Agencia Española de Medicamentos y Productos Sanitarios

C/Campezo 1, Edificio 8
28022 – Madrid
España
(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

COLFIVE 5,000,000 IU/ml concentrate for oral solution

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0221/001/DC
COLFIVE 5,000,000 IU/ML concentrate for oral solution	COLFIVE 5,000,000 IU/ml concentrate for oral solution
Applicant	aniMedica España, S.L.U. Esmeralda, 19 E-08950 Esplugues de Llobregat (Barcelona) Spain
Active substance(s)	Colistin sulfate
ATC Vet code	QA07AA10
Target species	Cattle (calves), pigs, sheep (lambs), chickens and turkeys
Indication for use	Calves, lambs, pigs, chickens, turkeys: Treatment and metaphylaxis of enteric infections caused by non-invasive *E. coli* susceptible to colistin. The presence of the disease in the herd should be established before metaphylactic treatment.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies website (http://www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	24/02/2015
Date product first authorised in the Reference Member State (MRP only)	Pending
Concerned Member States for original procedure	AT, BE, CZ, DE, DK, EL, FR, HU, IE, IT, NL, PL, PT, RO, SI, SK, 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.

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 colistin (sulfate) 5,000,000 UI/ml and excipients benzyl alcohol (E 1519), sodium acetate anhydrous (E 262), acetic acid glacial (E 260) and purified water

The container/closure system consist of a high-density polyethylene (HDPE) bottle with a nominal capacity of 100 ml, 1 L and 5 L. The containers are heat-sealed with a polyethylene (PE) foil and are closed with a screw cap made of HDPE equipped with a security system to give an airtight sealing.

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

The choice of the presence of preservative are justified.

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 colistin sulphate, 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.

The CEP is included according to the European Pharmacopoeia.

D. 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.

E. Control on intermediate products (pharmaceuticals)

Not applicable.

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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

The retest period of the active substance is declared by the CEP.

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.

In-use stability after first opening the immediate packaging has been demonstrated for 3 months according to the relevant European guideline.

The claim of a 24 hour stability after reconstitution in water and 6 hour after reconstitution in milk is based on the demonstration of stability for a batch broached and stored 24 and 6 hours at 25°C.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT

As this is a hybrid application according to Article 13(3), and bioequivalence with the 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 the same 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(3) of Directive 2001/82/EC, as amended, and the bioequivalence with the reference product has been demonstrated, 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.
Colistin sulphate is very persistent in soils.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(3) of Directive 2001/82/EC and the biequivalence 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
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». MRL 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

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 hybrid application according to Article 13(3), and bioequivalence with the reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

As this is a hybrid application according to Article 13(3), and bioequivalence with the reference product has been demonstrated, pharmacology studies are not required.

Tolerance in the Target Species of Animals

As this is a hybrid application according to Article 13(3), and bioequivalence with the reference product has been demonstrated, tolerance studies are not required.

Resistance

As this is a hybrid application according to Article 13(3), and bioequivalence with the reference product has been demonstrated, data regarding development of resistance are not required.

Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

As this is a hybrid application according to Article 13(3), and bioequivalence with the reference product has been demonstrated, clinical trials are not required.

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