College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

GalluDoxx 50% powder for use in drinking water/milk replacer

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0203/001/DC
Name, strength and pharmaceutical form	GalluDoxx 50% powder for use in drinking water/milk replacer
Applicant	Huvepharma NV Uitbreidingstraat 80 2600 Antwerp, Belgium
Active substance(s)	Doxycyclin hyclate 500 mg
ATC Vetcode	QJ01AA02
Target species	Calves, chickens and turkeys
Indication for use	<u>Calves</u> For the treatment of: - Pneumonia and shipping fever caused by Pasteurella- and *Mannheimia haemolytica* infections; - Anaplasmosis caused by *Anaplasma marginale*. <u>Chickens and turkeys</u> For the treatment of: - Ornithosis caused by *Chlamydia psittaci* in turkeys; - Colibacillosis caused by *E. coli* in chickens and turkeys; - CRD caused by *Mycoplasma gallisepticum* in chickens and turkeys.

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MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13 (1) application of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	13-12-2016
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	Belgium, Bulgaria, Germany, Spain, France, Ireland, Italy, Poland, United Kingdom

I. SCIENTIFIC OVERVIEW

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. Qualitative and quantitative particulars

The product contains doxycycline hyclate 500mg (equivalent to 433 mg doxycycline).

The container/closure system consist of 1kg or 5kg bags formed from polyethylene/aluminium/polyethylene terephthalate laminate.

The choice of the formulation and the absence of preservative are justified.

The inactivation process and the detection limit of the control of inactivation are correctly validated.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines

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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 the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

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

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

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 sitehave been provided demonstrating compliance with the specification.

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.

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 after first opening the container: 3 months.

Shelf life after reconstitution in drinking water: 12 hours.

Shelf life after reconstitution in milk replacer: Use immediately. Do not store

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III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

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

The pharmacological and 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 and the environment.

III.A Safety Testing

Pharmacological Studies

The applicant has has provided bibliographical data which show that doxycycline inhibits bacteria, Mycoplasma, Chlamydia, Rickettsia and certain Protozoa.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that it must be kept out of sight and reach of children.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

A Phase I and Phase II environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

Phase I:

A Phase II ERA is required as the Phase I assessment showed that the initial predicted environmental concentration in soil (PECsoil initial (see table)) is greater/ equal to 100 µg/kg and no mitigations exist that alter the PECsoil.

Target animal	PEC_{soil} [µg kg_{soil}^{-1}]
Calve	**346**
Broiler	**1075**
Replacement layer	**238**
Broiler breeder	67.7
Turkey	**536**

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Phase II:

A Phase II data set was provided according to the requirements of the CVMP/VICH guideline GL38 and the CVMP guideline on the Environmental Impact Assessment for Veterinary Medicinal Products in support of the VICH guidelines GL6 and GL38 (EMEA/CVMP/ERA/418282/2005-Rev.1), The data were considered to be complete and acceptable.

Physical-chemical properties			
Study type	**Test protocol**	**Result**	**Remarks**
Water solubility	OECD 105	66440 mg/L 57580 mg/L 59200 mg/L	pH 5 pH 7 pH 9
Dissociation constants in water pKa	OECD 112	pKa = 3.10 6.83	20°C 20°C

Environmental fate			
Soil Adsorption/Desorption	OECD 106 or …	Koc =71177, 106088 and 221723 L/kg Koc= 581969 and 4354116 L/kg K_d =	For silt loam soil, clay loam and loamy sand, respectively for the study of Kloppel For the study of Rushworth Koc values based on Kf values corrected for the low recovery List all values with pH, Corg, soil texture including clay content

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Risk characterisation

The Predicted Environmental Concentration (PEC) for each compartment was calculated in accordance with VICH guideline GL6 and the CVMP guideline on the Environmental Impact Assessment for Veterinary Medicinal Products in support of the VICH guidelines GL6 and GL38 (EMEA/CVMP/ERA/418282/2005-Rev.1)

Using the assessment factors (AF) in these VICH guidelines, predicted no effect concentrations (PNEC) were calculated and compared with the PEC values. This results in a risk quotient (RQ) for each compartment as follows:

Compartment	**PNEC**	**PEC**	**RQ**
surface water	Algea: 1.39 µg/l Crustacea:>68.1 µg/l Fish:>80.5 µg/l	µg/l Calve: 0.012 Broiler:0.037 Replacement Layer:0.008 Broiler breeder: 0.002 Turkey :0.018	<u>Algae</u> Calve : 0.009 Broiler:0.027 Replacement Layer :0.006 Broiler breeder: 0.001 Turkey : 0.013 <u>Crustacea</u> Calve :<0.001 Broiler: 0.001 Replacement Layer: <0.001 Broiler breeder: <0.001 Turkey :<0.001 <u>Fish</u> Calve: <0.001 Broiler <0.001 Replacement Layer <0.001 Broiler breeder:<0.001 Turkey :<0.001
groundwater		Calve: 0.035 Broiler: 0.110 Replacement Layer: 0.024	

		Broiler breeder: 0.007 Turkey :0.055	
soil	Micro-organisms: n.c Earthworms:≥86600 µg/kg Plants: 8660 µg/kg	Calve: 346 Broiler: 1080 Replacement: Layer 238 Broiler breeder: 68 Turkey: 536	<u>micro-organisms</u> Calve: n.c Broiler: n.c Replacement Layer :n.c Broiler breeder: n.c Turkey : n.c <u>Earthworms</u> Calve: 0.004 Broiler :0.012 Replacement Layla 0.003 Broiler breeder: 0.001 Turkey :0.006 <u>Plants</u> Calve :0.040 Broiler: 0.124 Replacement Layer: 0.027 Broiler breeder: 0.008 Turkey: 0.062

The risk characterisation resulted in risk quotients (RQs) below 1 for the surface water and groundwater compartments indicating that the product will not pose a risk to those compartments when used as recommended.

III.B Residues documentation

MRLs

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

	Bovine>	Porcine poultry
Muscle	100 µg/kg	100 µg/kg

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Liver	300 µg/kg	300 µg/kg
Kidney	600 µg/kg	600 µg/kg
Fat / skin		300 µg/kg

Withdrawal Periods

Based on the data provided above, a withdrawal period of 28 days for meat in calves and turkey is justified.

Based on the data provided above, a withdrawal period of 14 days for meat in chickens are justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic 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.

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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 Veterinary 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)**	**Approval date**
B.III.1.a.2 Updated certificate from an already approved manufacturer. (NL/V/0203/001/IA/001)	19th July 2017
B.III.1.a.2 Updated certificate from an already approved manufacturer. (NL/V/0203/001/IA/002)	9 July 2020