College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
3531 AH Utrecht
The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Ophtocycline 10 mg/g eye ointment for dogs, cats and horses

MODULE 1

PRODUCT SUMMARY

Dutch Registration number	119200
EU Procedure number	NL/V/0209/001/DC
Name, strength and pharmaceutical form	Ophtocycline 10 mg/g eye ointment for dogs, cats and horses
Applicant	Le Vet Beheer B.V. Wilgenweg 7 3421 TV Oudewater The Netherlands
Active substance(s)	Chlortetracycline hydrochloride
ATC Vetcode	QS01AA02
Target species	Dogs, cats and horses
Indication for use	Treatment of keratitis, conjunctivitis and blepharitis caused by *Staphylococcus* spp., *Streptococcus* spp., *Proteus* spp. and/or *Pseudomonas* spp. sensitive to chlortetracycline.

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MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website:

http://mri.medagencies.org/veterinary/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	24th of May 2017
Date product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NO, PL, PT, RO, SE, SI, SK, UK Repeat use: DE

I. SCIENTIFIC OVERVIEW

Ophtocycline 10 mg/g eye ointment for dogs, cats and horses 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.
Ophtocycline 10 mg/g eye ointment for dogs, cats and horses is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.
The efficacy of the product was demonstrated according to the claims made in the SPC.
The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product is an eye ointment containing 10 mg of Chlortetracycline hydrochloride as the active substance and wool fat, white soft paraffin and liquid paraffin as excipients.

The product is packed in an internal epoxy resin lacquered aluminium tube, with a content of 5 gram, with a HDPE cannula and screw cap.

The choice of the formulation is 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 at a licensed manufacturing site.

Process validation data on pilot scale batches of the product have been presented in accordance with the relevant European guidelines. The product is manufactured using conventional manufacturing techniques. A post-approval commitment for process validation of the first three full-scale batches is given.

C. Control of Starting Materials

The active substance is Chlortetracycline hydrochloride, an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice. The CEP procedure is used by the two suppliers of the active substance

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating full compliance with this specification are provided.

Declarations of compliance have been provided with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products.

D. Control on intermediate products

Not applicable.

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 adequately justified and the specification can be accepted.

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 proposed specification.

F. Stability

Stability data on the non-sterile active substance has been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

For the sterile active substance testing to ensure compliance with its specification immediately prior to its use in manufacture is performed.

Stability data on the finished product and in-use stability have been provided in accordance with applicable European guidelines. The claimed shelf-life of 24 months and storage condition of “Do not store above 25°C” can be granted. Also, the claimed in-use shelf of 14 days can be granted.

G. Other Information

None.

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III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic hybrid application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological, pharmacological and residue tests are not required.
However, the applicant provided additional information to alter the withdrawal period.

Warning statements and precautions as listed in the product literature are based on those of the reference product and supplemented with additional statements, based on increased knowledge and the current state of science. This information is considered adequate to ensure safety of the product to users, consumers and the environment.

III.A Safety Testing

User Safety

Being a generic procedure the applicant refers to the reference product for information on this section.

Additionally the applicant has provided a user safety assessment. Combined with increased knowledge and the current state of science, warning statements and precautions have been added to the product literature, ensuring safety to users of the product.

Environmental Risk Assessment

Phase I

The environmental risk assessment can stop in Phase I because the product is used only to treat individual animals.

Conclusion

Based on the data provided, the ERA can stop at Phase I. The product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

III.B Residues documentation

Residue Studies

No residue studies have been provided. Based on worst case assumptions, i.e. treatment of both eyes, administration of the maximum dosage per eye, the maximum duration of treatment, and a worst case bioavailability via the eyes of 100% and taking into account the half-life of the active substance, no residues in edible tissues are expected above acceptable levels at all time points.
By including an extra safety margin, it is concluded that a withdrawal period of 1 day is more than sufficient to protect consumer safety.

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MRLs

Chlortetracycline is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Marker residue	**Animal Species**	**MRL (µg/kg)**	**Target Tissues**	**Other provisions**
Sum of parent drug and its 4-epimer	All food producing species	100 300 600 100 200	Muscle Liver Kidney Milk Eggs	

Withdrawal Periods

Based on the above the following withdrawal periods are justified:

Meat and offal: 1 day

Not authorised for use in horses producing milk intended for human consumption.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic hybrid 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

The data submitted in the dossier demonstrate that 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 Heads of Vetrinary Medicines Agencies website (www.HMA.eu).

This section 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.

Summary of change (Application number)	**Section updated in Module 3**	**Approval date**
– Extension of the shelf life of the finished product - As packaged for sale (supported by real time data) – Change in test procedure for the finished product - Minor change in an approved test procedure NL/V/0209/001/IB/001/G	IIF	1 June 2018
Submission of updated Ph. Eur. certificate of suitability : For an active substance (2x) NL/V/0209/IA/002/G	-	6 February 2019
Repeat use to add DE as CMS NL/V/0209/001/E/001	-	3 July 2019
Introduction of a new Pharmacovigilance system which has been assessed by the EMA for another product of the same MAH NL/V/xxxx/WS/021	-	12 July 2019
Renewal NL/V/0209/001/R/001	-	22 June 2022