Publicly Available Assessment Report for a
Veterinary Medicinal Product

VALEMAS 50 mg/ml solution for injection for cattle, sheep, goats, pigs, dogs and cats.

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PRODUCT SUMMARY

EU Procedure number	IE/V/0445/001/DC
Name, strength and pharmaceutical form	VALEMAS 50 mg/ml solution for injection for cattle, sheep, goats, pigs, dogs and cats
Active substance(s)	Enrofloxacin
Applicant	FATRO S.p.A. Via Emilia 285 - 40064 Ozzano Emilia Bologna Italy
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of Authorisation/ completion of procedure	11/03/2019
Target species	Cattle (calves), sheep, pigs, dogs and cats
Indication for use	<u>Calves</u> 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*. <u>Sheep</u> 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 mastitis caused by enrofloxacin susceptible strains of *Staphylococcus aureus* and *Escherichia coli*. <u>Goats</u> Treatment of infections of the respiratory tract caused by enrofloxacin susceptible strains of *Pasteurella multocida* and *Mannheimia haemolytica*. 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 mastitis caused by enrofloxacin susceptible strains of *Staphylococcus aureus* and *Escherichia coli*. <u>Pigs</u> 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*. <u>Dogs</u> Treatment of infections of the alimentary, respiratory and urogenital tracts (including prostatitis, adjunctive antibiotic

	therapy for pyometra), skin and wound infections, otitis (externa/media) caused by enrofloxacin susceptible strains of *Staphylococcus spp*., *Escherichia coli*, *Pasteurella spp*., *Klebsiella spp*., *Bordetella spp*., *Pseudomonas spp*. and *Proteus spp*. Cats 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*.
ATCvet code	QJ01MA90
Concerned Member States	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 enrofloxacin (50 mg/ml) as the active substance and the excipients n-butyl alcohol, potassium hydroxide and water for injections.
The container/closure system is a Type II amber glass bottle containing 50 ml, 100 ml or 250 ml closed with chlorobutyl rubber stoppers and sealed with flip-off aluminium caps.
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.

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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 has 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 has been provided.

Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substance has 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 has 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 submitted in accordance with paragraph 1 of Article 13 of Directive 2001/82/EC, as amended, and an exemption from the requirement to demonstrate bioequivalence with a reference product has been satisfactorily justified, results of safety and residue tests are not required. The reference product is Baytril 50 mg/ml solution for injectioncontaining enrofloxacin (VPA 10021/020/002 – Bayer Limited) which was granted marketing authorisation on 01 October 1988. The reference product has been authorised within the Community for not less than 10 years based upon a full dossier and can be accepted as being a suitable reference product.

The safety aspects of this product are considered to be identical to that of 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 consumers of foodstuffs from treated animals and for the environment.

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 the requirement to conduct bioequivalence studies in accordance with paragraph 7.1(a) and (b) of the Guideline for Conduct of Bioequivalence Studies (EMEA/CVMP/016/00-Rev.2). Paragraph 7.1(a) of the guideline permits exemption from the requirement for bioequivalence studies where; '*the product is to be administered solely as an aqueous intravenous solution containing the same active substance as the currently approved product. However, if any excipients interact with the active substance (e.g. complex formation), or otherwise affect the disposition of the active substance, a bioequivalence study is required unless both products contain the same excipients in very similar quantity and it can be adequately justified that any difference in quantity does not affect the pharmacokinetics of the active substance*'. Paragraph 7.1(b) of the guideline permits exemption from the requirement for bioequivalence studies where; '*products intended for intramuscular, subcutaneous or systemically acting topical administration, bioequivalence studies are not required in cases when*

the product is of the same type of solution, contains the same concentration of the active substance and comparable excipients in similar amounts as the reference veterinary medicinal product, if it can be adequately justified that the difference(s) in the excipient(s) and/or their concentration have no influence on the rate and/or extent of absorption of the active substance.'

Based on the argumentation and quality data provided by the applicant, the claimed exemption is accepted. Studies have been conducted to determine the composition of this product compared with that of the reference product and it was accepted that the results confirm that the products are comparable in terms of composition and physicochemical properties. Consequently, systemic availability of the active substance following administration of 'Valemas 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 it was accepted that 'Valemas 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), i.e. a generic application. Based on the argumentation/quality data presented, it was accepted that exemption from the requirement to conduct an *in-vivo* bioequivalence study was justified and that the test product can be considered bioequivalent to the reference product. Accordingly, the applicant is not required to provide the results of safety and residue tests or of pre-clinical and clinical trials.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that that the product does not present any greater risk to the user than that presented by 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 Phase I 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 for this application. It wsa accepted 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.Therefore, the omission of studies investigating the depletion of residues was considered acceptable.

MRLs

Enrofloxacin is listed in table1 of the Annex to Commission Regulation (EU) No. 37/2010 as follows:

	Bovine, ovine, caprine	**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. Accordingly the following withdrawal periods for cattle (calves), sheep, goats and pigs are considered appropriate:

Calves:

Following intravenous injection:	Meat and offal:	5 days
Following subcutaneous injection:	Meat and offal:	12 days

Not authorised for use in animals producing milk for human consumption.

Sheep:

Meat and offal:	4 days.
Milk:	72 hours.

Goats:

Meat and offal:	6 days.
Milk:	96 hours.

Pigs:

Meat and offal:	13 days.

IV. CLINICAL ASSESSMENT

As this is a generic application according to Article 13(1), and exemption from the requirement to demonstrate bioequivalence with the reference product has been satisfactorily justified, 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 requirement to demonstrate bioequivalence with the reference product has been satisfactorily justified no tolerance studies have been provided. It is accepted 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

Appropriate prudent use warnings, as recommended in the relevant guidelines, are included in the product literature.

IV.B Clinical Studies

Field Trials

As this is a generic application according to Article 13, and exemption from requirement to demonstrate bioequivalence with the reference product has been satisfactorily justified, field efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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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:
None.