Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

CTC Spray, 78.6 mg/g, cutaneous spray, suspension for pigs, sheep and cattle (UK)

Cyclospray 78.6 mg/g, cutaneous spray, suspension for pigs, sheep and cattle (Croatia, Cyprus, Czech Republic, Estonia, Latvia, Portugal, Romania, Slovakia, Slovenia)

Cyclospray vet 78.6 mg/g, cutaneous spray, suspension for pigs, sheep and cattle (Finland, Iceland, Sweden)

Date Created: February 2016

PuAR correct as of 05/09/2018 when RMS was transferred to PT. Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0564/001/DC
Name, strength and pharmaceutical form	CTC Spray, 78.6 mg/g, cutaneous spray, suspension for pigs, sheep and cattle
Applicant	Eurovet Animal Health B.V. Handelsweg 25 5531 AE Bladel The Netherlands
Active substance(s)	Chlortetracycline HCl
ATC Vetcode	QD06AA02
Target species	Cattle, sheep and pigs
Indication for use	Supportive treatment of infections of superficial traumatic origin or surgical wounds caused by micro-organisms sensitive to chlortetracycline. The veterinary medicinal product can be used as part of a treatment for superficial foot infections, in particular interdigital dermatitis (foot rot) in sheep, and digital dermatitis in cattle.

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	23 September 2015
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Croatia, Cyprus, Czech Republic, Estonia, Finland, Iceland, Latvia, Portugal, Romania, Slovakia, Slovenia, Sweden.

I. SCIENTIFIC OVERVIEW

CTC Spray has been developed as a generic of Cyclo Spray Chlortetracycline HCl 2.45% w/w, cutaneous spray, suspension for pigs, sheep and cattle. The reference product was first authorised in the UK in August 2006 and is also marketed by Eurovet Animal Health B.V. Clinical equivalence with the reference product is claimed on the basis that the products are identical and an exemption from studies was granted.

The product is indicated for the treatment of infections caused by micro-organisms sensitive to chlortetracycline in superficial or surgical wounds. The product can also be used as part of treatment of superficial foot infections. The product is contraindicated in cases of hypersensitivity to the active substance or any of the excipients.

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, 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[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.

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

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains chlortetracycline HCl as the active substance and the excipients patent blue V (E131), butane (Butan 100), colloidal anhydrous silica (Aerosil 200), isopropyl alcohol and sorbitan trioleate (Span 85).

The container/closure system consists of a 270 ml (containing 130.76 g) or 520 ml (containing 261.52 g) pressurized container of coated tin plate with a plastic valve mechanism and spraying nozzle. The particulars of the containers and controls performed are provided and conform to the regulation.

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.

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 manufacturing method consists of mixing the active substance with the excipients, excluding butane. The suspension is then filled into containers, which are fitted with a container top before adding butane under high pressure. Finally a spray nozzle is fitted and the containers are capped. Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is chlortetracycline hydrochloride, an established active substance described in the European Pharmacopoeia ((Ph. Eur.). The active substance is manufactured in accordance with Ph. Eur. Certificates of Suitability. The active substance is 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.

All excipients, apart from patent blue V and butane, are described in a pharmacopeia and comply with their respective European monographs. The specifications have been provided for patent blue V and butane. Certificates of analysis have been supplied.

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. Control tests on the finished product include those for identification and assay of the active substance, net fill weight, pressure testing, leakage testing, delivery rate and microbiological quality.

Satisfactory validation data for the analytical methods have been provided. Batch analytical data from the proposed production sites have been provided demonstrating compliance with the specification.

II.F. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. A retest period of 4 years has been determined.

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 of the finished product stored in upright and inverted positions at 25°C/60%RH for 36 months and 40°C/75%RH for 18 months.

In addition stability studies were performed for refrigerated and frozen conditions. Data were provided for batches stored at 5°C and -20°C for 6 months.

G. Other Information

Shelf life
Shelf life of the finished product as packaged for sale is 3 years.

Special precautions for storage
Extremely flammable aerosol. Pressurised container, may burst if heated. Protect from sunlight. Do not expose to temperatures exceeding 50°C. Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological Studies

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

Toxicological Studies

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC as amended, and equivalence with a reference product has been demonstrated, 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 product is identical to the reference product therefore the risk to the user remains the same. The same user warnings as were authorised on the reference product are included on the product literature. The warnings and precautions are adequate to ensure safety to users of the product.

- Direct contact with the skin should be avoided because of sensitisation, contact dermatitis and possible hypersensitivity reactions to chlortetracycline.
- Wear appropriate impermeable gloves whilst handling the product.
- Because of risk of eye irritation, contact with the eyes should be avoided. Protect the eyes and face.
- Do not spray on an open flame or other ignition source. Do not pierce or burn the container, even after use.
- Avoid inhaling vapours. Apply the product in open air or in a sufficiently ventilated area.
- Wash hands after use.
- Do not eat or smoke whilst administering the product.
- In case of accidental ingestion, or in case of contact with eyes, seek medical advice immediately and show the label to the physician.

Environmental Safety

An Environmental Risk Assessment (ERA) has been submitted as part of the application. The assessment was performed in accordance with VICH and CVMP guidelines.

Phase I:
The product will be used to treat individuals or a small number of animals in a flock or herd and as such environmental exposure will be low. The product is not expected to pose a risk to the environment when used as recommended on the SPC. A Phase II ERA was not required.

III.B.2 Residues documentation

Residue Studies

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

MRLs

Chlortetracycline is listed in Table 1 of Regulation 37/2010 and MRLs have been established for edible tissues and milk. The marker substance is sum of parent drug and its 4-epimer. All of the excipients have been evaluated by the CVMP and no MRLs are required.

MRLs are listed below:

	All food producing species
Muscle	100 µg/kg
Liver	300 µg/kg
Kidney	600 µg/kg
Milk	100 µg/kg

Withdrawal Periods

The same withdrawal periods as authorised for the reference product have been approved.
Meat and offal: Zero days
Milk: Zero hours
Do not use on the udder of lactating animals if milk is intended for human consumption.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Pharmacology

As the product is identical to the reference product, equivalence with the reference product can be assumed. Therefore, an exemption from studies was granted and no data are required for this section.

Pharmacodynamics
Chlortetracycline is primarily a bacteriostatic antibiotic and exerts its action by inhibiting protein synthesis within the bacterial cell, impairing cell division and formation of the cell wall. Chlortetracycline binds to the bacterial ribosome and interferes with RNA binding.

Pharmacokinetics
Following cutaneous administration of the spray the absorption of chlortetracycline is negligible. Therefore, the product only has a local effect and systemic effects are not anticipated.

Tolerance in the Target Species

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

Resistance

Information was provided on the current state of resistance to chlortetracycline. The references showed that the MIC_{50} of most of the common foot pathogens to tetracyclines is between 0.25 and 0.5 µg/ml. Some isolates were found to have an increased MIC of 4 µg/ml. There appears to be a slight increase in MICs over time, however tetracyclines have been used for a number of years. The topical application of the product should continue to have efficacy against target pathogens when used in accordance with the SPC. Adequate warnings and precautions appear on the product literature.

IV.II. Clinical Documentation

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

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

.

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.

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