FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
AGENCE NATIONALE DU MEDICAMENT VETERINAIRE
8 rue Claude Bourgelat –
Parc d'activités de la grande
Marche – Javené – CS
70611 – 35306
FOUGERES

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

HIDROCOL, 4000000 IU/ml solution for use in drinking water/milk

DATE: 21/06/2016

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0294/001/DC
Name, strength and pharmaceutical form	HIDROCOL, 4000000 IU/ml solution for use in drinking water/milk
Applicant	SP VETERINARIA SA Crta Reus Vinyols km 4.1 Riudoms (43330) Spain
Active substance(s)	Colistin (as sulfate)
ATC Vetcode	QA07AA10
Target species	Cattle (calves), sheep (lambs), pigs, chickens and turkeys.
Indication for use	Treatment and metaphylaxis of enteric infections caused by non-invasive *Escherichia coli*, susceptible to colistin. The presence of the disease should be established in the group or herd before metaphylactic treatment.

MODULE 2

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

The Summary of Product Characteristics (SPC) for this product is available on the website http://www.anmv.anses.fr/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Hybrid application in accordance with Article 13 (3) of Directive 2001/82/EC as amended.
Date of completion of the decentralised procedure	25/05/2016
Concerned Member States for original procedure	BG, CY, EL, ES, HU, IE, IT, MT, PL, PT, RO and UK

I. SCIENTIFIC OVERVIEW

***For public assessment reports for the first authorisation in a range**:*

HIDROCOL contains Colistin (sulfate). It is intended for an oral use for the treatment and metaphylaxis of enteric infections caused by non-invasive *E. coli*, susceptible to colistin. The presence of the disease should be established in the group or herd before metaphylactic treatment.

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 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 4000000 UI/mL of colistin sulfate and the following excipients: trihydrate sodium acetate, glacial acetic acid, benzyl alcohol, glycerol and purified water.
The product is packaged as described in the SPC. 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 colistin sulfate, an established active 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.

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

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.
The shelf-life after opening the packaging, the shelf-life after dilution in water and the shelf-life after dilution in milk as detailed on the SPC have been supported by appropriate data.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

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

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 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 studies of the product regarding the pharmacology, toxicology or other safety of the product.

User Safety

The applicant has provided a user safety 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 product.

"This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

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 t «muscle and skin in natur proportions». MRL for fat, liver ar 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

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.
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance

An overview of the level of resistance to colistin in target pathogens and commensal bacteria based on recent bibliographical has been provided to address bacterial resistance to colistin.
Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

Efficacy data have not been presented.

Since the tested product and the reference product are bioequivalent and are intended to be used in drinking water/milk to prepare medicated water/milk of the same concentration, it can be concluded that the clinical effects of the two products will be the same and no clinical studies are 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.