# IPAR

# Publicly Available Assessment Report for a Veterinary Medicinal Product

Floxibac 50 mg/ml Solution for Injection for Cattle, Pigs, Dogs and Cats

## PRODUCT SUMMARY

| | |
|---|---|
| EU Procedure number | IE/V/0224/001/DC |
| Name, strength and pharmaceutical form | Floxibac 50 mg/ml Solution for Injection for Cattle, Pigs, Dogs and Cats |
| Active substance | Enrofloxacin |
| Applicant | Chanelle Pharmaceuticals Manufacturing Ltd.<br>Loughrea<br>County Galway<br>Ireland |
| Legal basis of application | Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended. |
| Date of completion of procedure | 27th January 2010 |
| Target species | Cattle, Pigs, Dogs and Cats |
| Indication for use | Calves:<br>Treatment of infections of respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida, Mannheimia haemolytica* and *Mycoplasma* 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*.<br>Treatment of acute mycoplasma-associated arthritis due to enrofloxacin susceptible strains of *Mycoplasma bovis.*<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 alimentary tract caused by enrofloxacin susceptible strains of *Escherichia coli.*<br>Treatment of septicaemia caused by enrofloxacin susceptible strains of *Escherichia coli.*<br><br>Dogs:<br>Treatment of infections of the alimentary, respiratory and urogenital tracts (including prostatitis, adjunctive antibiotic therapy for pyometra), skin and wound infections and otitis (externa/media) caused by enrofloxacin susceptible strains of *Staphylococcus* spp., *Escherichia coli, Pasteurella* spp., *Klebsiella* spp., *Bordetella* spp., *Pseudomonas* spp. and *Proteus* spp.<br><br>Cats:<br>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<br>. |
| ATCvet code | QJ01MA90 |
| Concerned Member States | DE, FR, 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 50 mg/ml Enrofloxacin and the excipients n-butanol, potassium hydroxide and water for injections.

The container/closure system a 100 ml or 250 ml Type I amber glass vial with a teflonised chlorobutyl stopper and an aluminium cap.

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 for the manufacturing process has been presented in accordance with the relevant European guidelines.

### *C. Control of Starting Materials*

The active substance is Enrofloxacin, an established active substance. 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.

### *G. Other Information*

Not applicable.

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

As this is a generic application according to Article 13.1 and an exemption from the demonstration of bioequivalence with a reference product has been justified, results of safety and residue tests are not required.

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

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

### *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 and therefore data on pharmacodynamics are not required.

The applicant claims exemption from bioequivalence studies in accordance with paragraph 4(b) of the Guideline for Conduct of Bioequivalence Studies (EMEA/CVMP/016). Paragraph 4(b) of the guideline permits exemption from the requirement for bioequivalence studies where *'the product is to be parenterally or orally 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.'* Based on the argumentation and chemical data provided by the applicant, the claimed exemption is accepted. Studies have been conducted to determine the composition of this product compared with the reference product and the results confirm that the products are comparable in terms of composition and physiochemical properties. Consequently, systemic availability of the active substance following administration of 'Floxibac 50 mg/ml' is assumed to be equivalent to that achieved following administration of the reference product 'Baytril 50 mg/ml', with the result that 'Floxibac 50 mg/ml' and the reference product will have a similar safety and efficacy profile.

***Toxicological Studies***

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application and therefore data on toxicological studies are not required.

No data were presented and this is accepted.

*Studies on Metabolites, Impurities, Other Substances and Formulation*

The applicant has provided information regarding impurities. Comparative analytical studies confirm that the impurity profile in the test and reference products are comparable.

Excipients included in the product are commonly used in injectable veterinary pharmaceuticals.

***Observations in Humans***

The application is made in accordance with Article 13(1) of Council Directive 2001/82/EC (as amended), a generic application and therefore data on observations in humans are not required.

No data were presented and this is accepted.

***User Safety***

The applicant has provided a user safety assessment which shows that that the product does not present any greater risk to the user than the reference product.

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 full Phase I and Phase II environmental risk assessment in compliance with the relevant guideline. The assessment concluded that the product, when used as recommended, will not pose an unacceptable risk for the environment.

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 applicant successfully demonstrated that the similarity in formulation with the reference product was such that a difference between products with respect to residue depletion from both the primary target tissues and injection site is not to be expected.

***MRLs***

Enrofloxacin is listed in Annex I of Council Regulation 2377/90 as follows:

| | Bovine | Porcine |
|---|---|---|
| Muscle | 100µg/kg | 100µg/kg |
| Liver | 300µg/kg | 200µg/kg |
| Kidney | 200µg/kg | 300µg/kg |

| | | |
|---|---|---|
| Fat / skin | 100µg/kg | 100µg/kg |
| Milk | 100µg/kg | Not applicable |

***Withdrawal Periods***

Given that a difference between the test and reference products with respect to residue depletion is not to be expected, it is accepted that the withdrawal periods currently authorised for the reference product can be applied to the test product. The following withdrawal periods for cattle and pigs are justified:

- Cattle (meat & offal): 13 days (subcutaneous); 5 day (intravenous)
- Cattle (milk): Not permitted for use in lactating animals producing milk for human consumption.

- Pigs (meat): 12 days.

## IV CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13(1), and exemption from the demonstration of bioequivalence with the reference product has been efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

### *IV.A Pre-Clinical Studies*

***Tolerance in the Target Species of Animals***

As this is a generic application according to Article 13 (1) and exemption from the demonstration of bioequivalence with a reference product has been accepted, no tolerance studies have been provided. It is argued that the safety profile of the test product will be the same as that for the reference product.

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

Adequate warnings and precautions appear on the product literature.

***Resistance***

The SPC has been updated with appropriate prudent use warnings as recommended in the relevant guidelines.

### *IV.B Clinical Studies*

***Field Trials***

As this is a generic application according to Article 13, and exemption from the demonstration of bioequivalence with a reference product has been accepted, field 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.

**Changes:**

| **Summary of change** | **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).<br>C.I.1.A Update section 4.1, 4.2, 4.3, 4.4, 4.5, 4.8, 4.9, 4.11, 5.1 of the SPC - IE/V/xxxx/1A/035/G | 15/12/2014 |