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DEPARTAMENTO DE
MEDICAMENTOS
VETERINARIOS

Agencia Española de Medicamentos y Productos Sanitarios

C/Campezo 1, Edificio 8
28022 – Madrid
España
(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

**MARBOSYVA 100 mg/ml solution for injection for cattle and
pigs**

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0188/001/DC
Name, strength and pharmaceutical form	Marbosyva 100 mg/ml solution for injection
Applicant	Laboratorios SYVA, S.A.U. Avda. Párroco Pablo Diez, 49-57 24010-León SPAIN
Active substance(s)	Marbofloxacin
ATC Vet code	QJ01MA93
Target species	Cattle and pigs (sows)
Indication for use	<p><u>In cattle:</u></p> <p>-Treatment of respiratory infections caused by susceptible strains of <i>Histophilus somni</i>, <i>Mannheimia haemolytica</i>, <i>Pasteurella multocida</i> and <i>Mycoplasma bovis</i>.</p> <p>-Treatment of acute forms of mastitis induced by marbofloxacin-susceptible <i>Escherichia coli</i> strains, during lactation.</p> <p><u>In pigs (sows):</u></p> <p>-Treatment of Postpartum Dysgalactiae Syndrome, PDS (Metritis Mastitis Agalactia Syndrome) caused by marbofloxacin-susceptible bacterial strains.</p>



MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies website (<http://www.hma.eu>).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	22 de octubre de 2012
Date product first authorised in the Reference Member State (MRP only)	---
Concerned Member States for original procedure	AT; BE; BG; DE; DK; FR; HU; IE; IT; NL; PL; PT; UK.

I. SCIENTIFIC OVERVIEW

For public assessment reports for the first authorisation in a range:

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.

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 product contains marbofloxacin (100 mg/ml) and excipients (metacresol, monothioglycerol, gluconolactone, disodium edetate, water for injections).

The container/closure system are type II amber glass vials of 50, 100 and 250 ml with type I bromobutyl stopper and aluminium cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the presence of preservatives are justified.

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 and sterilised 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.

C. *Control of Starting Materials*

The active substance is marbofloxacin, 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 specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with these specifications have been provided.

Copies of the ASMFs of Zhejiang Guobang Pharmaceutical Co. Ltd. (China) and F.I.S. Fabbrica Italiana Sintetici S.p.A., manufacturers of the active substance, have been included.

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*

Tests performed on the bulk product are described.

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 from the proposed production site have been provided demonstrating compliance with the specification.

G. Stability

Stability data on the active substance 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 product when stored under the approved conditions.

The claim of 28 days stability after broaching is based on the demonstration of stability for four pilot batches (two batches packaged in 50 ml vials and two batches packaged in 250 ml vials) broached and stored 28 days at $30\pm 2^{\circ}\text{C}/65\pm 5\% \text{RH}$.

H. Genetically Modified Organisms

None of the starting materials used in the manufacture of the product contains genetically modified organisms.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with reference products has been demonstrated, the results of toxicological and pharmacological tests are not required.

The aspects of safety of this product are identical to the reference products.

Warnings and precautions as listed on the product literature are the same as those of the reference products and are adequate to ensure safety of the product to users, the environment and consumers.

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with reference products has been demonstrated, the results of pharmacological tests are not required.

Toxicological Studies

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with reference products has been demonstrated, the results of toxicological tests are not required.

User Safety

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with reference products has been demonstrated, the applicant has provided a user safety assessment in compliance with the relevant guideline EMEA/CVMP/543/03.

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

Ecotoxicity

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

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

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with reference products has been demonstrated, the results of residue depletion studies are not required.

MRLs

Marbofloxacin is listed in Commission Regulation (EU) No 37/2010 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin.

MRLs are listed below:

Pharmacologically active Substance	Marker residue	Animal Species	MRL	Target Tissues	Other Provisions (according to Article 14 (7) of Regulation (EC) No 470/2009)	Therapeutic classification
Marbofloxacin	Marbofloxacin	Bovine, porcine	150 µg/kg 50 µg/kg 150 µg/kg 150 µg/kg	Muscle Fat Liver Kidney	For porcine species the fat MRL, relates to skin and fat in natural proportions	Anti-infectious agents/Antibiotics
		Bovine	75 µg/kg	Milk		

Withdrawal Periods

Since the bioequivalence with reference products has been demonstrated, the withdrawal period proposed are identical to those authorised for reference products.

Cattle:

Intramuscular use (8 mg/kg single dose):

Meat and offal: 3 days

Milk: 72 hours

Intramuscular or subcutaneous use (2 mg/kg single daily injection, for 3-5 days):

Meat and offal: 6 days

Milk: 36 hours

Pigs (sows):

Intramuscular use:

Meat and offal: 4 days

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13 (1), and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference products.

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with reference products has been demonstrated, the results of pharmacological tests are not required.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with reference products has been demonstrated, the results of tolerance studies are not required.

Resistance

As this is a generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with reference products has been demonstrated, the results of resistance development are not required.

Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

As this is generic application according to Article 13 (1) of Directive 2001/82/EC, as amended, and bioequivalence with reference products has been demonstrated, the results of clinical trials are not required.



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 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 veterinary Heads of 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.

None.