IPAR

KARIFLOX 25 mg/ml oral solution for calves [IE,ES,FR,NL]

ENRO-K 25 mg/ml oral solution for calves [DE]

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

1 PRODUCT SUMMARY

EU Procedure number	IE/V/0217/002/DC
Name, strength and pharmaceutical form	KARIFLOX 25 mg/ml oral solution for calves [IE,ES,FR,NL] ENRO-K 25 mg/ml oral solution for calves [DE]
Applicant	Laboratories Karizoo, S. A. Mas Pujades, 11-12 Pol. Ind. La Borda 08140 Caldes de Montbui Spain
Active substance(s)	Enrofloxacin
ATCvet code	QJ01MA90
Target species	Calves
Indication for use	- treatment of respiratory infections due to *Pasteurella multocida* and *Manheimia haemolytica.* - treatment of gastro-intestinal infection due to *Escherichia coli*.

2 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	Day 210 : 23rd March 2009
Date product first authorised in the Reference Member State (MRP only)	NA
Concerned Member States for original procedure	ES, FR, DE, NL

2.1 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 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.

2.2 II Quality Aspects

A. Composition

The product contains Enrofloxacin 25 mg/ml and the excipients benzyl alcohol, hypromellose, potassium hydroxide and purified water. The product is packaged in 250 ml, 500 ml and 1 litre white HDPE containers with white HDPE screw cap with induction disc. A graduated polypropylene measuring device with a capacity of 20 ml is provided with all containers.

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 an established active substance which is not described in the European/British Veterinary 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.

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.
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.

H. Genetically Modified Organisms

J. Other Information
Not applicable.

2.3 III Safety and residues assessment (pharmaco-toxicological)

III.A Safety Testing

Pharmacological Studies

2.1. Pharmacodynamics
The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application and therefore data on pharmacodynamics are not required.
The information proposed for inclusion in section 5.1 of the SPC for the test product reflects the text approved for section 5.1 of the SPC for the reference product in the RMS. The reference product is Baytril 2.5% Oral Solution (VPA 10021/21/1, Bayer Ltd).

2.2. Pharmacokinetics
The applicant claims exemption from bioequivalence studies in accordance with paragraph 4(e) of the Guideline for Conduct of Bioequivalence Studies (EMEA/CVMP/016) because:

- the product is an oral solution
- it contains an active substance or therapeutic moiety in the same concentration as a product approved for use in the target species that is the subject of the new application
- it contains no inactive substance that can significantly affect the absorption of the active substance or therapeutic moiety.

Given that the criteria as detailed in paragraph 4(e) of the Guideline for Conduct of Bioequivalence Studies (EMEA/CVMP/016) have been satisfied, it is accepted that the test product can be considered bioequivalent to the reference product, Baytril 2.5% Oral Solution, without the need for specific bioequivalence studies.
The information proposed for inclusion in section 5.2 of the SPC for the test product reflects the text approved for section 5.2 of the SPC for the reference product, Baytril 2.5% Oral Solution (VPA 10021/21/1), in the RMS.

Toxicological Studies
The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application.

Based on information provided in support of this application it is accepted that the test product is bioequivalent to the reference product (Baytril 2.5% Oral Solution). Consequently, specific toxicological data relating to the active substance are not presented.
Note that the safety of the final formulation in the target animal is commented on in Part IV of this report.

User Safety
The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. As such, it can be assumed that the risk to the user arising from the active substance is not going to be any greater for the test product, compared to the reference product.
The excipients are widely used in veterinary medicinal products.
Warnings and precautions as listed on the product literature are similar to those on the reference product and are adequate to ensure safety to users of the product.
Ecotoxicity
An Environmental Risk Assessment for the product in line with the guideline on the environmental impact assessment for veterinary medicinal products- Phase II (CVMP/VICH/ 790/03- Final) was provided. Based on the information provided, it can be concluded that the use of the product as recommended does not constitute a risk for the environment.

III.B Residues documentation
Exemption from bioequivalence studies (in accordance with paragraph 4(e) of the Guideline for Conduct of Bioequivalence Studies (EMEA/CVMP/016)) is accepted because the product is an oral solution containing an active substance in the same concentration as a product approved for use in the same target species, and it contains no inactive substance that can significantly affect the absorption of the active substance.
As the test product is bioequivalent to Baytril 2.5% Oral Solution, it is accepted that the safety profile will be similar to that of the reference product. In addition, it is accepted that there will be no difference between products with respect to depletion of residues of enrofloxacin. Further, it is noted that the excipients in the formulation are listed in Annex II of Council Regulation 2377/90 or are generally regarded as safe.
The proposed withdrawal period for the test product for bovine meat and offal (11 days) is in line with the withdrawal period authorised for the reference product in a number of CMS and is considered adequate.

2.4 IV Clinical Assessment

IV.A Pre-Clinical Studies

Pharmacology
See Part IIIA

Tolerance in the Target Species of Animals
A target animal safety study specific to the test product has not been presented
with the application. Given that:

- the product is an oral dose form,
- bioequivalence with an authorised reference product is claimed,
- the toxicological profile of the active substance is well known, and
- the excipients are recognised as being safe,

the absence of tolerance studies specific to the test product can be accepted.

Resistance
The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. As such, the resistance profile is expected to be the same as for the reference product.

The warnings and precautions that appear on the product literature are in line with the prudent use statements recommended by CVMP for fluoroquinolones containing products intended for food animals (see **EMEA/CVMP/416168/06**).

IV.B Clinical Studies

Exemption from bioequivalence studies (in accordance with paragraph 4(e) of the Guideline for Conduct of Bioequivalence Studies (EMEA/CVMP/016)) is accepted because the product is an oral solution containing an active substance in the same concentration as a product approved for use in the same target species, and it contains no inactive substance that can significantly affect the absorption of the active substance.

As the test product is accepted to be bioequivalent to Baytril 2.5% Oral Solution, it is accepted that the efficacy profile will be similar to that of the reference product.

The proposed SPC text reflects the authorised SPC of the reference product.

2.5 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.

2.6 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.

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.

None.