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)

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Vetrimoxin L.A. 150 mg/ml Suspension for injection

MODULE 1

PRODUCT SUMMARY

EU Procedure number	DE/V/0153/001/MR
Name, strength and pharmaceutical form	Vetrimoxin L.A. 150 mg/ml Suspension for injection
Applicant	Ceva Tiergesundheit GmbH Kanzlerstr. 4 D-40472 DÜSSELDORF, Germany
Active substance(s)	Amoxicillin trihydrate
ATC Vetcode	QJ01CA04
Target species	Cattle and pigs

Indication for use	In cattle: Treatment of respiratory infections caused by *Mannheimia haemolytica* and *Pasteurella multocida* susceptible to amoxicillin. In pigs: Treatment of respiratory infections caused by *Pasteurella multocida* susceptible to amoxicillin.

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	21.11.2012
Date product first authorised in the Reference Member State (MRP only)	17.03.2010
Concerned Member States for original procedure	AT, DK, FI, IE, IS, NL, SE, 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.

The safety and efficacy aspects of this product are identical to Vetrimoxin L.A. a product approved in Spain.

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

II. QUALITY ASPECTS

A. Composition

The product contains 150 mg amoxicillin (as amoxicillin trihydrate) and the excipients anhydrous colloidal silica, sorbitan oleate and propyleneglycol-dicaprylocaprate.

The suspension for injection is filled into plastic vials (polypropylene/ethylene vinyl alcohol/polypropylene) and closed with chlorobutyl rubber stoppers (type II) and aluminium/plastic flip capsules. 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.

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.

C. Control of Starting Materials

The active substance is amoxicillin trihydrate, 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.

A valid Certificate of suitability issued by the European Directorate for the Quality of Medicines (EDQM) has been presented.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

Compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been confirmed.

E. <Control on intermediate products> (pharmaceuticals)

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 site 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.

An in-use shelf-life of 28 days has been supported by appropriate data.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

None.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL) (*for pharmaceuticals only)*

As this is a generic application according to Article 13(1), and as Vetrimoxin LA 150mg/ml is identical with a reference product, studies on safety and residues are not required.

III.A Safety Testing

As this is a generic application according to Article 13(1), and as Vetrimoxin LA 150mg/ml is identical with a reference product, studies on toxicology are not provided.

User Safety

The applicant has not provided a user safety assessment. As this is a generic application according to Article 13(1), and as Vetrimoxin LA 150mg/ml is identical with a reference product, risk characterisation, hazard characterisation and risk mitigation measures are considered identical. Thus, 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 guidelines which showed that further assessment was required for the use of amoxicillin in weaner pigs, whereas no further assessment was necessary for cattle and pig subgroups other than weaner pigs.

The Phase II environmental risk assessment for amoxicillin concentrated on the major metabolite of amoxicillin in pig slurry, i.e. amoxicillin penicilloic acid (APA), since Amoxicillin has not been detected after 28 days in the respective study. The applicant provided the necessary ecotoxicological studies for APA.
Overall it could be concluded that the product is not expected to pose a risk for the environment when used in accordance with the SPC.

Warnings and precautions as listed in 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 Vetrimoxin L.A. 150mg/ml was authorised in Germany as a generic to the approved reference product Vetrimoxin LA from Spain. Both products are identical in the qualitative and quantitative composition of the active ingredient. The products were classified as bioequivalent.

MRLs

Amoxicillin is listed in Table 1 of Commission Regulation (EU) No 37/2010 for all food producing species with the following MRLs:

Pharmacologically active substance	Marker residue	Species	MRLs	Target tissue	Other provisions
Amoxicillin	Amoxicillin	All food producing species	50 µg/kg 50 µg/kg 50 µg/kg 50 µg/kg 4 µg/kg	Muscle Fat Liver Kidney Milk	For porcine species the fat MRL relates to 'skin and fat in natural proportions'.

Two excipients contained in Vetrimoxin L.A. 150 mg/ml – Sorbitan oleate and Propylene glycol dicaprylocaprate – are included in Table 1 of Commission Regulation (EU) No 37/2010 with no MRL required. Anhydrous colloidal silica is covered by entry for food additives with an E number (E551) according to European Parliament and Council Directive 95/2/EC.

Withdrawal Periods

The following withdrawal periods are justified.

Cattle:	Meat and offal:	18 days
	Milk:	3 days
Pigs:	Meat and offal:	20 days

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

As this is a generic application according to Article 13(1), and as Vetrimoxin LA 150mg/ml is identical with a reference product, studies on pharmacology are not required. The pharmacology claims for this product are equivalent to those of the reference product.

Tolerance in the Target Species of Animals

As this is a generic application according to Article 13(1), and as Vetrimoxin LA 150mg/ml is identical with a reference product, target animal tolerance studies are not required. The tolerance claims for this product are equivalent to those of the reference product.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance

As this is a generic application according to Article 13(1), and as Vetrimoxin LA 150mg/ml is identical with a reference product, studies on bacterial resistance are not required. The resistance claims for this product are equivalent to those of the reference product.

However, the Applicant has provided publications on the bacterial resistance development towards amoxicillin and on the *in-vitro* susceptibility of relevant respiratory tract pathogens from cattle and pigs towards this substance, which had been collected between 1998 and 2004. It was demonstrated that resistance rates of *Pasteurella multocida* and *Mannheimia haemolytica* towards amoxicillin were in general still low.

Regarding bacterial resistance development, adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies (pharmaceuticals and immunologicals)

As this is a generic application according to Article 13(1), and as Vetrimoxin LA 150mg/ml is identical with a reference product, 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 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.

<None>