ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
KT15 3LS
(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Karidox 100mg/ml Oral Solution for use in drinking water for Chickens and Pigs

PuAR correct as of 28/02/2019 when RMS was transferred to ES.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0250/001/DC
Name, strength and pharmaceutical form	Karidox 100mg/ml Oral Solution for use in drinking water for Chickens & Pigs
Applicant	Laboratorios Karizoo SA, Polígono Industrial La Borda, Mas Pujades 11-12, 08140 Caldes de Montbui (Barcelona), Spain
Active substance	Doxycycline
ATC Vetcode	QJ01AA02
Target species	Chickens and Pigs
Indication for use	Chickens (Broilers) Prevention and treatment of chronic respiratory disease (CRD) and mycoplasmosis caused by microorganisms sensitive to doxycycline. Pigs Prevention of clinical respiratory disease due to *Pasteurella multocida* and *Mycoplasma hyopneumoniae* sensitive to doxycycline.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	26 March 2008
Date product first authorised in the Reference Member State (MRP only)	n/a
Concerned Member States for original procedure	Czech Republic Denmark France Hungary Italy The Netherlands Poland Romania Slovak Republic Spain

I. SCIENTIFIC OVERVIEW

Karidox 10 % Oral Solution contains doxycycline 100 mg/ml as the active ingredient. It is indicated for use as a broad-spectrum antimicrobial to treat bacterial respiratory disease in pigs and bacterial respiratory and alimentary tract disease in chickens.

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; the slight reactions observed are indicated in the SPC.
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 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. Composition

The product contains the active substance doxycycline as doxycycline hyclate and excipients pyrrolidone and propylene glycol.

The container/closure system comprises white high-density polyethylene containers of 1 litre and 5 litres. Containers are closed with a screw cap of the same material with induction sealing. 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.

B. Method of Preparation of the Product

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 European guidelines.

C. Control of Starting Materials

The active substance is doxycycline as doxycycline hyclate, an established active substance described in the European Pharmacopoeia. 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.

Each excipient is the subject of a monograph in the European Pharmacopoeia, which forms the raw material specification. Each specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with these specifications have been provided.

The dossier includes copies of the suppliers' specifications for the packaging materials and statements of compliance with European requirements for containers for food and pharmaceutical use.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

E. Control on intermediate products

There are no intermediate products.

F. 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 sites have been provided demonstrating compliance with the specification.

G. Stability

Stability data on the active substance and finished product has 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.

The claim of 24 hour stability after reconstitution is based on the demonstration of stability for a batch broached and stored 28 days at 25°C/60%RH.

H. Genetically Modified Organisms

Not applicable

J. Other Information

Shelf life
Shelf life of the veterinary medicinal product as packaged for sale: 15 months
Shelf life after dilution according to directions: 24 hours
Shelf-life after first opening the immediate packaging: 28 days

Special precautions for storage
Do not store above 25ºC.
Protect from light.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of pharmacological tests are not required.

The pharmacological aspects of this product are identical to the reference product.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

Toxicological Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological tests are not required.

The toxicological aspects of this product are identical to the reference product.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which considers all of the potential routes of exposure.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that further assessment was required. The requirements of VICH Phase II risk assessment were addressed. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of residues studies are not required.

The residues aspects of this product are identical to the reference product.
Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to consumers.

MRLs

Doxycycline is listed in Annex I of Council Regulation 2377/90. The marker substance is Doxycycline.
MRLs are listed below:

	Swine	Chickens
Muscle	100 µg/kg	100 µg/kg
Liver	300 µg/kg	300 µg/kg
Kidney	600 µg/kg	600 µg/kg
Fat / skin	300 µg/kg	300 µg/kg

Withdrawal Periods

Based on the data provided above, a withdrawal period of 7 days for meat and offal in chickens (broilers) and pigs is justified.
Not permitted for use in laying birds producing eggs for human consumption

IV CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, pharmacological studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, target species tolerance studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

Resistance

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, resistance studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, clinical 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 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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