studies*

Bibliographical data has been provided. The preparation combines three active ingredients:
- marbofloxacin, a synthetic bactericidal agent belonging to the fluoroquinolone family that acts by inhibiting DNA gyrase. It exhibits a broad spectrum of activity against Gram-positive bacteria (e.g. Staphylococcus intermedius) and against Gram-negative organisms (Pseudomonas aeruginosa, Escherichia coli and Proteus mirabilis).
- clotrimazole, an anti-fungal agent that belongs to the imidazole family and which acts by causing changes in membrane permeability, allowing intracellular compounds to leak from the cell and thus inhibiting cellular molecular synthesis. It exhibits a wide spectrum of activity and is aimed, in particular, at Malassezia pachydermatis;
- dexamethasone acetate, a synthetic glucocorticoid exhibiting anti-inflammatory and anti-pruritic activity.
Pharmacokinetics studies in dogs at the therapeutic dosage have shown that:
Marbofloxacin plasma concentrations peak at 0.06 µg/ml on the 14th day of treatment. Marbofloxacin binds weakly to plasma proteins (< 10% in dogs) and is eliminated slowly, mainly in the active form, over 2/3 in urine and over 1/3 in faeces. Clotrimazole absorption is extremely poor (plasma concentration < 0.04 µg/ml). Dexamethasone acetate plasma concentration reaches 1.25 ng/ml on the $14^{th}$ day of treatment. Dexamethasone resorption is not increased by the inflammatory process induced by otitis.

### *Toxicological Studies*

The applicant has provided bibliographical data.

### *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. Therefore the following applicant's user recommendations are appropriate:

People with known hypersensitivity to marbofloxacin, dexamethasone, clotrimazole should avoid contact with the veterinary medicinal product.

This veterinary medicinal product may cause skin and eye irritation. Avoid contact with skin and eyes. In case of accidental contact, wash exposed area thoroughly with water.

Wash hands after use.

In case of accidental ingestion or if skin and eye symptoms persist seek medical advice immediately and show the package leaflet or the label to the physician.

### *Environmental Safety*

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

**Phase I:**

The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required.

## IV. CLINICAL DOCUMENTATION

### *IV.I. Pre-Clinical Studies*

Not required as bioequivalence was established with the reference product.

### *IV.II. Clinical Documentation*

Not required as bioequivalence was established with the reference product.

## V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that 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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