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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

AMPROLINE
400 mg/mL
solution for use in drinking water for chickens and turkeys
DATE : 26 July 2016

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0284/001/DC
Name, strength and pharmaceutical form	AMPROLINE 400 mg/mL solution for use in drinking water for chickens and turkeys
Applicant	QALIAN 34 RUE JEAN MONNET BP 20341 49503 SEGRE CEDEX
Active substance(s)	Amprolium (as hydrochloride)
ATC Vetcode	QP51AX09
Target species	Chickens (broilers, pullets, layers and breeder hens) Turkeys
Indication for use	Treatment of intestinal coccidiosis caused by *Eimeria spp* susceptible to amprolium

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website http://mri.medagencies.org/veterinary/

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 original decentralised procedure	25/01/2016
Concerned Member States for original procedure	ES – IT – PL - PT – UK

I. SCIENTIFIC OVERVIEW

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

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 efficacy claims for this product are equivalent to those of the reference products

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

II. QUALITY ASPECTS

A. Composition

The product contains 452 mg of amprolium hydrochloride per mL and excipients sorbic acid and purified water.
The container/closure system is composed of opaque, rectangular, white can of 100 mL, 1L and 5 L, made of polyethylene, closed with a white cap made of

polyethylene. 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 using conventional manufacturing techniques. Process validation for full-scale batches will be performed post-authorisation.

C. Control of Starting Materials

The active substance is amprolium hydrochloride, an established substance described in the British Veterinary 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.
An in-use shelf-life as detailed in the SPC has been supported by appropriate data,as well a shelf-life after dilution.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

This application is submitted in agreement with the Article 13(3), as hybrid application since the test and reference product NEMAPROL 10.6% ORAL SOLUTION differ by a change in strength (quantitative change of the active substance).
Based on information provided in support of this application, it is accepted that the test product is bioequivalent to the reference product.
The pharmacological aspects of this product are identical to the reference product.

Toxicological Studies

As this is an hybrid application according to Article 13 (3), and bioequivalence with a reference product has been demonstrated, results of toxicological tests are not required.

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

Observations in Humans

The applicant has provided bibliographical data which show that amprolium may act as a sensitiser in susceptible persons although this phenomenon was only rarely reported and only in case of massive exposure to amprolium.

From MRL assessment, a toxicological ADI of 100 µg/kg (6 mg/person for a 60 kg adult) was established.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the user's safety can be considered as good when the product is used as directed.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a phase I and a phase II environmental risk assessment in compliance with the relevant guidelines. The assessment concluded that amprolium is a persistent molecule in soils, is neither bioaccumulative nor toxic.

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

The oral test solution and the reference product NEMAPROL can be considered bioequivalent. Thus, no specific residue studies with AMPROLINE 40% are required.

MRLs

a. Active substance

Amprolium is listed in Table 1 of MRL Regulation 470/2009. MRLs are listed below:

Marker residue	Animal species	MRL	Target tissues	Other provisions	Therapeutic classification
Not applicable	Poultry	No MRL required	Not applicable	For oral use only	Anti-infectious agents/Antibiotics

b. Excipients

The MRL status of the excipient of the product AMPROLINE 400 mg/mL is indicated in the following table.

Excipient	MRL status
Sorbic acid	Table 1, no MRL required

Withdrawal Periods

The withdrawal periods agreed for the reference product can be applied to the AMPROLINE 40%, as follows:

Species	Tissues	**Withdrawal periods**
Chicken	Meat & offal	Zero days
	Eggs	Zero days

IV. CLINICAL ASSESSMENT (EFFICACY)

For generics, insert in the relevant sections as appropriate:

As this is a generic hybrid application according to Article 13, 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

Due to the nature of the application no tolerance studies were required.
The bioequivalence is established between the test product and the reference one, the toxicological profile of both products is expected to be similar in target species.

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

Resistance

An update on parasitic resistance of amprolium based on published literature has been provided. Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies

Considering that the test and reference product can be considered as bioequivalent, no specific clinical data are required to demonstrate equivalent efficacy and benefits.

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 benefit/risk profile for the target species is favourable and the quality and safety of the product for humans and the environment are 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 (http://mri.medagencies.org/veterinary/).

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>

or

Complete this section for extensions to the same VPA range or defined, significant variations, using the table shown below.

Some examples of significant changes in safety or efficacy data are:

- *Changes to pharmacokinetic data leading to a change in the SPC*
- *Changes to toxicological data leading to a change in the SPC*
- *Changes to user safety warnings*
- *Changes to ecotoxicological information as given in the SPC or changes to disposal warnings*
- *New residue studies in new target species or tissues*
- *Reassessment of residue data or new studies resulting from changes to MRL*
- *Changes to withdrawal period*
- *Changes to target species*
- *Changes to target species tolerance data leading to change in warnings/precautions for target species*
- *New or changed indications*

Significant changes in administrative or quality data include any Type II change, which affects the initial report. The following Type IA or IB changes may also apply:

- *Name of product [Type IA: 2]*
- *Name of active substance [Type IA: 3}*
- *MAH [Type IA: 1]*
- *Composition of the medicinal product [Type IB: 18, Type IA/B: 25, 34, 35, 39]*
- *Container/closure system [Type 1/B: 26, 28, 29, 36, 41, 43]*
- *Method of preparation [Type 1B: 33]*
- *Active substance specification [Type IB: 25]*

- *CEP [Type IA/B: 15]*
- *Re-test period or storage conditions of active substance [Type IB: 17]*
- *Excipient specifications [Type 1A/B: 25]*
- *Packaging materials[Type 1A/B: 28, 29, 36, 41, 43]*
- *TSE [Type 1A: 16, 22]*
- *Shelf-life or storage conditions of the finished product [Type 1B: 42]*

Quality changes

Summary of change **(Application number)**	**Section updated in Module 3**	**Approval date**
<Example: Change to active substance specification> (MS/V/XXX/X/IB/XX)	N/A	

Safety/efficacy changes

Summary of change **(Type; application number)**	**Section updated in Module 3**	**Approval date**
<Example: Addition of target species - pigs> (MS/V/XXX/X/II/XX)	<IIIA> <IIIB> <IV>	