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Publicly Available Assessment Report for a
Veterinary Medicinal Product

ASHIDOX 500 mg/g, powder for use in drinking water/milk for cattle (pre-ruminant), pigs and chickens

PRODUCT SUMMARY

EU Procedure number	IE/V/0584/001/DC
Name, strength and pharmaceutical form	Ashidox 500 mg/g, powder for use in drinking water/milk for cattle (pre-ruminant), pigs and chickens
Active substance	Doxycycline hyclate
Applicant	Ashish Life Science Holding B.V. Herengracht 454 Amsterdam Noord-Holland 1017 CA Netherlands
Legal basis of application	Generic application in accordance with Article 18 of Regulation (EU) 2019/6.
Date of completion of procedure	01/05/2025
Target species	Cattle (pre-ruminant), pigs, chickens.
Indication for use	For the treatment of the following specified infections of the respiratory tract and the alimentary tract. Cattle (pre-ruminant): - Bronchopneumonia and pleuropneumonia caused by *Pasteurella* spp., *Streptococcus* spp., *Arcanobacterium pyogenes*, *Histophilus somni* and *Mycoplasma* spp.. Pigs: - Atrophic rhinitis caused by *Pasteurella multocida* and *Bordetella bronchiseptica*; - Bronchopneumonia caused by *Pasteurella multocida*, *Streptococcus suis* and *Mycoplasma hyorhinis*; - Pleuropneumonia caused by *Actinobacillus pleuropneumoniae*. Chickens: - Infections of the respiratory tract caused by *Mycoplasma* spp., *Escherichia coli*, *Haemophilus paragallinarum* and *Bordetella avium*; - Enteritis caused by *Clostridium perfringens* and *Clostridium colinum*.
ATCvet code	QJ01AA02
Concerned Member States	BG, CZ, ES, HU, IT, RO

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in relevant articles of Regulation (EU) 2019/6. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland. The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.
It has been shown that the VMP can be safely used in the target species.
The VMP 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 VMP 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

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A. Qualitative and Quantitative Particulars

The product contains doxycycline 433 mg (equivalent to 500 mg doxycycline hyclate) and the excipients citric acid, anhydrous and lactose monohydrate.
The product is packaged in a 100 g poly laminated aluminium silver coloured foil sachet and a 1000 g poly laminated aluminium silver coloured pouch.

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 for the manufacturing process has been presented in accordance with the relevant European guidelines.

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 has been provided.

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.

D. Control on Intermediate Products

Not applicable.

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 has been provided. Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substance 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 has 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

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing
Pharmacological Studies

As this is a generic application according to Article 18 of Regulation (EU) 2019/6 and bioequivalence with the reference product DOXYLIN 50% WSP, powder for oral solution (Dopharma Research B.V.) has been demonstrated, results of pharmacodynamic or pharmacokinetic tests are not required.

Toxicological Studies

As this is a generic application according to Article 18 of Regulation (EU) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of toxicological tests are not required.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline.
The product contains the same concentration of the active substance and the same excipients in similar amounts as the reference veterinary medicinal product. In addition, the product is intended to be administered by the same route of administration at the same dose and for the same indications for use in the same species as the reference product. Given no qualitative or quantitative difference in terms of active substance and as any difference in the quantitative composition of the excipients is not expected to alter the risk to the user, it is accepted that the inherent toxicity of the product and exposure scenarios can be expected to be the same for both products.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

The applicant has not provided a Phase II environmental risk assessment, instead, reference to the 'Reflection paper on the interpretation of Article 18(7) of Regulation (EU) 2019/6' (EMA/CVMP/ERA/622045/2020) has been made. As noted in the reflection paper, an environmental risk assessment is no longer routinely required in support of a generic application, subject to a number of criteria being satisfied.
As the reference product is supported by a Phase II environmental risk assessment in line with VICH GL38 conducted after 1 October 2005 it is accepted that an ERA data package is in place and that the need for risk mitigation measures has been considered. As the product literature of the reference product does not contain environmental risk mitigation measures the absence of risk mitigation measures is appropriate.

III.B Residues Documentation

Residue Studies

No residue depletion studies were conducted on the basis that bioequivalence with the reference product was accepted. The CVMP Guideline on determination of withdrawal periods for edible tissues (EMA/CVMP/SWP/735325/2012 Rev.2) provides the following guidance for generic products:
"When the formulation (active and inactive ingredients), the dose schedule, the route(s) of administration and the target species of a specific generic product, are identical to a currently approved product (i.e. the reference product), or it has been adequately justified that any differences in formulation are so minor such that they will not impact on residue depletion, then the withdrawal period of the latter can be used for the former."
Considering the following:

- the product and reference product have the same qualitative and quantitative amount of active substance and have the same excipients (citric acid and lactose monohydrate) in similar amounts,
- the product is an aqueous oral solution at time of administration and contains an active substance in the same concentration as an approved reference veterinary medicinal product presented as an aqueous oral solution at time of administration,
- doxycycline is a highly soluble and completely absorbable active substance (BCS-Class I),
- the product is intended to be administered by the same route of administration (in drinking water or milk replacer), at the same dose, and for the same indications for use in the same species as the reference product,

the rate and extent of absorption of the active substance in the target animal is not expected to differ between the products.

Maximum Residue Limits

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

Pharmacologically active substance	Marker residue	Animal species	MRL (µg/kg)	Target tissue	Other provisions
Doxycycline	Doxycycline	All food-producing species	100 300 300 600	Muscle Fat Liver Kidney	For fin fish the muscle MRL relates to 'muscle and skin in natural proportions'. MRLs for fat, liver and kidney do not apply to fin fish. For porcine and

					poultry species the fat MRL relates to 'skin and fat in natural proportions'. Not for use in animals from which milk or eggs are produced for human consumption.

Withdrawal Periods
Based on the data provided, the following withdrawal periods are justified:
Meat and offal:
Cattle (pre-ruminant): 7 days
Pigs: 8 days
Chickens: 5 days
Not for use in birds producing eggs for human consumption.
Not authorised for use in animals producing milk for human consumption.

IV. CLINICAL ASSESSMENT

IV.A Pre-Clinical Studies
As this is a generic application according to Article 18 of Regulation (EU) 2019/6 and bioequivalence with a reference product has been demonstrated, pre-clinical 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
No target animal tolerance data specific to the product have been presented, however, given the legal basis of the application and the similarity of formulations, it was accepted that the product will not present any greater risk to the target animal than that posed by the reference product. The omission of product-specific target animal tolerance study data was therefore accepted.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance
Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies
As this is a generic application according to Article 18 of Regulation (EU) 2019/6 and bioequivalence with a reference product has been demonstrated, clinical trials 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 benefit/risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

VI. 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 in the Union Product Database (UPD).
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.

Changes:
None.