ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Soludox 500 mg/g Powder for Use in Drinking Water for Turkeys

PuAR correct as of 30/08/2018 when RMS was transferred to NL.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0437/001/DC
Name, strength and pharmaceutical form	Soludox 500 mg/g Powder for Use in Drinking Water for Turkeys
Applicant	Eurovet Animal Health BV Handelsweg 25 Bladel 5531 AE The Netherlands
Active substance(s)	Doxycyline hyclate
ATC Vetcode	QJ01AA02
Target species	Turkeys
Indication for use	Treatment of clinical respiratory infections associated with *Mycoplasma gallisepticum* susceptible 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	Generic hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	05 July 2012
Date product first authorised in the Reference Member State (MRP only)	Not Applicable
Concerned Member States for original procedure	France, Germany, Hungary, Italy, The Netherlands, Poland.

I. SCIENTIFIC OVERVIEW

This was a generic hybrid application submitted in accordance with Article 13(3) of Directive 2001/82/EC. The reference product for Soludox 500 mg/g Powder for Use in Drinking Water for Turkeys is Doxyprim 40% vizoldhato pulvis A.U.V authorised in Hungary on 17 July 2001 for which bioequivalence is claimed. Pharmaceutical equivalence is being claimed with the reference veterinary medicinal product authorised in the UK which is Pulmodox 500 mg/g Granules for Oral Solution for Pigs, Chickens and Turkeys, via the global marketing authorisation. This is a generic hybrid application because there is a change in strength of the active substance compared to the reference product. The applicant was exempt from submitting a bioequivalence study under paragraph d) of Section 7 of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products.

Soludox 500 mg/g Powder for Use in Drinking Water for Turkeys in intended for the treatment of clinical respiratory infections associated with *Mycoplasma gallisepticum* susceptible to doxycycline in turkeys. It is administered orally with drinking water. The recommended dosage is 25 mg doxycycline (corresponding to 29 mg doxycycline hyclate) per kg of bodyweight daily (equivalent to 58 mg product per kg bodyweight) administered for 5 consecutive days.

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[1]. The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when

[1] Summary of Product Characteristics

used as recommended. Suitable warnings and precautions are indicated in the SPC. The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains 500 mg doxycycline hyclate (corresponding to 433 mg doxycycline) and the excipient tartaric acid.

The product is presented as bags of 1 kg. Sachets of 100 grams packed per 10 in a carton box

1000 g bag: polyester, polyethylene, aluminium, polyethylene and an inner layer of polyethylene

1000 g bag: polyethylene terephtalic acid, aluminium, polyamide and an inner layer of polyethylene.

100 g sachet: polyester, polyethylene, aluminium and an inner layer of ionomer (surlyn).

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.

The manufacture consists of a simple mixing process. The excipient and the active substance are passed through a sieve separately before being mixed together and filled into the primary packaging. During the product preparation process the product is checked for fill weight and appearance.

C. Control of Starting Materials

The active substance is 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 for each of the proposed suppliers. The active

substance is manufactured in accordance with Certificates of Suitability (CEPs) granted by the EDQM[2].

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

Not applicable.

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 for two production batches from the proposed production site have been provided demonstrating compliance with the specification. Tests include those for solubility, weight, pH, microbiological quality and identification of doxycycline hyclate.

G. Stability

Stability data on the active substance has been provided for one of the active substance manufacturers in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. Other manufacturers have re-test periods stated on the certificates of suitability. A re-test period of 4 years for the active substance, regardless of its source was proposed and is considered acceptable.

Stability data on two commercial scale batches of the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product when stored under the approved conditions. Tests include those for solubility, loss on drying, microbiological quality, assay of doxycycline hyclate and total doxycyxline hyclate impurities. No special storage conditions were considered to be necessary.

H. Genetically Modified Organisms

Not Applicable.

J. Other Information

The shelf life of the finished product as packaged for sale is 3 years. After first opening the immediate packaging a shelf life of 6 months applies. After

[2] European Directorate for the Quality of Medicines & HealthCare

reconstitution with water, any product remaining after 24 hours should be discarded.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, the applicant is claiming exemption from providing *in vivo* bioequivalence studies citing pharmaceutical equivalence with Pulmodox 500 mg/g Granules for Oral Solution for Pigs, Chickens and Turkeys via the global marketing authorisation, under paragraph d) of Section 7 of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products. Therefore, the results of pharmacological and toxicological studies are not required.

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the product is not expected to pose a risk for users when used as recommended. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant has provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the product is not expected to pose a risk to the environment when used in accordance with the SPC.

III.B Residues documentation

Residue Studies

As this is a generic application according to Article 13, on the basis of citing pharmaceutical equivalence to Pulmodox 500 mg/g Granules for Oral Solution for Pigs, Chickens and Turkeys, the results of residues studies are not required. The product has the same withdrawal period as the product being cited for pharmaceutical equivalence. The withdrawal period for meat and offal is 12 days. There is no Maximum Resisdues Limit (MRL) set for eggs and therefore the product is not to be used in birds producing eggs for human consumption.

IV CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, on the basis of citing pharmaceutical equivalence to Pulmodox 500 mg/g Granules for Oral Solution for Pigs, Chickens and Turkeys, the applicant is exempt from the requirement to provide pre-clinical and clinical studies. The formulation of Soludox 500 mg/g

Powder for Use in Drinking Water for Turkeys is very similar to that of the reference product and bioequivalence of bioavailability and therefore efficacy can be claimed.

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)