College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

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PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Kelamoxil LA 150 mg/ml suspension for injection for cattle and pigs

PRODUCT SUMMARY

EU procedure number	NL/V/0390/001
Name, strength, and pharmaceutical form	Kelamoxil LA 150 mg/ml suspension for injection for cattle and pig
Applicant	Kela nv Sint Lenaartseweg 48 2320 Hoogstraten Belgium
Active substance(s)	Amoxicillin
ATC vetcode	QJ01CA04
Target species	Cattle and pigs
Indication for use	In cattle: Treatment of respiratory infections caused by *Mannheimia haemolytica* and *Pasteurella multocida*. In pigs: Treatment of respiratory infections caused by *Pasteurella multocida*.

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Kela NV	DCP
Publicly available assessment report	

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Generic application in accordance with Article 18 of Regulation (EC) 2019/6 as amended.
Reference product (RP)	Vetrimoxin L.A. 150 mg/ml suspension for injection
Marketing authorisation holder	CEVA Sante Animale
MS where the RP is or has been authorised	ES
Marketing authorisation number EU procedure number	1223 ESP
Date of authorisation	29 October 1998
Date of completion of the original decentralised procedure	31 May 2023
Date veterinary medicinal product first authorised in the Reference Member State (MRP only)	-
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IS, IT, LT, LU, LV, NI (UK), NO, PL, PT, RO, SE, SI, SK
Concerned Member States for subsequent recognition procedure	-
Withdrawn CMS during original decentralised procedure	-

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of referenceability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

1. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.

It has been shown that the VMP can be safely used in the target species; the reactions observed are indicated in the SPC.

The VMP 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 VMP was demonstrated according to the claims made in the SPC.

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

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The proposed veterinary medicinal product is a non-aqueous suspension for injection for intramuscular administration to cattle and pigs. The product contains 150 mg/mL amoxicillin (as trihydrate) and the excipients sorbitan oleate, colloidal anhydrous silica and propylene glycol dicaprylocaprate.

The product is packed in 100 mL and 250 mL clear type II glass vial or clear PET vial closed with type I laminated chlorobutyl rubber stopper and aluminium cap.

The choice of the formulation has been justified. The absence of preservatives has been fully justified.
The product is an established pharmaceutical form, and its development is sufficiently described in accordance with the relevant European guidelines.

B. Description of the manufacturing method

The product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

The manufacturing process is regarded as a standard process. Process validation results have been provided for three production scale batches.

The applicant committed that post-authorisation process validation will be conducted on the first three full scale production batches.

C. Production and control of starting materials

The active substance is amoxicillin trihydrate, an established active substance described in the European Pharmacopoeia (monograph 0260). For the active substance a CEP is used. 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 for two batches. Analytical data of one more batch are awaited.

A TSE declaration of compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been provided.

D. Control tests carried out on isolated intermediates during the manufacturing process

An intermediate process step has been identied and properly justified. Required quality control parameters are in place.

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, are considered appropriate to adequately control the quality of the product.

Satisfactory validation data for the analytical methods have been provided. The stability indicating nature of the HPLC method has been investigated by stress testing and the laser diffraction method for particle-size distribution has also been validated.

Batch analytical data have been submitted for two pilot scale batches and one production batch, demonstrating compliance with the specification.

F. Stability tests

Stability data on the active substance has been assessed as part of granting the CEP. The retest period of the active substance is 6 years if stored in a polyethylene bag in a sealed laminate bag place in a carton box.

Stability data on the finished product has been provided. In accordance with applicable European guidelines. Based on the submitted stability data, the claimed shelf-life and storage conditions can be granted.

The claimed in-use shelf-life of 28 days can be granted.

A commitment is included to perform stability studies of the first three full-scale batches at long-term and accelerated conditions post-authorisation.

Applicant’s commitment for in-use stability testing on an aged batch approaching the end of shelf-life is also submitted.

G. Other information

Not applicable.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, results of safety tests are not required.

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

Warning statements and precautions as listed in the product literature are based on those of the reference product and supplemented with additional statements, based on increased knowledge and the current state of science. This information is considered adequate to ensure safety of the product to users, consumers, and the environment.

User safety

Being a generic procedure, the applicant refers to the reference product for information on this section. Additionally, the applicant has provided a user safety risk assessment in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the VMP.

Environmental Risk Assessment

Following the CVMP Reflection paper on the interpretation of Article 18(7) of Regulation (EU) 2019/06 (EMA/CVMP/ERA/622045/2020, 25 February 2022) an ERA is not required as there are similar VMPs with an acceptable ERA authorised in the EU/EEA after 1 October 2005.

However, a discussion underpinned with references from the recent scientific literature on the risk of selection of antimicrobial resistance (AMR) in the environment resulting from the use of the veterinary medicinal product according to Regulation (EU) 2019/6, Article 8(2), and Annex II, Part II.3A.4.3 has been provided.

B. Residues documentation

Residue tests

The applicant has conducted injection site residue depletion studies which show that the residue levels at the injection sites are below MRL at the proposed withdrawal periods as adopted from the reference product, i.e. 18 and 20 days respectively for cattle and pigs

The analytical method was a LC-MS/MS method. The method was fully validated.

No residue depletion studies in milk were conducted because this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated.

Maximum Residue Limits

Amoxicillin is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance	**Marker residue**	**Animal Species**	**MRL**	**Target tissues**	**Other provision**	**Therapeutic Classification**
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	Anti-infectious agents/Antibiotics

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Withdrawal Periods

Based on the data provided above, the following withdrawal periods are justified:

Cattle:

Meat and offal: 18 days

Milk: 72 hours

Pigs:

Meat and offal: 20 days

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a generic application according to Article 18 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, efficacy studies are not required. The efficacy claims for this VMP are equivalent to those of the reference VMP.

The applicant submitted two *in-vivo* bioavailability studies (one in each target species) in support of bioequivalence with the reference product.

Development of resistance and related risk in animals

Information was provided about the level of resistance, as known from bibliographic data, according to what is stated in Delegated Regulation 2021/805 Section IV.1.3, for a generic veterinary medicinal product application containing an antimicrobial substance.

Adequate warnings and precautions appear on the product literature.

Tolerance in the target species of animals

The product literature accurately reflects the type and incidence of adverse effects, which might be expected. Evidence to demonstrate that target animal tolerance at the administration site is identical to the reference product was provided.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMP 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 VMP for humans and the environment is acceptable.

POST-AUTHORISATION PROCEDURES

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the VMP. The current SPC is available in the Union Product Database (UPD).

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 VMP.

None