College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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The Netherlands

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Doxybactin (vet) 50-200-400 mg tablets for dogs (and cats)
NL/V/0218/002-004/DC

Created: 5-9-2018
Updated: 7-2-2022

CMS: AT, BE, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NO, PL, PT, RO, SE, SI, SK, UK

MODULE 1

PRODUCT SUMMARY

Dutch Application numbers	REG NL 119711, 119712 and 119713
EU Procedure number	NL/V/0218/002-004/DC
NL Case numbers registration	539949, 539950, 539951
Names, strengths and pharmaceutical form	Doxybactin (vet) 15 mg tablets for dogs and cats (withdrawn) Doxybactin (vet) 50 mg tablets for dogs and cats Doxybactin (vet) 200 mg tablets for dogs Doxybactin (vet) 400 mg tablets for dogs
Applicant	Le Vet Beheer B.V., Oudewater, The Netherlands
Active substance(s)	Doxycycline (as doxycycline hyclate)
ATC Vetcode	QJ01AA02
Target species	Dogs (and cats)
Indication for use	<u>Dogs:</u> Rhinitis caused by *Bordetella bronchisepticum* and *Pasteurella* spp.; Bronchopneumonia caused by *Bordetella* spp., *E. coli* and *Pasteurella* spp.; Pyelonephritis caused by *E. coli* and gram-positive cocci; Interstitial nephritis caused by *Leptospira* spp., *E. coli* and gram-positive cocci; Otitis media caused by gram-positive cocci and *Pasteurella* spp. <u>Cats (if applicable):</u> Rhinitis caused by *Bordetella bronchisepticum* and *Pasteurella* spp.; Bronchopneumonia caused by *Bordetella* spp., *E. coli* and *Pasteurella* spp.; Pleuritis sicca caused by gram-positive cocci; Pneumonitis caused by *Chlamydophila felis*; Pyelonephritis caused by *E. coli* and gram-positive cocci; Interstitial nephritis caused by *Leptospira* spp., *E.coli* and gram-positive cocci; Otitis media caused by gram-positive cocci and *Pasteurella* spp.

Doxybactin (vet) 50-200-400 mg tablets for dogs (and cats)	NL/V/0218/002-004/DC
Le Vet Beheer B.V.	DCP
	Publicly available assessment report

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).

Or on the Dutch website:

https://www.diergeneesmiddeleninformatiebank.nl/nl/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(3) of Directive 2001/82/EC as amended (Hybrid application).
Date of completion of the original decentralised procedure	28-06-2017
Concerned Member States for original procedure	AT, BE, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NO, PL, PT, RO, SE, SI, SK, UK

I. SCIENTIFIC OVERVIEW

Doxybactin (vet) 50-200-400 mg tablets for dogs (and cats) 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.
Doxybactin (vet) 50-200-400 mg tablets for dogs (and cats) 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. Composition

The tablets contain 57.71 mg, 230.83 mg and 461.66 mg doxycycline hyclate equivalent to 50.0 mg, 200.0 mg and 400.0 doxycycline and the following core excipients: Colloidal silicon dioxide, Sodium starch glycolate (type A), Magnesium stearate, Microcrystalline cellulose, Yeast and Chicken flavour.
The tablet is cross scored and meant to be broken into equal halves or quarters.
The products are packed in PVC/PE-PVDC-Al blisters, each containing 10 tablets.
The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.
A bioequivalence study is waived since it is similar to the reference product.

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 product is manufactured using conventional manufacturing techniques. However, suitable pre-approval validation results on three pilot scale batches have been provided.

The tests performed during production are described.

C. Control of Starting Materials

The active substance is Doxycycline hyclate is an established active substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.
CEP procedures has been employed and no concerns were raised.

The active substance specification is considered adequate to control the quality of the material from both suppliers. Batch analytical data demonstrating compliance with this specification have been provided.

All excipients are in conformity with the Ph.Eur. requirements with the exception of the yeast and chicken flavour which have been adequately specified.

The packaging is conformity with the Ph. Eur. and EU Food Directive.

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

The magnesium stearate is of vegetable origin. In regard to chicken flavour A TSE declaration and Viral Safety Evaluation are provided.

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. Relevant 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.

G. Stability

Stability data on the active substance has been assessed by the EDQM in order to be granted a CEP.

Stability data on the finished product have been provided in accordance with applicable European guidelines. According to the stability results provided the claimed shelf life of 30 months can be granted. Shelf life of divided tablets: 3 days.

H. Genetically Modified Organisms

Not applicable.

Doxybactin (vet) 50-200-400 mg tablets for dogs (and cats)	NL/V/0218/002-004/DC
Le Vet Beheer B.V.	DCP
	Publicly available assessment report

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 (1) for the lowest strength and hybrid applications according Article 13 (3) for the higher strengths (Doxybactin 50 mg, 200 mg and 400 mg) and bioequivalence with a reference product has been demonstrated results of safety tests or of the pre-clinical and clinical trials tests are not required except for the larger tablets of the higher strengths for which a URA has been provided.

Warnings, precautions and other statements as listed on the product literature are derived from the reference product and adapted to the results of the URA.
Moreover additional statements have been added, based on increased knowledge, the current state of science and the discussions with the CMS.
In conclusion the veterinary medicinal product is safe if used in accordance with the product information.

III.A Safety Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline.

Warnings, precautions and other statements as listed on the product literature are derived from the reference product and adapted to the results of the URA and the discussions with the CMS.

These conclusions included the increased knowledge and the current state of science.

In conclusion the veterinary medicinal product is safe for the user if used in accordance with the product information

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

As the products are for use in dogs and cats (non-food animals) the Phase I decision tree stops at Question 3. It is therefore not necessary to submit a Phase II assessment.

Doxybactin (vet) 50-200-400 mg tablets for dogs (and cats)	NL/V/0218/002-004/DC
Le Vet Beheer B.V.	DCP
	Publicly available assessment report

III.B Residues documentation

No residue depletion studies were conducted because the applications are for dogs and cats.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13 (1) for the lowest strength and hybrid applications according Article 13 (3) for the higher strengths (Doxybactin 50 mg, 200 mg and 400 mg), and bioequivalence with a reference product has been demonstrated, results of the pre-clinical and clinical tests are not required.

The data in the product information regarding target animal safety and efficacy are in compliance with the data in the reference product and adapted to the results of the assessment of the dossier and the discussion with the CMS.

When the product is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable

Doxybactin (vet) 50-200-400 mg tablets for dogs (and cats)	NL/V/0218/002-004/DC
Le Vet Beheer B.V.	DCP
	Publicly available assessment report

V . OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the veterinary medicinal 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.

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	**Section updated**	**Approval date**
NL/V/xxxx/WS/021 C.II.7.b. introduction of a new Pharmacovigilance system which has been assessed by the relevant national competent authority/EMA for another product of the same MAH.	N/A	12-7-2019
NL/V/0218/IB/002/G B.II.b.1.e - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product; Site where any manufacturing operation(s) take place, except batch release, batch control, primary and secondary packaging, for non-sterile medicinal products. B.II.b.1.a - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product; Secondary packaging site. B.II.b.1.b - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product; Primary packaging site. B.II.b.2.c.2 - Change to batch release arrangements and quality control testing of the finished product; Replacement or addition of a manufacturer responsible for importation and/or batch release; Including batch control/testing. B.II.b.3. a) Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product; Minor change in the manufacturing process.	N/A (Package leaflet updated)	24-1-2022
Renewal		ongoing