Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Mometamax Ultra Ear Drops Suspension for Dogs

Date Created: May 2023

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Mometamax Ultra Ear Drops Suspension for Dogs, Gentamicin (8.6 mg/ml) Posaconazole (2.6 mg/ml) Mometasone Furoate (2.1 mg/ml)
Applicant	MSD Animal Health UK Limited Walton Manor, Walton Milton Keynes Buckinghamshire MK7 7AJ
Active substance	Gentamicin, posaconazole and mometasone furoate
ATC Vetcode	QS02CA91
Target species	Dogs
Indication for use	Treatment of acute otitis externa and acute exacerbation of recurrent otitis externa caused by mixed infections of susceptible strains of bacteria sensitive to gentamicin (*Staphylococcus pseudintermedius*) and fungi sensitive to posaconazole (*Malassezia pachydermatis*).

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	Fixed combination application in accordance with Article 13(b) of Directive 2001/82/EC as amended.
Date of conclusion of the procedure	17/02/2023

I. SCIENTIFIC OVERVIEW

This application was submitted in accordance with Article 13(b) of Directive 2001/82/EC as a new combination of the active substances.

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, 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.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains gentamicin, mometasone furoate and posaconazole and the excipients paraffin liquid and plasticised hydrocarbon gel.

The container/closure system consists of a high-density polyethylene (HDPE) bottle closed with a low-density polyethylene (LDPE) 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.

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

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

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of pre-suspension, mixing and homogenisation.

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 first active substance is gentamicin sulphate, an established active substance described in the European Pharmacopoeia. The active substances mometasone furoate monohydrate and Posaconazole are both registered in the EU via a centralised procedure, with the former being tested according to the current Ph. Eur. monograph and the latter being controlled by in-house specifications.

The active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substance specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with these specifications have been provided.

There is a CEP for gentamicin sulphate.

Paraffin liquid is described in the Ph. Eur. Plasticised hydrocarbon gel is not described in Ph. Eur. or the USP but is used in veterinary medicinal products.

The packaging materials comply with both the EU and US regulatory guidelines.

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. 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, density, water, identification and

assay of mometasone furoate and Posaconazole, identification and assay of gentamicin, mometasone furoate and Posaconazole degradation products, gentamicin impurities, microbial quality, particle size, viscosity, resuspendability and morphology and agglomeration.

II.F. 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.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 24 months.
Shelf life after first opening the immediate packaging: 3 months.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

Bibliographical data has been provided which show how the actives act.

Gentamicin is an aminoglycoside bacterial antibiotic which acts by inhibiting protein synthesis. Its spectrum of activity includes Gram-positive and Gram-negative bacteria, such as pathogenic organisms isolated from the ears of dogs.

Posaconazole is a broad-spectrum triazole antifungal agent.

Mometasone furoate is a corticosteroid with high topical potency, but few systemic effects. It has anti-inflammatory and anti-pruritic properties.

The applicant has also provided bibliographical data which show the pharmacokinetic aspects of the actives.

Gentamicin is minimally absorbed after oral administration due to the polar nature and high aqueous solubility.

Posaconazole is poorly absorbed by the oral route of exposure, although absorption can be significantly enhanced in the fed state or by the use of a liposomal formulation designed to provide greater lipid solubility and bioavailability.

Mometasone furoate is also poorly absorbed by the oral route of exposure.

Toxicological Studies

Auricular administration to puppies at up to 5 times the recommended dose to both ears on 3 occasions at 2-week intervals was well-tolerated.

For tolerance in the target species and studies of other effects (skin and eye irritation, and skin sensitisation), GLP-compliant studies were conducted specifically for gentamicin, posaconazole and mometasone furoate ear drops suspension.

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:

- In case of accidental eye or skin contact, rinse thoroughly with water.
- In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
- It is recommended that this veterinary product is administered only by veterinarians or under their close supervision.

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

Pharmacology

The applicant has provided bibliographical data describing the pharmacodynamic and pharmacokinetic properties of the active substance. The results suggested that there is no pharmacological interaction between the active substances contained within the product that would impact the efficacy of the products.

Tolerance in the Target Species

The applicant has conducted a target animal tolerance study using multiples of the recommended dose in the target species. A placebo was used as a control. All doses were administered by the intra-aural route on 5 occasions.
Parameters evaluated were clinical signs, body weights, body weight gains, food consumption, veterinary physical examinations, otoscopic examinations, functional evaluation, ophthalmology, electrocardiography, clinical pathology parameters, ACTH stimulation, gross necroscopy findings, organ weights and histopathologic examinations.

Minimal adverse effects were seen following doses up to 3 and 5 times the recommended dose.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance

Adequate warnings and precautions appear on the product literature.

IV.II. Clinical Documentation

Laboratory Trials

The applicant has provided bibliographical data which show that dose determination is inexact as efficacy will differ.

Dose confirmation studies:

A randomised negative control study in 16 dogs was submitted. The results of this were inconclusive.

Field Trials

A multicentre, randomised, investigator blinded, positive controlled parallel group design study was submitted. Overall, there were 316 dogs in the population (153 IVP dogs and 163 receiving the control product of Osurnia Otic gel for dogs).
The clinical field trial demonstrated that the IVP is non-inferior, compared to the control product, for the reduction of clinical signs of acute or acute recurrent otitis on study day 28, with mixed infections of *Staphylococcus pseudintermedius* and *Malassezia pachydermatis,* at the proposed dose.

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.

(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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