**IPAR**

# Publicly Available Assessment Report for a Veterinary Medicinal Product

# Enrotron 100 mg/ml Solution for injection for cattle and pigs

**PRODUCT SUMMARY**

| | |
|---|---|
| EU Procedure number | IE/V/0270/003/DC |
| Name, strength and pharmaceutical form | Enrotron 100 mg/ml Solution for Injection for Cattle and Pigs |
| Active substance(s) | Enrofloxacin |
| Applicant | aniMedica GmbH<br>Im Südfeld 9<br>48308 Senden-Bösensell<br>Germany |

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| Legal basis of application | Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended. |
| Date of completion of procedure | 21st December 2011 |
| Target species | Cattle, pigs |
| Indication for use | Cattle<br><br>Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida, Mannheimia haemolytica* and *Mycoplasma spp*.<br>Treatment of acute severe mastitis caused by enrofloxacin susceptible strains of *Escherichia coli*.<br>Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.<br>Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*.<br>Treatment of acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of |



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| | *Mycoplasma bovis* in cattle less than 2 years old.<br><br>Pigs<br>Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida, Mycoplasma spp*. and *Actinobacillus pleuropneumoniae*.<br>Treatment of infections of the urinary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.<br>Treatment of post-partum dysgalactiae syndrome, PDS (MMA syndrome) caused by enrofloxacin susceptible strains of *Escherichia coli* and *Klebsiella spp*.<br>Treatment of infections of the alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli*.<br>Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli*. |
| ATCvet code | QJ01MA90 |
| Concerned Member States | EL, IT, PL, 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.

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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 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 enrofloxacin 100 mg and the excipients 1-butanol, potassium hydroxide, hydrochloric acid and water for injection.
The product is presented in 100 ml clear glass vial type I with teflonised rubber stopper sealed with an aluminium cap.
Cartons of 1 x 100 ml or 12 x 100 ml are available.

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.

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

### *C. Control of Starting Materials*


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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 IntermediateProducts*

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.

### *G. Other Information*

Not applicable.


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## III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

### *III.A Safety Testing Pharmacological Studies*

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application. Exemption from bioequivalence studies is claimed. This is accepted on the basis that:
"The product is to be parenterally … administered as a solution and contains the same active substance(s) and excipients in the same concentrations as a veterinary medicinal product currently approved for use in the target species which is the subject of the new application" (paragraph 4b, EMEA/CVMP/016/00-corr).

### *Toxicological Studies*

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

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users / the environment / consumers.

### *User Safety*

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 first phase environmental risk assessment in compliance with the relevant guideline which showed that further assessment was required. The assessment concluded that the product when used in accordance with label recommendations will not present a risk to the environment.No warnings regarding enrofloxacin are therefore required.

### *III.B Residues Documentation Residue Studies*

No residue depletion studies were conducted using the final formulation. Given that the test product is a simple solution with a formulation that can be considered equivalent to the reference product, it is accepted that a difference between


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products with respect to depletion from injection site is unlikely. As a consequence, the absence of confirmatory residue studies is justified and that the withdrawal periods authorised for the reference product can be applied to the test product.

***MRLs***

Enrofloxacin is included in Table 1 of the Annex of Commission Regulation (EU) No. 37/2010 (O.J. 20.1.2010, L 15/30).The marker substance is the sum of enrofloxacin and ciprofloxacin.
MRLs are listed below:

| | Cattle |
|---|---|
| Muscle | 100 µg/kg |
| Liver | 300 µg/kg |
| Kidney | 200 µg/kg |
| Fat | 100 µg/kg |
| Milk | 100 µg/kg |

| | Pig |
|---|---|
| Muscle | 100 µg/kg |
| Liver | 200 µg/kg |

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| | |
|---|---|
| Kidney | 300 µg/kg |
| Skin and fat in natural proporotions | 100 µg/kg |

***Withdrawal Periods***

The following withdrawal periods are justified:

Cattle: Subcutaneous use
Meat and offal: 12 days
Milk: 96 hours

Cattle: Intravenous use
Meat and offal: 5 days
Milk: 72 hours

Pigs: Intramuscular use
Meat and Offal 13 days

## IV. CLINICAL ASSESSMENT

### *IV.A Pre-Clinical Studies 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 test and reference product are qualitatively and quantitatively similar in terms of active substance and excipient content,
· The toxicological profile of the active substance is well known,
· The proposed indications and posology for the test product are identical to the authorised indications and posology of the reference product, the absence of tolerance studies specific to the test product can be accepted.


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The information relating to adverse reactions and overdose included on the SPC for the test product is the same as that included on the SPC of similar enrofloxacin containing products.

***Resistance***

As this is a generic application according to Article 13(1), and bioequivalence with a reference product has been accepted, it can be said that the risk of development of resistance to the active substance in the product is no different to that of the reference product. Adequate warnings and precautions appear on the product literature.

***IV.B Clinical Studies***

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

Exemption from bioequivalence studies is claimed on the basis that:
"The product is to be parenterally … administered as a solution and contains the same active substance(s) and excipients in the same concentrations as a veterinary medicinal product currently approved for use in the target species which is the subject of the new application" (paragraph 4b, EMEA/CVMP/016/00-corr).

As the test product is considered to be bioequivalent to Baytril 10% Solution for Injection, it is accepted that the efficacy profile will be equivalent to that 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.


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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<br><br>(Type; application number) | Section updated | Approval date |
|---|---|---|
| Change in the Summary of Product Characteristics, Labelling or 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 forveterinary medicinal products, which contain the active substance Enrofloxacin (Decision number: C (2014) 6268 Final). (Type C.I.1.a)<br><br>IE/V/0270/01_2_3/IA/03/G | Product summary and<br><br>Part IIIB | 04/11/2014 |

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