Bundesamt für
Verbraucherschutz und
Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
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(Germany)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Marbosol 20 mg/ml Solution for Injection for Calves and Piglets

Date: 18 April 2017

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0175/001
Name, strength and pharmaceutical form	Marbosol 20 mg/ml solution for injection for calves and piglets
Applicant	CP-Pharma Handelsgesellschaft mbH Ostlandring 13 31303 Burgdorf Germany
Active substance(s)	Marbofloxacine
ATC Vetcode	QJ01MA93
Target species	Cattle (pre-ruminating calves), piglets
Indication for use	Pre-ruminating calves: For treatment and prevention of respiratory infections caused by marbofloxacin susceptible Mannheimia haemolytica and Pasteurella multocida strains, where the presence of the disease has been established in the group. Piglets: For the treatment of respiratory infections caused by marbofloxacin susceptible Actinobacillus pleuropneumoniae, Mycoplasma hyopneumoniae and Pasteurella multocida strains.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original Decentralised procedure	21 December 2012
Date product first authorised in the Reference Member State (MRP only)	n.a.
Concerned Member States for original procedure	AT, BE, DK, ES, FR, DE, HU, IE, IT, PT, UK
Current Concerned Member States	ES, HU

I. SCIENTIFIC OVERVIEW

Marbosol 20 mg/ml solution for injection for calves and piglets is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.

It can be considered that Marbosol 20 mg/ml solution for injection for calves and piglets can be safely used in the target species; the reactions that may be expected are indicated in the SPC and that Marbosol 20 mg/ml solution for injection for calves and piglets is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.

The efficacy of Marbosol 20 mg/ml solution for injection for calves and piglets is considered as demonstrated in respect of the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

The safety and efficacy aspects of Marbosol 20 mg/ml solution for injection for calves and piglets are based on bioequivalence with the reference product authorised in the Netherlands MARBOCYL 2 %, oplossing voor injectie voor niet-herkauwend kalf en big, REG NL 9169. Warnings and precautions are added based on increased knowledge and the current state of science.

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The application concerns Marbosol 20 mg/ml solution for injection for calves and piglets containing marbofloxacin (20 mg/ml).

The product contains the following excipients: Metacresol, Disodium edetate, Gluconolactone, Mannitol, Monothioglycerol and Water for injections

The solution for infusion is packed in 50 and 100 ml Amber type II glass bottles, fitted with red chlorobutyl 20 mm stoppers and aluminium 20 mm caps.

The product represents 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 fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The product is manufactured according to a standard manufacturing process using conventional manufacturing techniques.

A process validation protocol has been included. The process validation protocol is considered appropriate to control the critical step in the manufacturing process. The 50 L pilot batches used are considered applicable to the commercial batch size of 500 L.

The process validation will be performed post-approval.

The tests performed during production are described. Adequate in-process specifications are provided.

C. Control of Starting Materials

The active substance is marbofloxacin for veterinary use, 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 have been provided.

The excipients are in conformity with the requirements of their Ph.Eur. monographs and USP/NF. For the auxiliary substance nitrogen an in-house specification is used.

The glass vials and stoppers are in conformity with the Ph.Eur. requirements.

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

Not applicable

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.

G. Stability

The ASMFs from the active substance manufacturers confirm the retest period 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 throughout the claimed shelf life of 36 months without any special storage conditions.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been accepted based on exemption a) and d) of section 7.1 of the CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products, EMA/CVMP/016/00-Rev.-2, results of toxicological, pharmacological and residue tests are not required.

Warnings and precautions as listed on the product literature are based on those of the reference product but supplemented using provided safety studies, increased knowledge and the current state of science and are adequate to ensure safety of Marbosol 20 mg/ml solution for injection for calves and piglets to users / the environment / consumers.

III.A Safety Testing

Pharmacological Studies

For this generic procedure, the applicant refers to the reference product, MARBOCYL 2 %, oplossing voor injectie voor niet-herkauwend kalf en big, REG NL 9169, for which it was shown that Marbofloxacin acts by inhibition of DNA gyrase and has a broad-spectrum activity against Gram-positive bacteria and against Gram-negative bacteria.

Toxicological Studies

The applicant refers to the reference product for this generic procedure, MARBOCYL 2 %, oplossing voor injectie voor niet-herkauwend kalf en big, REG NL 9169, from which the SPC warnings have been derived. These are supplemented using increased knowledge and the current state of science.

User Safety

The applicant refers to the reference product for this generic procedure, MARBOCYL 2 %, oplossing voor injectie voor niet-herkauwend kalf en big, REG NL 9169 authorised in the Netherlands.

Additionally the applicant has provided a brief user safety assessment. Combined with increased knowledge and the current state of science, warnings and precautions are added to the product literature ensuring safety to users of Marbosol 20 mg/ml solution for injection for calves and piglets.

Environmental Risk Assessment

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

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because Marbosol 20 mg/ml solution for injection for calves and piglets is considered to be identical to their reference products, respectively Marbocyl 2% oplossing voor injectie voor niet-herkauwend kalf en big, REG NL 9169 (translated: Marbocyl 2% solution for injection for non-ruminating calves and piglets. Therefore, the withdrawal periods as established for Marbocyl 2% can be adopted for Marbosol 20 mg/ml solution for injection for calves and piglets.

MRLs

Active substance marbofloxacin is listed in Table 1 of Council Regulation 37/2010

The marker substance is Marbofloxacin.

MRLs (in µg/kg) are listed below:

	Bovine	Porcine
Muscle	150	150
Liver	150	150
Kidney	150	150
Fat / skin	50	50
Milk	75	

Withdrawal Periods

Based on the data provided above, a withdrawal period of 6 days for meat in non-ruminating calves and 3 days for meat in piglets is justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with the reference product, Marbocyl 2% oplossing voor injectie voor niet-herkauwend kalf en big, REG NL 9169, has been accepted based on exemption a) and d) of section 7.1 of the CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products, EMA/CVMP/016/00-Rev.-2, efficacy studies are not required. The efficacy claims for this product are essentially equivalent to those of the reference product.

Tolerance in the Target Species of Animals

The applicant refers to the reference product for this generic procedure.

Additionally, based on increased knowledge and the current state of science, warnings and precautions are added to the product literature ensuring safety to the target animals.

Resistance

Adequate warnings and precautions appear on the product literature.

V . OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when Marbosol 20 mg/ml solution for injection for calves and piglets 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 Marbosol 20 mg/ml solution for injection for calves and piglets is acceptable for humans and the environment.

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 Medicinal 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.

18 April 2017

RMS change from NL/V/0168/001-002/DC and withdrawal of CMS: AT, BE, DK, FR, IE, IT, NL, PT, UK

Quality changes

Summary of change **(Application number)**	**Section updated in Module 3**	**Approval date**
B.II.f).1.b). 1 Extension of the shelf life of the finished product As packaged for sale (supported by real time data) (NL/V/0168/002/IB/001)	II.G	09/01/2015