IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

Quinoflox 100 mg/ml solution for injection for cattle and pigs

PRODUCT SUMMARY

EU Procedure number	IE/V/0290/001/DC
Name, strength and pharmaceutical form	Quinoflox 100 mg/ml solution for injection for cattle and pigs
Active substance(s)	Enrofloxacin
Applicant	GLOBAL VET HEALTH SL c/Capcanes nº12-bajos. Polígon Agro-Reus. REUS (43206) Spain
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of procedure	26th September 2012
Target species	Cattle and pigs
Indication for use	**Cattle** Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida, Mannheimia haemolytica* and *Mycoplasma* spp. Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*. Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*. Treatment of acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of *Mycoplasma bovis* in cattle less than 2 years old. **Pigs** Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida, Mycoplasma* spp. and *Actinobacillus pleuropneumoniae.* Treatment of infections of the urinary tract caused by enrofloxacin susceptible strains of *Escherichia coli.* Treatment of post-partum dysgalactiae syndrome, PDS (MMA syndrome) caused by enrofloxacin susceptible strains of *Escherichia coli* and *Klebsiella* spp. Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*. Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*.
ATCvet code	QJ01MA90
Concerned Member States	BG, PL, PT, RO, UK

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 the active substance enrofloxacin (100 mg/ml) and the excipients benzyl alcohol, lactic acid, disodium edetate and water for injections.

The container/closure system consists of amber polypropylene vials of 50 ml, 100 ml and 250 ml with rubber butyl stoppers.

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 enrofloxacin an established 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.

The in-use shelf-life is supported by the data provided.

G. Other Information

Not applicable.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13(1), and bioequivalence with a reference product has been demonstrated, results of pharmacological tests are not required.

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

A bioequivalence study was conducted demonstrating that this product was bioequivalent to the reference product, Baytril 10% Solution for Injection when administered by the subcutaneous route to cattle at a dose of 2.5 mg enrofloxacin/kg bodyweight.

Similarly, a bioequivalence study was conducted demonstrating that this product was bioequivalent to the reference product, Baytril 10% Solution for Injection when administered by the intramuscular route to pigs at a dose of 2.5 mg enrofloxacin/kg bodyweight

Toxicological Studies

As this is a generic application according to Article 13(1), and bioequivalence with a reference product has been demonstrated, results of toxicological tests are not required.

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

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product and reflect those of similar products recently considered in the context of European procedures.

Environmental Risk Assessment

The Applicant has conducted a detailed ERA for the product Quinoflox 100 mg/ml solution for injection. Based on the data provided, it is accepted that this product is unlikely to constitute a risk to the environment when used in accordance with the recommended posology.

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

Residue depletion studies at the injection site of the product using the final formulation have also been conducted in cattle and pigs. Samples of injection site were taken from animals at several time points. Results show that residues depleted to below the MRL at the injection site before the end of the withdrawal period.

The analytical method was a fully validated HPLC (high performance liquid chromatography) with fluorescence detection.

No residue depletion studies were conducted in milk because bioequivalence between the product and Baytril 10% Solution for Injection was demonstrated and it is expected that the rate of depletion of residues will be the same.

MRLs

Enrofloxacin is listed in Table 1 of the Annex of Council Regulation 37/2010. The marker substance for enrofloxacin is the sum of enrofloxacin and ciprofloxacin.

MRLs are listed below:

	BOVINE	**PORCINE**
Muscle	100 µg/kg	100 µg/kg
Liver	300 µg/kg	200 µg/kg
Kidney	200 µg/kg	300 µg/kg
Fat / skin	100 µg/kg	100 µg/kg
Milk	100 µg/kg	Not applicable.

Withdrawal Periods

Based on the available information, a withdrawal period of 5 days for meat in cattle and 72 hours for milk following intravenous use are justified. When the product is administered by subcutaneous injection a withdrawal period of 12 days for meat in cattle and 96 hours for milk are justified.In the case of pigs, a withdrawal period of 13 days for meat are justified.

IV CLINICAL ASSESSMENT (EFFICACY)

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 this product are equivalent to those of the reference product.

Tolerance in the Target Species of Animals

The applicant has conducted two target animal tolerance studies using the recommended dose in the target species. The authorised reference product, Baytril 10% Solution of Injection, containing the same active substance was used as a control. For cattle a dose of 2.5 mg/kg bodyweight was administered by the subcutaneous route for 5 days as recommended. For pigs a dose of 2.5 mg/kg bodyweight was administered by the intramuscular route for 3 days as recommended.

Parameters evaluated were clinical observation, including injection site assessment.

In the studies conducted, the test product was well tolerated. Local reactions characterised by pain at the time of administration and swelling (skin thickening) following administration were observed in cattle. In the pig study, reactions at the injection site were not evident clinically in any animal following administration of the test or reference products at the recommended dose. There was no difference between the test and reference products in terms of local tolerance in the studies conducted.

The product literature accurately reflects the type and incidence of adverse effects which might be expected.

IV.B Clinical Studies

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 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 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.

Safety/Efficacy Changes

Summary of change (Application number)	**Approval date**
Change in the Summary of Product Characteristics, labelling and package leaflet intended to implement the outcome of a Union referral procedure concerning: in the framework of Article 35 of Directive 2001/82/EC of the European Parliament and of the Council, the marketing authorisations for "Baytril 2.5% injectable, Baytril 5% injectable, Baytril 10% injectable and associated names", and related veterinary medicinal products, which contain the active substance "Enrofloxacin" (Decision number: C (2014) 6268 Final). (IE/V/0290/001/IA/001)	dd/mmmm/yyyy