ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
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(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Quiflor Multi 100 mg/ml Solution for Injection for Cattle and Pigs (Sows)

UK/V/0361/001/DC

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0361/001/DC
Name, strength and pharmaceutical form	Quiflor Multi 100 mg/ml Solution for Injection for Cattle and Pigs (Sows)
Applicant	Krka, d.d., Novo mesto Šmarješka cesta 6 8501 Novo mesto Slovenia
Active substance	Marbofloxacin
ATC Vetcode	QJ01MA93
Target species	Cattle, Pigs
Indication for use	**Cattle** Treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica*, *Mycoplasma bovis* and *Histophilus somni.* Treatment of acute mastitis caused by *Escherichia coli* strains sensitive to marbofloxacin during the lactation period. **Sows** Treatment of Metritis Mastitis Agalactia Syndrome caused by bacterial strains sensitive to marbofloxacin.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	23rd March 2011.
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Austria, Belgium, Denmark, France, Germany, Greece, Ireland, Italy, The Netherlands, Portugal, Spain

I. SCIENTIFIC OVERVIEW

Originally, this report was compiled for Ubiflox 20 mg/ml Solution for Injection for Cattle and Pigs, and Ubiflox 100 mg/ml Solution for injection for Cattle and Pigs (Sows). The 20 mg product was expired, and the 100 mg product had a name change to Quiflor Multi 100 mg/ml Solution for Injection for Cattle and Pigs (Sows). The reference products were Marbocyl 2% Solution for Injection, Marbocyl 10% Solution for Injection and Marbocyl Solo 10% Solution for Injection, authorised in the UK since 1998,1997and 2007 respectively. Bioequivalence was claimed in accordance with exemption 4.b of the Guidelines for the Conduct of Bioequivalence Studies for Veterinary Products.

For Quiflor Multi mg/ml Solution for Injection for Cattle and Pigs (Sows), the indication in cattle is for the treatment of respiratory infections caused by sensitive strains of *Pasteurella multocida*, *Mannheimia haemolytica* and *Mycoplasma bovis*, and the treatment of acute mastitis caused by *Escherichia coli* strains sensitive to marbofloxacin during the lactation period. The second indication is for pigs, for the treatment of Metritis Mastitis Agalactia Syndrome caused by bacterial strains sensitive to marbofloxacin in pigs (sows), given intramuscularly over 3 days. Refer to the Summary of product Characteristics (SPC) for dosage information.

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 SPCs. The efficacy of the product was demonstrated according to the claims

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

II. QUALITY ASPECTS

A. Composition

The product contains marbofloxacin and excipients gluconolactone, disodium edetate, metacresol, monothioglycerol and water for injections and mannitol.

The containers are amber glass bottles with bromobutyl stoppers and aluminium closures, in 50, 100 ml or 250 ml presentations. The particulars of the containers and controls performed are provided and conform to the regulation. The presence of preservative is justified.

The product is an established pharmaceutical form and their development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

The ingredients are added to water and mixed. Water is added to make up the final volume, and the products are filtered before being filled into the glass bottles.

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. Process validation data on three batches of 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. All excipients are described in the European Pharmacopoeia or USP/NF[1].

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 the product.

[1] USP/NF – United States Formulary/National Formulary.

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.

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.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf-life of the veterinary medicinal products as packaged for sale: 3 years.
Shelf-life after the first opening of the immediate packaging: 28 days.
Store in the original package in order to protect from light. Do not freeze.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this was a generic application according to Article 13 (1), and bioequivalence with reference products has been demonstrated, results of pharmacological, toxicological, user safety and residues tests were not required. These aspects of the product are identical to the reference products.

The user warnings are as follows:

- People with known hypersensitivity to (fluoro)quinolones should avoid contact with the veterinary medicinal product.
- Avoid contact of the skin and eyes with the product. In case of accidental spillage onto skin or eyes, rinse the affected area with large amounts of water.
- Avoid accidental self-injection, since this can cause local irritation. In case of self-injection or ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

- Wash hands after use.

III.A Safety Testing

Ecotoxicity

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 concluded that animals will be treated in housing, with marbofloxacin reaching the environment as manure when spread onto land. A Phase 1 Risk Assessment provided PEC_{soil}[2] values which were below the action limit of 100 µg/kg. The amount of exposure will therefore be minimal. 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 product was accepted as being identical to the reference products

MRLs

MRLs are listed below:

	Bovine (µg/kg)	Porcine (µg/kg)
Muscle	150	150
Liver	150	150
Kidney	150	150
Fat and/or skin	50	50
Milk	75	-

Withdrawal Periods

Based on the data provided above, withdrawal periods as described below are justified:-

Quiflor Multi mg/ml Solution for Injection for Cattle and Pigs (Sows)

Cattle:

8 mg/kg single dose

Meat and offal: 3 days

Milk: 72 hours

[2] PEC_{soil} – Prediction of concentration of product in the uppermost 5 cm soil layer.

2 mg/kg single daily injection, for 3 to 5 days:

Meat and offal: 6 days

Milk: 36 hours

Pigs (sows):

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 the 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), and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for the product are equivalent to those of the reference products.

Tolerance in the Target Species of Animals

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 the product are equivalent to those of the reference products.

Resistance

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 these products are equivalent to those of the reference products.

IV.B Clinical Studies

Laboratory Trials

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 the product are equivalent to those of the reference products.

Field Trials

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 the product are equivalent to those of 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.

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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