



MINISTERIO
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agencia española de
medicamentos y
productos sanitarios

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E - 28022 Madrid
Spain
(Reference Member State)**

DECENTRALISED PROCEDURE

**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL
PRODUCT**

**AQUACOLI 2000000 IU/ml, oral solution for use in drinking water
AQUACOLI 2000000 IU/ml, oral solution for cattle, sheep, swine and poultry (DE)**

MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0192/001/DC
Name, strength and pharmaceutical form	AQUACOLI 2000000 IU/ml, oral solution for use in drinking water AQUACOLI 2000000 IU/ml, Oral solution for cattle,sheep,swine and poultry (DE)
Applicant	Laboratorios Calier, S.A. C/Barcelonés, 26 (Plá del Ramassá) 08520 Les Franqueses del Vallés Barcelona-España
Active substance(s)	Colistin (sulfate)
ATC Vetcode	QA07AA10
Target species	Cattle (calves), sheep (lambs), swine and poultry
Indication for use	Treatment of gastrointestinal infections caused by non-invasive <i>Escherichia coli</i> susceptible to colistin.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v) website) (www.HEVRA.org).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 13(1) – Generic application, of Directive 2001/82/EC as amended
Date of completion of the original decentralised procedure	20/12/2013
Date product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	DE, IT, PL, PT

I. SCIENTIFIC OVERVIEW

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

II. QUALITY ASPECTS

A. Composition

The product contains as active substance colistin (as sulfate) (aprox. 86.96 mg/ml, equivalent to 2 MIU)

Excipients are: benzyl alcohol and purified water.

The container/closure system is high-density polyethylene bottle of 1L and 5 L provided with polyethylene stoppers with strapping and removable polyethylene sealing disk.

The particulars of the containers and controls performed are provided and conform to the regulation.

The pharmaceutical development is well documented. It justifies the chosen formulation and the manufacturing method to produce a homogeneous and stable product, suitable for the proposed use.

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. A flow chart is enclosed in the dossier. The manufacturing equipment is detailed. The manufacturing process has been described.

Process validation data on the product have been presented in accordance with the relevant European guidelines with three pilot batches. Analysis certificates of the batches also support the suitability of the process to produce a homogeneous product with a consistent quality.

C. Control of Starting Materials

The active substance is colistin sulfate, an established active substance described in the European Pharmacopoeia (monograph 0320). The active substance is manufactured in accordance with the principles of good manufacturing practices.

The active substance specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

The applicant justifies the quality of the raw material by means of a Certificate of Suitability CEP n° R1-CEP-2005-166-Rev00, valid from July 13th 2011.

Benzyl alcohol and purified water comply with their respective Eur.Ph monographs. Certificates of analysis are submitted.

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

Documentation from the suppliers to justify that starting materials have no risk of transmitting BSE are included.

E. Control Tests on the Finished Product

The routine controls have been considered enough for the proposed use of the finished product. In general, they have been designed according to procedures of the European pharmacopoeia. 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

The Certificate of Suitability for colistin sulfate provides a shelf life of 4 years

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 (36 months) without any special storage conditions.

The shelf life period once opened the package is 3 months. Shelf-life after dilution in drinking water is 24 hours, and 6 hours after dilution in milk replacer.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, 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 are similar as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

III.A Safety Testing

Pharmacological, toxicological and other safety studies

Since this is an application under Article 13(1) of Directive 2001/82/EC, as amended, the applicant is not required to provide data regarding the pharmacology, toxicology or other safety studies performed with the active ingredient.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that, implementing the indicated protective measures, the use of the product poses an acceptable risk.

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 guideline which showed that further assessment was required (Phase II). The assessment concluded that the product has an acceptable 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 studies are provided because the application has been submitted in accordance with article 13(1) of Directive 2001/82/EC and equivalence with the reference product has been demonstrated.

MRLs

The active substance, colistin, is included in table 1 of the MRL regulation 37/2010, as follows:

Marker residue	Animal Species	MRL	Target Tissues	Other Provisions	Therapeutic Classification	Regulation
colistin	All food producing species	150 µg/kg 150 µg/kg 150 µg/kg 200 µg/kg 50 µg/kg 300 µg/kg	Muscle Fat Liver Kidney Milk Eggs	For fin fish the muscle MRL relates to « muscle and skin in natural proportions ». MRLs for fat, liver and kidney do not apply for fish. For porcine and poultry, the MRL relates to “skin and fat in natural proportions”.	Anti-infectious agents/ Antibiotics	37/2010 of 22.12.2009

Withdrawal Periods

Based on the data provided above, a withdrawal period of 1day for meat in all target species and zero days for eggs are justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

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

IV.A Pre-Clinical Studies

Resistance

Adequate warnings and precautions appear on the product literature.

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 veterinary Heads of 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>