IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Citramox 500 mg/g powder for use in drinking water for chickens, turkeys, ducks and pigs

PRODUCT SUMMARY

EU Procedure number	IE/V/0326/001/DC
Name, strength and pharmaceutical form	Citramox 500 mg/g powder for use in drinking water for chickens, turkeys, ducks and pigs.
Active substance(s)	Amoxicillin trihydrate
Marketing Authorisation Holder	LABORATORIOS KARIZOO, S.A. Polígono Industrial La Borda Mas Pujades, 11-12 08140 – CALDES DE MONTBUI (Barcelona) Spain
Legal basis of application	Generic application in accordance with Article 13.1 of Directive 2001/82/EC, as amended.
Date of completion of procedure	18th June 2014.
Target species	Chickens, turkeys, ducks and pigs.
Indication for use	Treatment of infections in chickens, turkeys and ducks caused by bacteria susceptible to amoxicillin. Pigs: For the treatment of pasteurellosis
ATCvet code	QJ01CA04
Concerned Member States	AT, DE, DK, ES, NL, PL, SI, UK

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.

The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

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

II. QUALITY ASPECTS

A.Qualitative and Quantitative Particulars

The product contains the active substance amoxicillin 436 mg/g (as amoxicillin trihydrate 500 mg/g) and the excipient anhydrous citric acid.
The container/closure system consists of a 400 g or 1 kg thermosealed bag made of polyester, aluminium and polyethylene complex.
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 at 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 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.

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.

D.Control on Intermediate Products

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.

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 has been provided.

Batch analytical data from the proposed production site has 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 when stored under the approved conditions.

G.Other Information

Not applicable

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

This is a generic application submitted in accordance with Article 13.1 of Directive 2001/82/EC, as amended. The product is a powder for oral administration after mixing with drinking water, to pigs, chickens, turkeys and ducks.
The active substance is amoxicillin trihydrate which is a bactericidal antimicrobial belonging to the β-lactam class. The product contains amoxicillin trihydrate at a concentration of 500 mg/g powder.
The reference product cited is Amoxinsol 50% w/w powder for oral solution (Vetoquinol UK Limited).

As this is a generic application according to Article 13.1, 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 considered to be identical to the reference product.

Warnings and precautions as listed on the product literature are in line with those approved for the reference product and other similar products recently authorised via European procedures. The warnings are considered to be adequate to ensure safety of the product to users, the environment and consumers.

Safety Testing

Pharmacological Studies

No pharmacological studies were provided. The formulation of the product is the same as that of the reference product. Consequently, no *in-vivo* comparative bioavailability studies were required. The product can be accepted as being bioequivalent with the reference product.

Toxicological Studies
No toxicological study data was provided. Given that the product can be accepted as being bioequivalent with the reference product, the omission of toxicological data can be accepted.

User Safety

No formulation specific user safety assessment was provided. As the formulation of the product is the same as that of the reference product, no increased risk to the user of the product is expected when compared with that of the reference product.

The user safety warnings are in line with those approved for the reference product and other similar products recently authorised via European procedures.

Warnings are considered adequate to ensure user safety when handling, storing, administering and disposing of the product.

Ecotoxicity
Phase I

A Phase II ERA is required as the Phase I assessment showed that the predicted environmental concentration for the main metabolite of amoxicillin exceeded the relevant trigger value for a phase II risk assessment.

Phase II Tier A
A Phase II Tier A assessment was conducted.

The applicant provided studies in order to characterise any risk to the terrestrial and aquatic compartments of the environment.

Based upon the data provided, it can be accepted that the product will not present an unacceptable risk for the environment and a Tier B assessment is not necessary.

Conclusion
Based on the data provided, the product is not expected to pose an unacceptable risk for the environment when used according to the SPC.

Residues documentation

Residue Studies
No residue depletion studies were conducted because the formulation of the product is the same as that of the reference product and is intended for administration to the same target species at the same dose rates using the same administration route (drinking water).

MRLs
The pharmacologically active substance (amoxicillin) is included in table 1 of Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance	Marker residue	Animal species	MRL	Target tissue	Other relevant provisions	Therapeutic classification
Amoxicillin	Amoxicillin	All food-producing species	50 microgram/kg 50 microgram/kg 50 microgram/kg 50 microgram/kg 4 microgram/kg	Muscle Fat Liver Kidney Milk	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

Given that the formulation of the product can be accepted as being the same as that of the reference product, the same withdrawal periods approved for the reference product were applied; namely,

Meat and offal:
Chickens 1 day
Ducks 9 days
Turkeys 5 days
Pigs 2 days

The product is not authorised for use in laying birds producing eggs for human consumption or within 3 weeks of the onset of lay.

IV. CLINICAL ASSESSMENT

As this is a generic application according to Article 13.1 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.

Pre-Clinical StudiesPharmacology

No pharmacological studies were provided. The formulation of the product is the same as that of the reference product. Consequently, no *in-vivo* comparative bioavailability studies were required. The product can be accepted as being bioequivalent with the reference product.

Tolerance in the Target Species of Animals
The formulation of the product is the same as that of the reference product and is intended for oral administration in the drinking water. Consequently, no difference with the reference product in terms of target animal tolerance is expected.
The omission of target animal tolerance studies can therefore be accepted.

Resistance

The product contains the same amount of the active substance (amoxicillin trihydrate) as the reference product and is to be administered to the same target species, at the same dose rate as approved for the reference product.
Consequently, no increased risk for development of antimicrobial resistance is anticipated when compared with that which exists for the reference product.
Adequate warnings and precautions appear on the product literature to ensure prudent use of the product.

Clinical Studies
The product meets the guideline requirements to justify the omission of *in-vivo* bioequivalence studies. Consequently, no clinical study data was required.

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 is acceptable.

VI. 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 HPRA website.

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.