IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Marfloxin 100 mg/ml solution for injection

PRODUCT SUMMARY

EU Procedure number	IE/V/0262/002/DC
Name, strength and pharmaceutical form	Marfloxin 100 mg/ml solution for injection
Active substance(s)	Marbofloxacin
Applicant	Krka, d.d., Novo mesto, Smarjeska cesta 6, 8501 Novo mesto, Slovenia.
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of procedure	23/03/2011
Target species	Cattle and pigs
Indication for use	In cattle: - treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica* and *Histophilus somni*. - treatment of acute *E.coli* mastitis. In pigs: - treatment of Metritis Mastitis Agalactia (MMA) syndrome caused by susceptible strains of organisms.
ATCvet code	QJ01MA93
Concerned Member States	BG, PL, RO, SI

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

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

II QUALITY ASPECTS

A. Qualitative and Quantitative Particulars

The product contains 100 mg/ml marbofloxacin as the active substance and the following excipients: gluconolactone, disodium edetate, metacresol, monothioglycerol and water for injections.

The product is packaged in 50 ml 100 ml or 250 ml amber glass vials (Ph. Eur. type II) which are sealed with bromobutyl rubber stoppers and aluminium closures.

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 fully in accordance with the principles of good manufacturing practice at 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 specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

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.

D. Control on Intermediate Products

Not applicable.

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 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.

F. 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 throughout its shelf life when stored under the approved conditions.

G. Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13.1, and acceptable justification for the omission of bioavailability studies to demonstrate bioequivalence with the reference products Marbocyl 10% Solution for Injection and Marbocyl Solo 10% Solution for Injection (Vetoquinol Ireland Ltd) has been provided, bioequivalence with the reference products can be accepted. The results of safety and residue tests or of pre-clinical and clinical trials are therefore not required.

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

Warnings and precautions as listed on the product literature are in line with 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

The test product has been formulated to include the same active substance and same excipients in the same concentrations as the reference products. It can be accepted that the product is essentially similar to the reference products (Marbocyl 10% Solution for Injection and Marbocyl Solo 10% Solution for Injection) in terms of the quantitative composition of both the active substance and excipients and that exemption from the requirement for in vivo bioequivalence data is justified.

Toxicological Studies

No data provided given that bioequivalence with the reference products can be accepted.

Microbiological Studies

Given the essential similarity with the reference products, Marfloxin 100 mg/ml is expected to demonstrate the same antimicrobial effect as the reference products against the target bacterial pathogens.

Excipients are commonly used in injectable veterinary pharmaceuticals.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the same risk management measures for the reference product are applicable for Marfloxin 100 mg/ml solution for injection. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product and are in line with those agreed for other injectable fluoroquinolone containing products recently authorised through European procedures.

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. The assessment determined that all PECsoil values fall below the trigger value of 100 µg/Kg. No additional warnings regarding the environment are therefore 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

No residue depletion studies were conducted because the formulation of the product is considered to be sufficiently similar to that of the reference products to be considered equivalent and bioequivalence with the reference products can be accepted.

MRLs

Marbofloxacin is listed in Table 1 of Council Regulation (EU) No 37/2010. The marker substance is Marbofloxacin.

MRLs are listed below:

	BOVINE	PORCINE
Muscle	150 µg/kg	150 µg/kg
Liver	150 µg/kg	150 µg/kg
Kidney	150 µg/kg	150 µg/kg
Fat / skin	50 µg/kg	50 µg/kg
Milk	75 µg/kg	N/A

Withdrawal Periods

Based on the withdrawal periods of the reference product in the RMS, the following withdrawal periods are justified:

Cattle:

2 mg/kg for 3 to 5 days (IV/IM/SC)
Meat and offal: 4 days.
Milk: 24 hours.

8 mg/kg on a single occasion (IM)
Meat and offal: 3 days.
Milk: 72 hours.

Pigs:

Meat and offal: 2 days.

IV CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13.1, and acceptable justification for the omission of bioavailability studies to demonstrate bioequivalence with the reference products has been provided, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference products.

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

No studies were conducted given that the product is essentially similar to the reference products. The same information in respect of expected adverse reactions as appears in the SPC of the reference products is included in the SPC of Marfloxin 100 mg/ml.

Resistance

Adequate warnings and precautions appear on the product literature. The SPC includes MIC data for the target pathogens.

IV.B Clinical Studies

Field Trials

No field trials have been conducted given that the product is accepted as being essentially similar to the 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.

VI 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 HPRA website.

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.