IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Enroxil Max 100 mg/ml solution for injection for cattle

PRODUCT SUMMARY

EU Procedure Number	IE/V/0424/001
Name, Strength, Pharmaceutical Form	Enroxil Max 100 mg/ml solution for injection for cattle
Active Substances(s)	Enrofloxacin
Applicant	KRKA, d.d., Novo mesto Šmarješka cesta 6, 8501 Novo mesto Slovenia
Legal Basis of Application	Mutual recognition application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Target Species	Cattle
Indication For Use	Treatment of bovinem respiratory disease associated with *Mannheimiahaemolytica, Pasteurella multocida, Histophilus somni and Mycoplasmaspp. where clinicalexperience,supportedwherepossible bysensitivitytesting of thecausalorganism,indicates enrofloxacin as the drug of choice.*
ATC Code	QJ01MA90
Date of completion of the original mutual recognition procedure	2 July 2008
Date product first authorised in the Reference Member State (MRP only)	1 August 2007 (UK) 19 September 2008 (IE)
Concerned Member States for original procedure	Austria, Czech Republic, Germany, Hungary, Ireland (now RMS), Italy, Latvia, Lithuania, Poland, Portugal, Romania, Slovak Republic, Slovenia, Added as CMS via RMS change: United Kingdom

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

Enroxil Max 100 mg/ml Solution for injection contains enrofloxacin 100 mg/ml for use as treatment of bovine respiratory disease associated with *Mannheimia haemolytica*, *Pasteurella multocida,Haemophilus somnus* and *Mycoplasma* spp, where clinical experience, supported where possible by sensitivity testing of the causal organism, indicates enrofloxacin as the drug of choice.
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 possible reactions 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 the active substance enrofloxacin and excipients benzyl alcohol, n-butyl alcohol, L-Arginine and water for injection.

The product is packed in clear, amber Type II glass vials of capacity 100 ml. Vials are sufficiently transparent to permit a test for visible particles to be included in the finished product specification. Vials are closed with grey bromobutyl rubber closures secured with aluminium collars. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and presence of preservative are justified. Since the product is a multi-dose aqueous injection solution, n-butyl alcohol and benzyl alcohol are included as antimicrobial preservatives. The purpose of each ingredient is explained.

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 from a licensed manufacturing site. The manufacturing formula, method of manufacture (description and flow diagram) and in-process controls are considered appropriately described.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance enrofloxacin is an established active substance and supporting data have been provided in the form of a European Drug Master File (EDMF). It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitably justified.

The requirements of the monographs of the European Pharmacopoeia are applied in the raw material specifications for benzyl alcohol, arginine and water for injections. In the absence of a monograph in the European Pharmacopoeia or the pharmacopoeia of a member state, the requirements of the monograph in the United States Pharmacopoeia National Formulary are applied in the raw material specification for n-butyl alcohol. For benzyl alcohol, arginine and n-butyl alcohol, the pharmacopoeial requirements are supplemented by adequate additional tests.

The vials used in the manufacture of the product must comply with the requirements of the applicant's specification and must meet the requirements of the European Pharmacopoeia for Type II glass containers, using results from the supplier supplemented with suitable checks conducted in house.

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

There are no intermediate products.

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 throughout its shelf life when stored under the approved conditions.

In-use stability testing has been carried out adequately to justify a 28 day in-use shelf life.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf life

Shelf-life of the veterinary medicinal product as package for sale: 5 years

Shelf-life after first opening the immediate packaging: 28 days

Special precautions for storage

Keep the container in the outer carton in order to protect from light.

Do not freeze.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13 of Directive 2001/82/EC as amended by 2004/28/EC and the applicant had justified the exemption from submitting bioequivalence study under Article 13(2)(b) of the Directive hence results of pharmacological tests are not required.

The pharmacological aspects of this product are identical to the reference product.

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.

Toxicological Studies

As this is a generic application according to Article 13 of Directive 2001/82/EC as amended by 2004/28/EC and the applicant had justified the exemption from submitting bioequivalence study under Article 13(2)(b) of the Directive hence results of toxicological tests are not required.

The toxicological aspects of this product are identical to the reference product.

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.

User Safety

As this is a generic application according to Article 13 of Directive 2001/82/EC as amended by 2004/28/EC and the applicant had justified the exemption from submitting bioequivalence study under Article 13(2)(b) of the Directive hence it is not required to provide a user risk assessment.

Warnings and precautions as listed on the product literature (see the warnings in the box below) are adequate to ensure safety to users of the product and are identical to the reference product.

This product is an alkaline solution. Any spillage onto the skin should be washed off immediately with water. In the event of accidental splash into the eye, rinse with copious amounts of clean water. If irritation occurs, seek medical advice. Do not eat, drink or smoke whilst using the product. Care should be taken to avoid accidental self-injection. In case of accidental self injection, seek medical advice immediately and show the package leaflet or the label to the physician. People with known hypersensitivity to fluoroquinolones should avoid contact with the veterinary medicinal product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was 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 of Directive 2001/82/EC as amended by 2004/28/EC and the applicant had justified the exemption from submitting bioequivalence study under Article 13(2)(b) of the Directive hence results of residues studies are not required.

The residues aspects of this product are identical to the reference product. 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 consumers.

MRLs

Enrofloxacin is listed in Annex I of Council Regulation 2377/90. The marker substances are the sum of enrofloxacin and ciprofloxacin.
MRLs are listed below:

	Bovine, Ovine, Caprine
Muscle	100 µg/kg
Liver	300 µg/kg
Kidney	200 µg/kg
Fat	100 µg/kg
Milk	100 µg/kg

All the excipients are included in Annex II of Regulation 2377/90, with the exception of Water for Injection, which is out of scope of that Regulation.

Withdrawal Periods

Based on the information provided, a withdrawal period of 14 days for meat and offal in cattle and 84 hours for milk are justified.

IV. CLINICAL ASSESSMENT

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13 of Directive 2001/82/EC as amended by 2004/28/EC and the applicant had justified the exemption from submitting bioequivalence study under Article 13(2)(b) of the Directive hence results of pharmacological tests are not required.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13 of Directive 2001/82/EC as amended by 2004/28/EC and the applicant had justified the exemption from submitting bioequivalence study under Article 13(2)(b) of the Directive hence results of target species tolerance studies are not required.

Resistance

As this is a generic application according to Article 13 of Directive 2001/82/EC as amended by 2004/28/EC and the applicant had justified the exemption from submitting bioequivalence study under Article 13(2)(b) of the Directive hence results of resistance studies are not required.

IV.B Clinical Studies

As this is a generic application according to Article 13 of Directive 2001/82/EC as amended by 2004/28/EC and the applicant had justified the exemption from submitting bioequivalence study under Article 13(2)(b) of the Directive hence results of clinical studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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.