Bundesamt für
Verbraucherschutz und
Lebensmittelsicherheit

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)
Federal Office of Consumer Protection and Food Safety
Mauerstraße 39-42
10117 Berlin
(Germany)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Powerflox 50 mg/ml solution for injection for cattle, pigs, dogs and cats

Date: 30.01.2018

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0183/001
Name, strength and pharmaceutical form	Powerflox 50 mg/ml solution for injection for cattle, pigs, dogs and cats
Applicant	Virbac 1ére Avenue 2065M L.I.D. F-06516 CARROS France
Active substance(s)	Enrofloxacin
ATC Vetcode	QJ01MA90
Target species	Cattle, pigs, dogs and cats
Indication for use	Cattle: Treatment of respiratory and alimentary tract diseases of bacterial or mycoplasmal origin (pasteurellosis, mycoplasmosis, coli-bacillosis and coli-septicaemia) and secondary bacterial infections subsequent to viral conditions (e.g. viral pneumonia). Pigs: Treatment of respiratory and alimentary tract diseases of bacterial or mycoplasmal origin (pasteurellosis, mycoplasmosis, coli-bacillosis and coli-septicaemia) and multifactorial diseases such as enzootic pneumonia. Dogs and cats: Treatment of bacterial diseases of the respiratory (Pasteurella spp., Haemophilus spp.), alimentary (E.coli., Salmonella spp.) and urogenital tracts (E. coli), skin and secondary wound infections (Staphylococcus spp.).

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicinal Agencies website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	22 July 2009
Date product first authorised in the Reference Member State (MRP only)	n.a.
Concerned Member States for original procedure	Austria, Germany (RMS), Ireland, Netherlands, United Kingdom (previous RMS)

I. SCIENTIFIC OVERVIEW

Powerflox 50 mg/ml solution for injection for cattle, pigs, dogs and cats enrofloxacin contains the active substance enrofloxacin. The product is authorised to be used in cattle, pigs, dogs and cats. In cattle, the product is used in the treatment of respiratory and alimentary tract diseases of bacterial or mycoplasmal origin (pasteurellosis, mycoplasmosis, coli-bacillosis and coli-septicaemia) and secondary bacterial infections subsequent to viral conditions (e.g. viral pneumonia). In pigs, the product is used in the treatment of respiratory and alimentary tract diseases of bacterial or mycoplasmal origin (pasteurellosis, mycoplasmosis, coli-bacillosis and coli-septicaemia) and multifactorial diseases such as enzootic pneumonia. In dogs and cats, it is used in treatment of bacterial diseases of the respiratory (Pasteurella spp., Haemophilus spp.), alimentary (E.coli., Salmonella spp.) and urogenital tracts (E. coli), skin and secondary wound infections (Staphylococcus spp.).

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 and 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..

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The product contains enrofloxacin as active substance and n-butyl alcohol, potassium hydroxide and water for injection as excipients.

The product is packaged in an amber Type 1 glass vial with a grey bromobutyl rubber stopper and aluminium cap.

The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation is justified.

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.

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 an Active Substance Master File (ASMF). It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitably justified.

There are three excipients used in the formulation and each has been used previously in veterinary medicines. Potassium hydroxide and water for injections have monographs in the Ph. Eur. and each comply with the requirements of the current edition of the Ph. Eur. In the absence of a monograph in the European Pharmacopoeia, the requirements of the monograph in the United States Pharmacopoeia National Formulary are applied in the raw material specification for n-butyl alcohol.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

Scientific data has been provided which states that Powerflox 50 mg/ml Solution for Injection for cattle, pigs, dogs and cats complies with the combined CVMP/CPMP note for guidance on TSE risk (EMEA/410/01) and the CVMP position paper (EMEA/CVMP/121/01).

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. The satisfactory validation data for the analytical methods have been provided.

G. Stability

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. The shelf-life of the veterinary medicinal product as packaged for sale is 2 years. An in-use shelf life of 28 days is justified.

H. Genetically Modified Organisms

Not applicable

J. Other Information

Special Precautions for Storage:
Do not store above 25ºC.
Keep the vial in the outer carton in order to protect from light.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

Since the application is made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, on the basis of being a generic of a reference medicinal product, data on pharmacodynamics and pharmacokinetics are not required.

Toxicological Studies

Since the application is made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, on the basis of being a generic of a reference medicinal product, data on toxicology are not required.

Other Studies

Since the application is made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, on the basis of being a generic of a reference medicinal product, applicant has not submitted any data for this section.

User Safety

The following operator warnings are included in the SPC and product literature:

This product is an alkaline solution. Direct contact with the skin should be avoided because of sensitisation, contact dermatitis and possible hypersensitivity reactions. Wear gloves. Wash hands after use. Wash any splashes from skin and eyes immediately with water.

Do not eat, drink or smoke whilst using the product.

Care should be taken to avoid accidental self-injection. If accidental injection occurs, seek medical advice immediately.

Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline. In accordance with the Phase I decision tree, the treatment of cats and dogs does not result in extensive exposure of the environment. The assessment can end at Phase I for cats and dogs. Since the product is also indicated to be used in cattle and pigs, it was necessary to calculate PEC_{soil} values. PEC_{soil} values were calculated for all types of cattle and pigs raised intensively using the equations provided by the CVMP guideline. The default value of 50 % of animals treated for bacterial infections provided by the CVMP guideline was used. The dose and duration of treatment together with the PEC_{soil} values are shown in the following table:

Target animal	**Dose (mg/kg bodyweight)**	**Duration of treatment (days)**	**PEC_{soil} (µg/kg)**
Dairy cow	5	5	40.1
Calf			71.4

Target animal	Dose (mg/kg bodyweight)	Duration of treatment (days)	PEC_{soil} (µg/kg)
Cattle (0-1 year)			63.0
Cattle (>2 years)			72.9
Weaner pig	5	3	65.2
Fattening pig			44.2
Sow			15.7

The assessment ended at Phase I as all the PEC_{soil} values are below 100 µg/kg. The 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 the product has same pharmaceutical form and the same qualitative and quantitative composition as the reference product, it was not necessary to provide any data on bioequivalence in accordance with paragraph 4b of the CVMP guidelines for the conduct of bioequivalence studies for veterinary medicinal products (EMEA/CVMP/016/00-corr-FINAL).

MRLs

All the excipients are listed in Annex II of Regulation 2377/90, with the exception of Water for Injection.
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

Withdrawal Periods

Cattle: Meat and offal: 14 days
Pigs: Meat and offal: 10 days

Not permitted for use in lactating animals producing milk for human consumption.

IV. CLINICAL ASSESSMENT (EFFICACY)

Pharmacology

Since the application is made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, on the basis of being a generic of a reference medicinal product, data on pharmacodynamics and pharmacokinetics are not required.

Tolerance in the Target Species of Animals

As the product has same pharmaceutical form and the same qualitative and quantitative composition as the reference product, no new target species tolerance data have been presented. This complies with exemptions specified under Article 13 (2)(b) of Directive 2001/82/EC as amended by 2004/28/EC.

Resistance

Fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials. Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to potential cross-resistance.

IV.B Clinical Studies

Since the application is made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, on the basis of being a generic of a reference medicinal product, data on clinical efficacy are not required.

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.

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 Heads of Veterinary Medicinal Agencies website (www.hma.eu).

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.

•	13 April 2015	Deletion of a non-significant specification parmameter
•	13 April 2015	Submission of a new certificate of suitability
•	13 April 2015	Submission of a new certificate of suitability
•	30 January 2018	RMS transfer from UK to DE