Veterinary Medicines Directorate

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

(Reference Member State)

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Soludox 500 mg/g Powder for Use in Drinking Water for Pigs and Chickens

PuAR correct as of 01/06/2018 when RMS was transferred to IE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0349/001/E/001
Name, strength and pharmaceutical form	Soludox 500 mg/g Powder for Use in Drinking Water for Pigs and Chickens
Applicant	Eurovet Animal Health BV Handelsweg 25 5531 AE Bladel The Netherlands
Active substance(s)	Doxycycline hyclate
ATC Vetcode	QJ01AA02
Target species	Pigs and chickens (broiler, pullet, breeder)
Indication for use	Pigs: For the treatment of the clinical signs associated with porcine respiratory disease caused by *Actinobacillus pleuropneumoniae, Pasteurella multocida*, and *Mycoplasma hyopneumoniae* susceptible to doxycycline. Chickens: Where clinical disease is present in the flock, to reduce mortality, morbidity, and clinical signs and to reduce lesions due to Pasteurellosis caused by *Pasteurella multocida* or to reduce morbidity and lesions in respiratory infections caused by *Ornithobacterium rhinotracheale (ORT)*.

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	Generic application in accordance with Article 13 (3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	28 July 2010
Date product first authorised in the Reference Member State (MRP only)	7th September 2011
Concerned Member States for original procedure	First Use Czech Republic, Italy, Slovakia Repeat Use First Wave Bulgaria, Croatia, Cyprus, Ireland, Malta, Romania, Slovenia

I. SCIENTIFIC OVERVIEW

This application was originally for a marketing authorisation for a generic hybrid product, submitted in accordance with Article 13 (3) of Directive 2001/82/EC as amended by Directive 2004/28/EC. Subsequently, European SPCs[1] for the product were harmonised via variation, (following CMD(v)[2] decision), in order to include a second species, chickens. The stated reference product is Doxycycline HCL 1000 mg/g Powder for Oral Solution. The UK reference product is Soludox 500 mg/g Water Soluble Powder for Pigs, authorised in the UK since April 2007.

In pigs, the product may be used for the treatment of clinical signs associated with porcine respiratory disease caused by *Actinobacillus pleuropneumoniae, Pasteurella multocida*, and *Mycoplasma hyopneumoniae* susceptible to doxycycline. In chickens, where clinical disease is present in the flock, the product may be used to reduce mortality, morbidity and clinical signs, and to reduce lesions caused by Pasteurellosis attributable to *Pasteurella multocida,* or to reduce morbidity and lesions in respiratory infections caused by *Ornithobacterium rhinotracheale (ORT)*.

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

[1] SPC – Summary of Product Characteristics.
[2] CVMP(v) – Co-ordination Group for Mutual Recognition and Decentralised Procedures – Veterinary.

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 benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains 500 mg doxycycline hyclate per gram, corresponding to 433 mg doxycycline, and the excipient tartaric acid.

The container system consists of sachets of 100 g, 250 g, 500 g, 1 kg and 10 x 100 g of product in a carton box.

The carton box is formed from one of the following:

- Polyester / polyethylene / aluminium / polyethylene and an inner layer of polyethylene.
- Polyester / polyethylene / aluminium and an inner layer of ionomer (surlyn).
- Polyethylene terephtalic acid / aluminium / polyamide and an inner layer of polyethylene.

The particulars of the containers and controls performed are provided and conform to the regulation.

The absence of preservative and the choice of formulation are 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. A portion of tartaric acid is placed in a mixing bin, followed by doxycycline hyclate and the remainder of the tartaric acid. The product is blended, prior to being filled into appropriate packs.

C. Control of Starting Materials

The active substance is doxycycline hyclate, an established active substance described in the European Pharmacopoeia (Ph. Eur.). The active substance is manufactured in accordance with the principles of good manufacturing practice, and certificates of suitability were provided.

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.

The applicant applied the current Ph. Eur. monograph specification for tartaric acid, and suitable specifications, in line with Ph.Eur and the Food and Drug Administration were received for the packaging materials.

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

Compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

E. Control on intermediate products

Not applicable, 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 site have been provided demonstrating compliance with the specification. Analytical tests include those for appearance, solubility, pH, microbiological quality, appropriate assays and impurities.

G. Stability

Active Substance
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. Data supported a retest interval of 4 years.

Finished Product
Stability tests were performed in accordance with VICH[3] Guidelines on a suitable number of commercially prepared batches. Long-term and accelerated study results supported demonstration of stability of the product for all four pack sizes.

In-Use Stability Testing

All parameters tested over short and long-term studies supported the established shelf-life.

[3] VICH – International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products.

Stability in Drinking Water
Studies showed that a slight increase in impurities occurred. No other adverse effect was noted.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

A declaration was made that no Class 1, Class 2 or Class 3 solvents are used in the manufacture of the product, complying with the VICH Guideline on new veterinary medicinal products. The shelf-life of the product was established as being 3 years for the product as packaged for sale, 9 months after first opening, and 24 hours after dilution or reconstitution. Any remaining product prepared for use and not utilised should be discarded.

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 pharmacological, toxicological and user safety tests are not required. These 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.

III.A Safety Testing

Ecotoxicity

The applicant provided a Phase II environmental risk assessment in compliance with the relevant guideline which showed that on the receipt of additional information no further assessment was required. 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

Suitable residues data were received for both target species.

Withdrawal Periods

Pigs:
Meat and offal: 4 days.

Chickens:
Meat and offal: 3 days, following a dose rate of 10 mg/kg body weight for 4 days.
Meat and offal: 9 days, following a dose rate of 20 mg/kg body weight for 4 days.
Not authorised for use in birds producing eggs for human consumption.
Do not use within 4 weeks of onset of laying.

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 were not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

Pharmacodynamics

The formulation of the test product and reference product are identical, therefore the pharmacodynamics of the new product may be considered the same as the reference product. No new data were presented.

Pharmacokinetics

The formulation of the test product and reference product are identical, therefore the pharmacokinetics of the new product may be considered the same as the reference product. No new data were required.

Tolerance in the Target Species of Animals

The formulation of the test product and reference product are identical, therefore the tolerance of the new product may be considered the same as the reference product. No new data were presented.

Resistance

Although resistance has been reported for the use of tetracyclines in chickens and pigs, no direct extrapolation can be made to doxycycline. No changes to the dosing regimens already used for pigs and chickens were made, thus it was considered there would be no increased risk to the environment.

Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

Laboratory Trials

The formulation of the test product is identical to that of the reference product, therefore the clinical efficacy of the product can be considered to be the same as the reference product. No further data were required in this section.

Field Trials

The formulation of the test product is identical to that of the reference product, therefore the clinical efficacy of the product can be considered to be the same as the reference product. No further data were required in this section.

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 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.

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