MINISTERIO DE SANIDAD
agencia española de medicamentos y productos sanitarios

DEPARTAMENTO DE MEDICAMENTOS VETERINARIOS

Agencia Española de Medicamentos y Productos Sanitarios

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(Reference Member State)

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Dobroxine 500 mg/g + 50 mg/g powder for use in drinking water/milk for calves (Doxycycline hyclate, Bromhexine hydrochloride)

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PRODUCT SUMMARY

EU procedure number	ES/V/0446/001/DC
Name, strength and pharmaceutical form	Dobroxine 500 mg/g + 50 mg/g powder for use in drinking water/milk for calves
Applicant	Laboratorios Karizoo S.A.
Active substance(s)	Doxycycline hyclate, Bromhexine hydrochloride
ATC vetcode	QJ01AA20
Target species	Cattle (pre-ruminant calves).
Indication for use	Treatment of respiratory infections caused by *Pasteurella multocida* and *Mannheimia haemolytica.*

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Decentralised procedure application in accordance with Article 19 of Regulation (EU) 2019/6 as amended.
Reference product (RP)	DFV DOXIVET 100mg/ml + 10 mg/ml solución para administración en agua de bebida o en leche
Marketing authorisation holder	DIVASA-FARMAVIC, S. A
MS where the RP is or has been authorised	ES
Marketing authorisation number	2623 ESP
EU procedure number	
Date of authorisation	12 September 2012
Date of completion of the original decentralised procedure	30/04/2025
Date veterinary medicinal product first authorised in the Reference Member State (MRP only)	-
Concerned Member States for original procedure	CY, NL, PT, IT
Concerned Member States for subsequent recognition procedure	-
Withdrawn CMS during original <mutual recognition> <decentralised><subsequent recognition> procedure	-

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of referenceability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

1. 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 reactions observed are indicated in the SPC.

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.

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

2.A. Product description

The VMP contains 500 mg/g of doxycycline (as doxycycline hyclate) and 50 mg/g of bromhexine hydrochloride with citric acid and lactose monohydrate as excipients*)*.

The container/closure system is a thermosealed bag of 200 g and 1 kg made of polyester, aluminium and polyethylene complex.

The choice of the formulation is justified.

The VMP is an established pharmaceutical form, and its development is adequately described in accordance with the relevant European guidelines.

2.B. Description of the manufacturing method

The VMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site

Process validation data on the VMP have been presented in accordance with the relevant European guidelines.

2.C. Production and control of starting materials

The active substances Doxycycline hyclate and Bromhexine hydrochloride are established active substances described in the European Pharmacopeia/National pharmacopeia. They are manufactured in accordance with the principles of good manufacturing practice.

The active substances specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

Certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products for both active substances.

2.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 VMP.

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.

2.F. Stability tests

Stability data on the active substances have 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 have been provided in accordance with applicable European guidelines, demonstrating the stability of the VMP throughout its shelf life when stored under the approved conditions.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of results of pharmacological or toxicological tests are not required.

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows that risks after dermal and inhalation exposure may arise.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the VMP.

Environmental Risk Assessment

The application for marketing authorisation of Dobroxine 500 mg/g + 50 mg/g powder for use in drinking water/milk for calves is exempt from submitting an Environmental Risk Assessment (ERA) according to Article 18(7) of Regulation (EU) 2019/6 as an ERA has already been performed for the same active substance and exposure level in the EU in accordance with VICH GL38 (“Guideline on environmental impact assessment for veterinary medicinal products - Phase II” [CVMP/VICH/790/03-FINAL]). Therefore, as there are similar products already authorized in the EU after October 2005 (EMA/CVMP/ERA/622045/2020), a complete data package for environmental risk assessment is not required. No unacceptable environmental risk is expected when the product is used, handled and disposed according to the information included in the SPC.

3.B. Residues documentation

Residue tests

No residue depletion studies were conducted because bioequivalence with the reference product has been demonstrated and both products are used in the same species, at the same dose and treatment regimen as the reference product. Therefore, the same withdrawal periods can be applied.

Maximum Residue Limits

Doxycycline hyclate and bromhexine hydrochloride are included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substances	**Marker residue**	**Animal species**	**MRLs (µg/kg)**	**Target tissues**	**Other provisions**
Doxycycline	Doxycycline	Bovine	100 µg/Kg 300 µg/Kg 600 µg/Kg	Muscle Liver Kidney	Not for use in animals from which milk is produced for human consumption
Bromhexine	Not applicable	Bovine	No MRL required	Not applicable	Not for use in animals from which milk or eggs are produced for human consumption

Withdrawal Periods

Based on the data provided above, a withdrawal period of 16 days for meat in pre-ruminant calves is justified. The veterinary medicinal product is not authorised for use in animals producing milk for human consumption.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, efficacy studies are not required.
The efficacy claims for this VMP are equivalent to those of the reference VMP.

4.A. Pre-Clinical Studies

No pre-clinical studies were performed.

Pharmacology

Development of resistance and related risk in animals

Adequate warnings and precautions appear on the product literature.

Tolerance in the target species of animals

The product literature accurately reflects the type and incidence of adverse effects, which might be expected.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMP 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 VMP for humans and the environment is acceptable.

POST-AUTHORISATION PROCEDURES

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the VMP. 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 VMP.

None.