Agencia Española de Medicamentos y Productos Sanitarios

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

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Rhemox 500 mg/g powder for use in drinking water for pigs, chicken broilers, duck broilers and turkeys for meat production

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0236/001/MR
Name, strength and pharmaceutical form	Rhemox 500 mg/g powder for use in drinking water for pigs, chicken broilers, duck broilers and turkeys for meat production
Applicant	Industrial Veterinaria, S.A. Esmeralda, 19 E-08950 Esplugues de Llobregat (Barcelona) Spain
Active substance(s)	Amoxicillin trihydrate
ATC Vet code	QJ01CA04
Target species	Pigs Chicken (broiler), duck (duck broiler) and turkey (turkey for meat production)
Indication for use	Pigs: Treatment of infections caused by strains of *Streptococcus suis* sensitive to amoxicillin. Chicken broilers, duck broilers and turkeys for meat production: Treatment of pasteurellosis and colibacillosis caused by strains of *Pasteurella spp*. and *Escherichia coli* sensitive to amoxicillin.

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	Mutual Recognition application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	17/06/2015
Date product first authorised in the Reference Member State (MRP only)	06/05/2008
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EL, FI, FR, HU, IE, IT, NL, NO, PL, PT, RO, SE, SI, SK, 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 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 Amoxicillin trihydrate 500 mg and sodium hexametaphosphate, sodium dihydrogen phosphate anhydrous, sodium carbonate and silica, colloidal anhydrous

The container/closure system are sachets of 400 g and1 kg. They are made of a complex film comprising an outer layer of polyester, an intermediate layer of aluminium and an inner layer of transparent polyethylene. The particulars of the containers and controls performed are provided and conform to the regulation.

The product is an establishe 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 amoxicillin trihydrate, 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.

Certificate of suitability referenced for Zhuhai United Laboratories Co. Ltd (R1-CEP 2006-039-Rev 00) and North China Pharmaceutical Group Semisyntech Co. Ltd R1-CEP 2004-074-Rev 00 are included.

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.

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<s> 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 claim of a immediate use after broaching and 24-hour stability after reconstitution is based on the demonstration of stability for a batch broached and stored in a dry place, protect from light and below 25 ºC.

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 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

In accordance with Article 13(1) of the Directive 2001/82/EC, as the bioequivalence between the test product and the reference product has been demonstrated, no further pharmacological data are required.

Toxicological Studies

In accordance with Article 13(1) of the Directive 2001/82/EC, as the bioequivalence between the test product and the reference product has been demonstrated, no further toxicological data are required.

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 in Phase II. The assessment concluded that the product does not pose a risk for the environment when it is used as recommended in the SPC.
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 depletion studies are provided because this is a generic application and the bioequivalence is demonstrated.

MRL

Amoxicillin is included in Table 1 of Annex of Council Regulation (UE) 37/2010 with the following MRL:

Pharmacologically active substance	Marker residue	Animal species	MRL	Target tissues	Therapeutic classification
Amoxicillin	Amoxicillin	All food producing species	50 µg/kg 50 µg/kg 50 µg/kg 50 µg/kg 4 µg/kg	Muscle Fat Liver Kidney Milk	Anti-infectious agents/Antibiotics

Withdrawal Periods

Based on the data provided above, the following withdrawal periods are justified:

Meat and offal:

Pigs: 6 days.
Broilers: 1 day.
Turkeys for meat production: 5 days.
Duck broilers: 9 days.

Not authorised for use in birds producing eggs for human consumption and within 4 weeks before onset of the laying period.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Pharmacology

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.

Tolerance in the Target Species of Animals

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.

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

Resistance

The applicant has revised the main European Monitoring Programmes of Antimicrobial Resistance to obtain updated data on amoxicillin resistance in different pathogens.

The information provided suggests that antimicrobial resistance to amoxicillin exists in different pathogens from producing animals.

Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies (pharmaceuticals and immunologicals)

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.

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.

Summary of change (Application number)	Approval date
Deletion of the special storage conditions according to the results of stability studies carried out with the new composition Extension of the shelf-life of the finished product after first opening until 3 months Change of the specification proposed for filling weight as IPC Change in the mixing time in the manufacturing process Update the approved specifications for related substances according to the current knowledge Reduce the testing frequency of the microbiological quality test from every 3 batches to every 10 batches Deletion of the uniformity of mass test from the specifications and to update the current specification for filling weight from 98-102% to NLT 100% The composition of the veterinary medicinal product has been changed in order to improve its solubility characteristics. ES/V/0236/A/007/G	07/07/2023
Deletion of two of the four pack sizes approved (100 and 300g) VNRA 22/874	07/07/2023

MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD
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