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

Final

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Enrotron 25
Enrotron 50
Enrotron 100

Date: 24 September 2012

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/
Name, strength and pharmaceutical form	Enrotron 25 25 mg/ml Enrotron 50 50 mg/ml Enrotron 100 100 mg/ml
Applicant	aniMedica GmbH Im Südfeld 9, 48308 Senden-Bösensell Germany
Active substance(s)	Enrofloxacin
ATC Vetcode	
Target species	Dog, Cat, Pig, Rabbit, Rodents, Reptiles, Ornamental Birds; Cattle (Calves), Pig, Dog; Cattle, Pig
Indication for use	Dogs (25 mg/ml and 50 mg/ml): Treatment of infections of the alimentary, respiratory and urogenital tracts (including prostatitis, adjunctive antibiotic therapy for pyometra), skin and wound infections, otitis (externa/interna) caused by enrofloxacin susceptible strains of Staphylococcus spp., Escherichia coli, Pasteurella spp., Klebsiella spp., Bordetella spp., Pseudomonas spp. and Proteus spp. Cats (25 mg/ml and 50 mg/ml): Treatment of infections of the alimentary, respiratory and urogenital tracts (as adjunctive antibiotic therapy for pyometra), skin and wound infections, caused by enrofloxacin susceptible strains of, e. g.: Staphylococcus spp.,

	Escherichia coli, Pasteurella spp., Klebsiella spp., Bordetella spp., Pseudomonas spp. and Proteus spp. Rabbits (25 mg/ml): Treatment of infections of the alimentary and respiratory tracts, caused by enrofloxacin susceptible strains of Escherichia coli, Pasteurella multocida and Staphylococcus spp. Rodents, Reptiles, Ornamental Birds (25 mg/ml): Treatment of infections of the alimentary and respiratory tracts where clinical experience, if possible, supported by susceptibility testing of the causal organism, indicates enrofloxacin as the substance of choice. Calves (50 mg/ml): 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. Cattle (100 mg/ml): Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of Pasteurella multocida, Mannheimia haemolytica and Mycoplasma spp. Treatment of acute severe mastitis caused by enrofloxacin susceptible strains of Escherichia coli. 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 (25 mg/ml and 50 mg/ml): 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 alimentary tract caused by enrofloxacin susceptible strains of Escherichia coli. Treatment of septicaemia caused by enrofloxacin susceptible strains of Escherichia coli. Pigs (100 mg/ml): 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. Enrofloxacin should be used where clinical experience, supported where possible by

	susceptibility testing of the causal organism, indicates enrofloxacin as the drug of choice.

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 Mutual recognition procedure Decentralised procedure	25 July 2012
Date product first authorised in the Reference Member State (MRP only)	n.a.
Concerned Member States for original procedure	AT, SI

I. SCIENTIFIC OVERVIEW

The quality, safety and efficacy aspects of the products are identical to original product Baytril - Das Original 5% - Injektionslösung, authorised in Germany in 1989, marketing authorisation number: 13113.01.00. Reference is also made to Baytril - Das Original 2,5% - Injektionslösung and Baytril - Das Original 10% - Injektionslösung, authorised in Germany in 2005, marketing authorisation number: 400614.00.00 and 400721.00.00, respectively. The initial application for original product Baytril - Das Original 5% - Injektionslösung was assessed before there was a requirement to have a public assessment report, therefore no details in this section are available.

II. QUALITY ASPECTS

A. Composition

The product contains 25 mg enrofloxacin/ml solution and the following excipients: 1-butanol, potassium hydroxide, hydrochloric acid and water for injections.

The product is packed in clear glass bottles of type I, closed with teflonised rubber stoppers and secured with aluminium caps. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the presence of preservative are justified.

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.

Process validation data on the product have been presented in accordance with the relevant European guidelines. The product is manufactured using conventional manufacturing techniques. Process validation for full-scale batches will be performed post-authorisation.

C. Control of Starting Materials

The active substance is enrofloxacin, 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.

The suitability of the European Pharmacopoeia monograph has been assessed by the EDQM (European Directorate for the Quality of Medicines & HealthCare). A certificate of suitability has 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 sites 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.

The claim of 28 days stability after broaching is based on the demonstration of stability for a batch broached and stored 28 days at +25°C.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13.1 of Directive 2001/82/EC based on the essential similarity of the reference and the generic products, results of safety tests are not required.

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

The applicant has made full reference to the SPCs of the reference products. However, as this was not fully identical to the SPCs authorised for the products in other concerned member states, the wording of advices in some sections of the SPCs aiming at ensuring the safe use of the product were harmonised with recently authorized enrofloxacin containing veterinary medicinal products in the EU.

Warnings and precautions as listed in the product literature are adequate to ensure safety of the products to the user and the environment.

III.A Safety Testing

User Safety

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is 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

No residue depletion studies were conducted because the products Enrotron 25, 50 and 100 are essentially similar to the German reference products Baytril - Das Original - 2.5 % Solution for injection, Baytril - Das Original - 5% Solution for injection and Baytril - Das Original - 10% Solution for injection.

MRLs

Enrofloxacin is listed in Table 1 of Commission Regulation (EU) No 37/2010 with the following MRLs:

	Bovine, ovine, caprine	Porcine, rabbit	Poultry	All other food producing species
Muscle	100 µg/kg	100 µg/kg	100 µg/kg	100 µg/kg
Liver	300 µg/kg	200 µg/kg	200 µg/kg	200 µg/kg
Kidney	200 µg/kg	300 µg/kg	300 µg/kg	200 µg/kg
Fat / skin	100 µg/kg	100 µg/kg	100 µg/kg	100 µg/kg
Milk	100 µg/kg	-	-	-

Based on the toxicological assessment establishment of maximum residue limits for the excipients n-Butanol and Hydrochloric acid was not considered as necessary.

Withdrawal Periods

Based on the data provided above, the following withdrawal periods are justified.

Enrotron 50

Calves	Intravenous injection	Meat and offal	5 days
	Subcutaneous injection	Meat and offal	12 days
Not authorised for use in animals producing milk for human consumption.			
Pigs		Meat and offal	13 days

Enrotron 25

Pigs	Meat and offal	13 days
Rabbits	Meat and offal	6 days
Do not use in birds intended für human consumption.		

Enrotron 100

Cattle	Subcutaneous injection	Meat and offal	12 days
		Milk	4 days
	Intravenous injection	Meat and offal	5 days
		Milk	3 days
Pigs	Intramuscular injection	Meat and offal	13 days

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13.1 of Directive 2001/82/EC based on the essential similarity of the reference and the generic products, efficacy studies are not required. The efficacy claims for the products 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 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.

Quality changes

Summary of change **(Application number)**	**Section updated in Module 3**	**Approval date**
<Example: Change to active substance specification> (MS/V/XXX/X/IB/XX)	N/A	

Safety/efficacy changes

Summary of change **(Type; application number)**	**Section updated in Module 3**	**Approval date**
Implementation of the outcome of the art 35 referral concerning 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" (DE/V/0147/001-003/IA/003)	IIIB	13/11/2014

Implementation of Commission Decision (2014) 6267 final of the Art. 34 Referral Procedure EMEA/V/A/091 concerning 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" – addition of target species rodents, reptiles and ornamental birds DE/V/0147/001/II/008	IIIB, IV	05.02.2018