DEPARTAMENTO DE
MEDICAMENTOS
VETERINARIOS

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

CRYPTISEL 0.5 MG/ML ORAL SOLUTION FOR CALVES

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0374/001/DC
Name, strength and pharmaceutical form	Cryptisel 0.5 mg/ml oral solution for calves
Applicant	LIVISTO INT'L, S.L. Avinguda Universitat Autònoma 29, Cerdanyola Del Vallès, Barcelona, 08290, Spain
Active substance(s)	Halofuginone lactate
ATC Vetcode	QP51AX08
Target species	Cattle (Newborn calves)
Indication for use	• Prevention of diarrhoea due to diagnosed *Cryptosporidium parvum*, in farms with history of cryptosporidiosis. Administration should start in the first 24 to 48 hours of age. • Reduction of diarrhoea due to diagnosed *Cryptosporidium parvum*. Administration should start within 24 hours after the onset of diarrhoea. In both cases, the reduction of oocysts excretion has been demonstrated.

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(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	23/09/2020
Date product first authorised in the ReferenceMemberState (MRP only)	N/A
Concerned Member States for original procedure	AT, CY, CZ, DE, DK, EE, EL, HU, IE, IT, LT, LV, NL, NO, PL, PT, RO, SE, 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. Qualitative and quantitative particulars

The product contains halofuginone (as lactate salt) as the active substance (0.50 mg/ml), benzoic acid as preservative and the excipients lactic acid, tartrazine (colouring agent) and purified water.

The container/closure system is high-density polyethylene (HDPE) bottles of 300, 500 and 1000 ml (containing 290, 490 and 980 ml of the medicinal product, respectively), sealed with polyethylene terephthalate (PET) foil and closed with a screw cap made of polypropylene (PP). The medicinal product can be supplied with or without a 4 ml metering pump, made of PP with low-density polyethylene (LDPE) suction pipe.

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 several licensed manufacturing sites.

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 halofuginone lactate salt, is not described in Ph. Eur. 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 information on the active substance is provided according to the Active Substance Master File (ASMF) procedure.

Confirmation is provided regarding compliance of the finished product with the current Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products.

D. Control on intermediate products

Not applicable.

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, 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 sites have been provided demonstrating compliance with the specification.

F. 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 (30 months) when stored under the approved conditions.

Data submitted on in-use stability studies are considered sufficient to support an in-use shelf life of 6 months after opening.

G. Other Information

Not applicable.

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 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 the consumers.

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13(1), and bioequivalence with a reference product has been demonstrated, results of pharmacological studies are not required.

Toxicological Studies

As this is a generic application according to Article 13(1), and bioequivalence with a reference product has been demonstrated, results of toxicological studies are not required.

Excipients are commonly used in oral veterinary medicines.

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which shows that the most likely route of exposure is dermal through skin contact with the product when handling a contaminated bottle, cap or syringe (metering pump). Ocular exposure may result from accidental splashing.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines. The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the predicted environmental concentration of the VMP in soil (PEC_{soil}) is less than the limit value 100 µg/kg.

No risk for the environment is envisaged if the product is used according to SPC.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because bioequivalence with the reference product has been demonstrated.

MRLs

The active substance Halofuginone is an allowed substance as described in table 1 of the annex to Commission Regulation (EU) No 37/2010:

MRLs are listed below:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs (µg/kg)	Target tissues	Other provisions
Halofuginone	Halofuginone	Bovine	10	Muscle	Not for use in animals from which milk is produced for human consumption
			25	Fat	
			30	Liver	
			30	Kidney	

Withdrawal Periods

The same withdrawal periods than the reference product are proposed for the VMP, as follows:

Meat and offal: 13 days.

IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been accepted in accordance with section 7.1.c of the Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMEA/CVMP/016/00-Rev.3), efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

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