MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
E IGUALDAD

agencia española de
medicamentos y
productos sanitarios

DEPARTAMENTO DE
MEDICAMENTOS
VETERINARIOS

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

APSASOL AMOXICILINA 500 mg/g

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0276/001/MR
Name, strength and pharmaceutical form	(Italy,United Kingdom) APSASOL AMOXICILLIN TRIHYDRATE 500 mg/g Powder for use in drinking water for pigs, chickens, ducks and turkeys (Bulgaria, Croatia, Cyprus, , Hungary, Greece, Portugal, Poland, Romania) APSASOL AMOXICILLIN 500 mg/g Powder for use in drinking water for pigs, chickens, ducks and turkeys (Spain) APSASOL AMOXICILINA 500 mg/g polvo para administracion en agua de bebida para porcino, pollos, pavos y patos
Applicant	ANDRES PINTALUBA S.A. Polígono Industrial Agro-Reus C/ Prudenci Bertrana nº 5 43206 - REUS (Tarragona) SPAIN
Active substance(s)	Amoxicillin trihydrate
ATC Vet code	QJ01CA04
Target species	Pig, chicken broiler, duck broiler and turkey for meat production
Indication for use	Chicken broiler, duck broiler and turkey for meat production: Treatment of pasteurellosis and colibacillosis caused by strains of *Pasteurella* spp. and *Escherichia coli* sensitive to amoxicillin Pig: Treatment of infections caused by strains of *Streptococcus suis* 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).

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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	22/02/2017
Date product first authorised in the Reference Member State (MRP only)	25/07/2014
Concerned Member States for original procedure	BG, CY, EL, HR, HU, IT, PL, PT, RO, 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. Composition

The product contains 500 mg /g of Amoxicillin trihydrate as active substance and citric acid as excipient

The container/closure system are 400 g and 1 kg multi-layer bags made of low density polyethylene (EP quality)/ aluminium/ polyethylene terephthalate (inside / middle / outside layers). The bags are closed by heat sealing (triple sealing). The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation is justified.

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 amoxicillin trihydrate an established 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.

The quality of the active substance is corroborated by two CEPs, R1-CEP 2007-315-Rev 01 and R0-CEP 2012-078-Rev 02.

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 (pharmaceuticals)

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.

The demonstration of the batch to batch consistency is based on the results of six batches produced according to the method described in the dossier.

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 24-hour stability after dilution according to directions is based on the demonstration of stability in accordance with applicable European guidelines.

The claim of 1-month stability after first opening the immediate packaging is based on the demonstration of stability in accordance with applicable European guidelines.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

As this is a generic application according to Article 13, and the product can be considered bioequivalent to the reference product according to condition 7.1 c) of the "Guideline on the conduct of bioequivalence studies for veterinary medicinal products", results of of toxicological, pharmacological or clinical 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 and the environment.

III.A Safety Testing

Pharmacological Studies

Since the application has been submitted in accordance with Article 13(1) (Directive 2001/82/EC, as amended by Directive 2004/28/EC), results of pharmacological tests are not required.

The pharmacological details of this product are the same as those of the reference product.

Amoxicilin is a broad spectrum betalactamic antibiotic belonging to the aminopenicillins group with bactericidal activity. The antibacterial mechanism of action of amoxicillin consists of the inhibition of the biochemical processes of bacterial cell wall synthesis by selectively and irreversible blocking different enzymes involved in such processes, largely transpeptidase, endopeptidase and carboxypeptidase. The inadequate synthesis of the bacterial wall in susceptible species produces an osmotic imbalance which particularly affects growing bacteria (when bacterial wall synthesis processes are especially important), finally leading to lysis of the bacterial cell.

Absorption of oral amoxicillin is independent from food intake and peak plasma concentrations are reached rapidly in most animal species, from 1 to 2 hours after the product's administration.
Amoxicillin binds sparingly to plasma proteins and rapidly spreads to the body fluids and tissues. Amoxicillin is widely distributed in the extracellular compartment. Its distribution to the tissues is facilitated by its low binding rate to plasma proteins.
The metabolism of amoxicillin is limited to hydrolysis of the β-lactam ring, leading to the release of inactive penicillanic acid (20%). Biotransformation takes place in the liver.
Most amoxicillin is eliminated through the kidneys in active form. It is also excreted in small quantities in milk and bile.

Toxicological Studies

Since the application has been submitted in accordance with Article 13 (1) (Directive 2001/82/EC, as amended by Directive 2004/28/EC), results of toxicological tests are not required.

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User Safety

Given that this application is submitted in accordance with Article 13(1) of the Directive and that the generic and reference products are identical in terms of both formulation and use, no further risk for the user is expected. 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. The assessment concluded that in conclusion, the use of the APSASOL AMOXICILINA 500 mg/g in the conditions recommended in the Summary of Product Characteristics does not pose a risk for the environment. No Warnings are therefore required.

III.B Residues documentation

Residue Studies

Since this is a generic application submitted according to Article 13(1) of Directive 2001/82/EC and bioequivalence with the reference product has been demonstrated, the applicant is not required to provide the results from residue depletion studies.

MRLs

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

MRLs are listed below:

Active substance	Marker residue	Animal species	MRL (µg/ kg)	Target tissues	Other provisions	Therapeutic classification
Amoxicillin	Amoxicillin	All food producing species	50 50 50 50 4	Muscle Fat Liver Kidney Milk	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 species the fat MRL relates to 'skin and fat in natural proportions'. Not for use in animals from which eggs are produced for human consumption	Anti-infectious agents/Antibiotics

Withdrawal Periods

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

Meat and offal:

Pigs: 6 days

Chicken broilers: 1 day

Duck broilers: 9 days

Turkeys for meat production: 5 days

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

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IV. CLINICAL ASSESSMENT (EFFICACY)

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.

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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.

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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.

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