FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

NEOIVEN 500 000 IU/g powder for use in drinking water/milk replacer

Date: 25/06/2018

French agency for food, environnemental and occupational health safety– French Agency for Veterinary Medicinal Products
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MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0327/001/DC
Name, strength and pharmaceutical form	NEOIVEN 500 000 IU/g powder for use in drinking water/milk replacer
Applicant	Laboratorios e Industrias IVEN, S.A. Luís I, 56 28031 MADRID (España).
Active substance(s)	Neomycin
ATC Vetcode	QA07AA01.
Target species	Cattle (calves), pigs (weaned and fattening pigs), chickens, layer hen, ducks, turkeys, turkey hen, goose, quail and partridge.
Indication for use	For treatment of gastrointestinal infections caused by *E. coli* sensitive to neomycin.

MODULE 2

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	Generic application in accordance with Article 13 (3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	06/06/2018
Concerned Member States for original procedure	BG, ES, IT, PL, PT, 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 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 500 000 IU/g neomycin (as neomycin sulphate) as the active substance, and the excipient lactose monohydrate.
The product is packed in bags. The particulars of the container and controls performed are provided and are conformed 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 neomycin 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.

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 (after dilution in water) as detailed on the SPC has been supported by appropriate data. After dilution in milk, the product should be administrated immediately.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

The tested product is bioequivalent to the reference product, NEOMYCINE 50% VIRBAC, 500 MG/G, POWDER FOR ORAL SOLUTION marketed by VIRBAC.
An exemption from the requirement to provide a bioequivalence study was accepted in respect of 7.1.c) of the Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2).

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

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

Toxicological Studies

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

User Safety

The applicant has not provided a user safety assessment. It is considered as acceptable in view of the legal basis of the type of application and taking into account that the tested product and the reference product contain the same excipient.

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

Ecotoxicity

The environmental risk assessment was performed according to EMA and VICH guidance.

The applicant has provided a Phase II risk assessment performed in compliance with the relevant guidelines. However, due to specific properties of neomycin and technical difficulties, no DT50 values could be established. Therefore a default DT50 value of 1000 days has be used in the ERA.
The risk characterization for the soil and aquatic compartments indicate that no risk for environment is expected.

III.B Residues documentation

Residue Studies

The applicant has provided one residue study in weaned piglets at the recommended dose.
The applicant has provided one residue study in eggs.

MRLs

a. active substances

The active substance is included in table 1 of the MRL regulation 470/2009, as follows:

NEOMYCIN (including FRAMYCETIN)						
Marker residue	**Animal Species**	**MRL**	**Target Tissues**	**Other Provisions**	**Therapeutic Classification**	**Regulation**
Neomycin B	All food producing species	500 µg/kg 500 µg/kg 500 µg/kg 5000 µg/kg 1500 µg/kg 500 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 to fin fish. For porcine and poultry, the fat MRL relates to "skin and fat in natural proportions".	Anti-infectious agents/ Antibiotics	37/2010 of 22.12.2009
Neomycin B	All food producing species	500 µg/kg 500 µg/kg **5500 µg/kg** **9000 µg/kg** 1500 µg/kg 500 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 to fin fish. For porcine and poultry, the fat MRL relates to "skin and fat in natural proportions".	Anti-infectious agents/ Antibiotics	1056/2013 of 29/10/13

b. excipients

The MRL status of excipients of the product is indicated in the following table:

Excipient	MRL status	ADI
Lactose monohydrate	Out of scope	-

Withdrawal Periods

The test product and the reference product have the same qualitative and quantitative composition in active ingredient, are both administered by oral route and it has been accepted that they are bioequivalent. Therefore, the withdrawal periods of the reference product can apply to the tested product.
For the weaned piglets, the residue study provided by the applicant justifies a withdrawal period of three days.

Cattle.
Meat and offal: 14 days.

Pigs.
Weaned and fattening pigs: 3 days

Chickens, layer hen, ducks, turkeys, turkey hen, goose, quail and partridge.
Meat and offal: 14 days.
Eggs: zero days.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

The applicant has not provided a tolerance study which is acceptable because:

- the tested product and the reference product are bioequivalent,
- The tested product and the reference product are to be administered orally and contain the same excipient.

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

Resistance

An overview of the level of resistance to neomycin in target pathogens and commensal bacteria based on recent bibliographical data has been submitted. Adequate warnings have been implemented in section 5.1 of the SPC.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, 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.