IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Marbocare 20 mg/ml solution for injection for cattle and pigs

PRODUCT SUMMARY

EU Procedure Number	IE/V/0457/001 (formerly UK/V/0409/001)
Name, Strength, Pharmaceutical Form	Marbocare 20 mg/ml solution for injection for cattle and pigs
Active Substances(s)	Marbofloxacin
Applicant	Emdoka bvba John Lijsenstraat 16 B-2321 Hoogstraten Belgium
Legal Basis of Application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Target Species	Cattle, Pigs
Indication For Use	In cattle: Treatment of respiratory infections caused by sensitive strains of Pasteurella multocida, Mannheimia haemolytica, Histophilus somni and Mycoplasma bovis Treatment of acute mastitis caused by E.coli strains sensitive to marbofloxacin during the lactation period. In pigs: Treatment of Metritis Mastitis Agalactia syndrome (postpartum dysgalactiae syndrome, PDS) caused by susceptible strains of organisms.
ATC Code	QJ01MA93
Date of completion of the original decentralised procedure	26 September 2012 (UK) 11 January 2013 (IE)
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	Austria, Belgium, France, Germany, Ireland (now RMS), Luxmebourg, The Netherlands, Portugal, Spain UK added via change of RMS

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the 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 Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. 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

These were applications for generic products submitted in accordance with Article 13 (1) of Directive 2001/82/EC as amended. Bioequivalence was claimed with Marbocyl 20 mg/ml Solution for Injection, Marbocyl 10% Solution for Injection and also a global marketing authorisation for Marbocyl 10% Solution for Injection for Cattle, 100 mg/ml. The reference products were first authorised in the UK in 1998, 1997 and 2007 respectively.

The indication in cattle is for the treatment of respiratory infections caused by susceptible strains of *Pasteurella multocida, Mannheimia haemolytica* and *Histophilus somni*. The product may also be used to treat acute *Escherichia coli* induced mastitis. In pigs, the product may be used to treat mastitis agalactia syndrome caused by susceptible strains of relevant organisms. The dose rate is 2 mg/kg bw/day, equivalent to 1 ml/50 kg in a single daily injection via the intramuscular, subcutaneous or intravenous routes for 3-5 days in cattle and via the intramuscular route in pigs. A single dose of 8 mg/kg bw, equivalent to 2 ml/25kg may alternatively be administered via intramuscular injection when treating respiratory infections in cattle.

The products are 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 products can be safely used in the target species the slight reactions observed are indicated in the SPC. The products are 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 products was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting marketing authorisations.

II. QUALITY ASPECTS

A. Composition
The products contain marbofloxacin and the excipients metacresol, monothioglycerol and disodiumedetate.

The container/closure system consists of Type II amber glass vials of 10, 20, 50, 100 and 250 ml. Vials are closed with bromobutyl rubber stoppers and sealed with an aluminium cap. Vials are packed individually in boxes. The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the formulation and the presence of preservative are justified.

The products are of established pharmaceutical form and development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product
The products are manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. Process validation data on the products have been presented in accordance with the relevant European guidelines. Sequential addition of components is followed by dissolution and filtration. The products are then filled into vials and sealed.

C. Control of Starting Materials
The active substance is marfloxacin, an established active substance described in the European Pharmacopoeia. Substance specification was provided. 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. All excipients are monographed in the Ph. Eur.

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 these products.

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. 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. Tests include those for appearance, volume, pH, relative density, identification, marbofloxacin related substances and sterility.

G. Stability
Stability data on the active substance were provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. The active substance must be protected from light, as it is not stable in sunlight. Various data which covered storage of the product over a variety of time points and at a

variety of temperatures confirmed a retest period of two years. Suitable data for stability tests performed on the finished product were also provided.

H. Genetically Modified Organisms
Not applicable.

J. Other Information
Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging (20, 50, 100, 250 ml vials): 28 days. The 10mL vials must be used immediately after the first opening.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is was generic application according to Article 13, and bioequivalence with a reference product was successfully claimed, results of pharmacological and toxicological tests are not required.
Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

III.A Safety Testing
User Safety
The applicant did not provide a user safety assessment as the proposed product is identical to the reference product. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

- People with known hypersensitivity to (fluoro)quinolones should avoid any contact with the product.
- If the product comes into contact with the skin or eyes, rinse with large amounts of water.
- Avoid accidental self-injection, since this can cause local irritation.
- Wash hands after use.
- In case of accidental self-injection or ingestion, seek medical advice immediately and show package leaflet or the label to the physician.

Ecotoxicity
The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required. The products are antibiotics, therefore assessment was not permitted to end until PEC_{soil} values were calculated. PEC_{soil} was calculated for all types of cattle and pigs that might be treated with the product, using equations stipulated in the relevant guidelines. Calculations were performed for both products, and it was concluded that PEC_{soil} (1) values were below the trigger value of 100 µg/kg. 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
No data were provided in this section as bioequivalence was claimed with the reference product.

Withdrawal Periods
Based on the data provided above, withdrawal periods are as follows:-
Cattle 2 mg/kg for 3 -5 days (IV/IM/SM) Meat and offal, 6 days, milk 36 hours.
Cattle 8 mg/kg single occasion (IM) Meat and offal 3 days, milk 72 hours.
Pigs Meat and Offal 4 days.

(1) PEC – Predicted Environmental Concentration.

IV. CLINICAL ASSESSMENT

For generics, insert in the relevant sections as appropriate:

As this is a generic application according to Article 13, and bioequivalence with a reference product was successfully claimed, efficacy studies were not required. The efficacy claims for this product are equivalent to those of the various reference products.

IV.A Pre-Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product was successfully claimed, efficacy studies were not required. The efficacy claims for this product are equivalent to those of the various reference products.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product was successfully claimed, efficacy studies were not required. The efficacy claims for this product are equivalent to those of the various reference products.

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.