Austrian
Federal Office for
Safety in Healthcare
BASG

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Enrox Max - 100 mg/ml solution for injection for cattle and pigs

AT/V/0010/001/DC

Last update: 21/11/2019

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Modules 1-3 reflect the scientific discussion for the approval of Enrox Max 100 mg/ml Solution for Injection. The procedure was finalised on 31/07/2013. For information on changes after this date please refer to module 4.

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MODULE 1

PRODUCT SUMMARY

EU procedure number	AT/V/0010/001/DC
Name, strength and pharmaceutical form	Enrox Max 100 mg/ml solution for injection for cattle and pigs
Applicant	Billev Pharma aps Elmegaardsvej 1A, Toerslev, 3630 Jaegerspris Denmark
Active substance(s)	Enrofloxacin
ATCvet code	QJ01MA90
Target species	Cattle and pigs
Indication for use	Cattle: For the treatment of respiratory tract infections caused by enrofloxacinsusceptible *Histophilus somni*, *Mannheimia haemolytica*, *Pasteurella multocida*, and *Mycoplasma* spp. For the treatment of mastitis caused by enrofloxacin-susceptible *E. coli*. Pigs: For the treatment of bacterial bronchopneumonia caused by enrofloxacin-susceptible *Actinobacillus pleuropneumoniae*, *Pasteurella multocida* and complicated by *Haemophilus parasuis* as secondary pathogen in pigs.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article Article 13 (1) of Directive No 2001/82/EC, as amended
Reference medicinal product	Baytril RSI 100 mg/ml Injektionslösung für Rinder und Schweine
Date of completion of the original <mutual recognition> <decentralised> procedure	31/07/2013
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	BE, BG, CZ, DE, ES, FR, HU, IT, LT, LV, PL, PT, RO, SI, SK, UK

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 risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

II.A Qualitative and quantitative particulars

The product contains:

Active substance: enrofloxacin (100 mg/ml) and

excipient(s): benzyl alcohol, butyl alcohol, arginine and water for injection

Container/closure system: a 100 ml brown glass bottle, type II, with bromobutyl rubber stopper and aluminium crimp cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

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II.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.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

II.C Control of Starting Materials

The active substance is enrofloxacin, an established active substance which is 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.

II.D Control on intermediate products (pharmaceuticals)

Not applicable.

II.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<s> have been provided demonstrating compliance with the specification.

II.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 claim of stability after broaching is acceptable, for details see section 6.3 of SPC.

II.G Other Information

Not applicable.

Shelf life

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

In-use shelf life

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

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Special precautions for storage

Store in the original package. Do not freeze.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

For generics, insert in the relevant sections as appropriate:

Since the application is made in accordance with Article 13(1) of Directive 2001/82/EC, as amended, for a generic veterinary medicinal product, data on pharmacodynamics and pharmacokinetics are not required. The data submitted are in accordance with the requirements of the applicable European bioequivalence guideline.

III.A Safety Testing

Pharmacological Studies

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

Toxicological Studies

As this is a generic application according to Article 13, and bioequivalence with the reference product has been demonstrated, results of pharmacodynamic and pharmacokinetic tests are not required.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the overall risk after exposure to the product is low, it is not expected to pose a risk for the user if used as recommended in the SPC.

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

Environmental Risk Assessment

The applicant provided a Phase I environmental risk assessment (ERA) for enrofloxacin in compliance with the relevant CVMP/VICH guidelines GL6 and GL38.

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the veterinary medicinal product will be used to treat a small number of animals in a flock herd. The results of the assessment for the terrestrial plants indicate that the initial predicted environmental concentration in soil is less than 100 µg/kg for all categories of the target animal species.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed in the SPC.

III.B Residues documentation

No residue depletion studies were conducted because, in accordance with the data requirements of the applicable European bioequivalence guideline, it was demonstrated that the product is a generic of Baytril RSI 100 mg/ml solution for injection for cattle and pigs and that the residue depletion profile will be the same.

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MRLs

Maximum Residue Limits (MRLs) for the active substance enrofloxacin is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010. The marker substance is the sum of enrofloxacin and ciprofloxacin. MRLs are listed below:

Pharmacologically active substance(s)	**Marker residue**	**Animal species**	**MRLs (µg/kg)**	**Target tissues**
Enrofloxacin	Sum of enrofloxacin and ciprofloxacin	Bovine, ovine, caprine	100	Muscle
			100	Fat
			300	Liver
			200	Kidney
			100	Milk
		Porcine, rabbit	100	Muscle
			100	Fat
			200	Liver
			300	Kidney

The excipients benzyl alcohol, butyl alcohol and L-arginine which are contained in the generic product are included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as "No MRL required". The excipient water for injection is "Out of Scope" of that Regulation.

Withdrawal Periods

The withdrawal periods for the proposed product are the same as those of the reference product as follows:

Cattle:

Meat and offal:	s.c.:	14 days
	i.v.:	7 days
Milk:	s.c.:	120 hours
	i.v.:	72 hours

Pigs:

Meat and offal:	i.m.:	12 days

IV. CLINICAL ASSESSMENT (EFFICACY)

For generics:

As this is a generic application according to Article 13, and bioequivalence with the reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13, and bioequivalence with the reference product has been demonstrated, pharmacodynamic and pharmacokinetic studies are not required.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13, and bioequivalence with the reference product has been demonstrated, tolerance studies are not required.

Resistance

The bibliography / information provided suggests that the intended target bacterial species are susceptible.

Adequate warnings and precautions appear on the product literature, for details see section 4.5 of SPC.

IV.B Clinical Studies

Laboratory Trials

As this is a generic application according to Article 13, and bioequivalence with the reference product has been demonstrated, laboratory studies are not required as they have already been presented for the reference product.

Field Trials

As this is a generic application according to Article 13, and bioequivalence with the reference product has been demonstrated, field studies are not required as they have already been presented for the reference product.

The product is efficacious when used according to the SPC.

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.

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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 Medicines 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.

Significant changes

Summary of change **(Application number)**	**Approval date**
This marketing authorization was renewed unlimited. (AT/V/0010/001/R/001)	04/07/2018

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