ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

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

NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Doxycycline Hyclate VMD 500 mg/g Powder for Use in Drinking Water for Chickens

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Doxycycline Hyclate VMD 500 mg/g Powder for Use in Drinking Water for Chickens
Applicant	V.M.D. n.v. Hoge Mauw 900 2370 Arendonk Belgium
Active substance(s)	Doxycycline hyclate
ATC Vetcode	QJ01AA02
Target species	Non-egg laying chickens
Indication for use	Treatment of the following specified infections of the respiratory tract and alimentary tract caused by micro-organisms susceptible to doxycycline. Non-egg laying chickens: Infections of the respiratory tract caused by *Mycoplasma spp, Escherichia coli, Avibacterium paragallinarum* and *Bordetella avium*. Enteritis caused by *Clostridium perfringens* and *Clostridium colinum.*

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Veterinary Medicines Directorate website (www.vmd.defra.gov.uk)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.

I. SCIENTIFIC OVERVIEW

Doxycycline Hyclate VMD 500 mg/g Powder for Use in Drinking Water for Chickens is authorised for use in non-egg laying chickens for the treatment of infections of the respiratory tract and alimentary tract caused by micro-organisms susceptible to doxycycline. The product is indicated for the treatment of respiratory tract infections caused by *Mycoplasma spp, Escherichia coli, Avibacterium paragallinarum* and *Bordetella avium*, and treatment of enteritis caused by *Clostridium perfringens* and *Clostridium colinum*.

The application for a national MA for a generic product was submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended by 2004/28/EC. The applicant claimed bioequivalence with the reference product, Doxycycline 50% WSP, marketed by Dopharma Research BV, which has been authorised in the Netherlands since December 1996. The applicant claimed exemption from bioequivalence studies in accordance with exemption 4.b) of the Guidelines for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products

The product is supplied in bags formed in a polyester/aluminium foil/polyethylene laminate containing either 100 gram or 1 kg of product. The product should not be administered to laying birds for 4 weeks before the start of lay and during lay; and should not be administered in combination with bactericidal antibiotics, such as penicillin and cephalosporins. Doxycycline absorption may be reduced by the presence of high quantities of calcium, iron, magnesium or aluminium in the diet.

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[1]. 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.

[1] Summary of Product Characteristics

II. QUALITY ASPECTS

A. Composition

The product contains doxycycline hyclate 500 mg/g as an active substance and excipients citric acid anhydrous and lactose monohydrate.

The product is supplied in bags formed in a polyester/aluminium foil/polyethylene laminate. The bags are of a 100 g or 1 kg size. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of formulation is justified.

The product is an established pharmaceutical form and its development has been 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. The applicant has provided details of the stages of, and method of manufacture. In-process controls have also been described. Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance doxycycline hyclate is an established active substance and supporting data have been provided in the form of a certificate of suitability. It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitable justified.

Both excipients are the subject of monographs in the European Pharmacopoeia. Compliance with the requirements of the pharmacopoeia is therefore applied as the specification for each of these ingredients.

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

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

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.

G. Stability

Active substance
Data have been provided which indicate that the active substance is stable when stored in the appropriate container under appropriate conditions. The retest period of 5 years is justified.

Finished Product
Data have been provided which indicate that the finished product is stable for 3 years.

In-Use
An in-use shelf life of 28 days is justified.

J. Other Information

- Shelf life of the veterinary medicinal product as packaged for sale: 3 years
- Shelf-life after first opening the immediate packaging: 28 days.
- Shelf life after reconstitution according to the directions: 24 hours.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

Since this generic application was made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, data on pharmacology and toxicology were not required.

III.A Safety Testing

Pharmacological Studies

Since this generic application was made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, data on pharmacology and toxicology were not required.

User Safety

The following operator warnings are included in the SPC and product literature:

- If you know you are allergic to the tetracycline class of antibiotics, special care should be taken when handling this product or the medicated solution.
- If contact with skin or eyes occurs, wash area immediately with plenty of fresh water.
- If irritation persists or accidental ingestion occurs seek medical advice.
- During preparation and administration of the medicated drinking water, skin contact with the drug and inhalation of dust particles should be avoided. Therefore, it is recommended to wear impermeable gloves (e.g. rubber or latex) and an appropriate dust mask (e.g. a disposable half-mask respirator conforming to European Standard EN 149 (FFP2) or a non-disposable respirator to European Standard EN 140 with a filter to EN 143).
- Wash hands and contaminated skin immediately after handling the product.

Ecotoxicity

The applicant provided a Phase II environmental risk assessment in compliance with the relevant guidelines. The PEC_{soil}[2] values derived from several studies were acceptable and in accordance with VICH[3] guidelines.

[2] Figure provided after calculation of the predicted concentration of active substance in the upper 5 cm of soil.
[3] International Co-operation on Harmonisation of Technical Requirements for Registration of Veterinary Products.

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

The applicant did not provide any residue depletion studies. As this was an application for a generic product, bioequivalence with the reference product was claimed, and the product is to be orally administered via the drinking water, the applicant was not required to provide any data for this section.

MRLs

Pharmacologically active substance	Marker residue	Animal species	MRLs	Target tissues	Other provisions
Doxycycline	Doxycycline	Poultry	100 µg/kg 300 µg/kg 300 µg/kg 600 µg/kg	Muscle Skin + fat Liver Kidney	Not for use in animals from which eggs are produced for human consumption

Withdrawal Periods

Meat and Offal: 5 days.
Not to be used in chickens laying 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 is established due to the nature of the products, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product. No further data were submitted.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and bioequivalence with a reference product is established due to the nature of the products, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product. No further data were submitted.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product is established due to the nature of the products, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product. No further data were submitted.

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.

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