IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Citramox 1000 mg/g powder for use in drinking water for chickens, ducks, turkeys and pigs

PRODUCT SUMMARY

EU Procedure number	IE/V/0353/001/DC
Name, strength and pharmaceutical form	Citramox 1000 mg/g powder for use in drinking water for chickens, ducks, turkeys and pigs
Active substance(s)	Amoxicillin Trihydrate
Applicant	Laboratorios Karizoo, S.A. P.I. La Borda, Mas Pujades 11-12 Caldes De Montbui 08140 Spain
Legal basis of application	Hybrid application in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of Authorisation	15/07/2016
Target species	Chickens, ducks, turkeys 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	CZ, EL, ES, HU, NL, PL, PT, RO, SK, UK RUP CMS: CY, DE, IT, LT, LV, SI

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 871.2 mg/g amoxicillin (as amoxicillin trihydrate 1000 mg/g) as the active substance. There are no

excipients in this product.
The container/closure system consists of a thermosealed bag made of polyester, aluminium and polyethylene complex of 200 g, 500 g or 1 kg in size.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
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 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 ASSESSMENT

Pharmacological Studies
As this was a generic application submitted in accordance with Article 13 of Directive 2001/82/EC, as amended and bioequivalence with the reference product was accepted, the applicant was not required to provide the results of pharmacological studies.

Toxicological Studies
As this was a generic application submitted in accordance with Article 13 of Directive 2001/82/EC, as amended and bioequivalence with the reference product was accepted, the applicant was not required to provide the results of toxicological studies.

User Safety
No user safety assessment was provided. Given that the candidate formulation was accepted as being essentially similar to the reference product and is to be indicated for use in the same target species using the same posology and route of administration, it was therefore accepted that the user of the product will not be exposed to a greater amount of the candidate formulation when compared to the reference product when handling, using, storing and disposing of the product.
The proposed user safety warnings are in line with those approved for the reference product and other similar products recently authorised via European procedures.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

Phase I

The applicant provided a Phase I environmental risk assessment. Based on the results of the Phase I assessment, it was concluded that a Phase II assessment was required.

Phase II

The applicant provided a Phase II environmental risk assessment. Based on the results of the Phase II assessment, it was concluded that the product will not present an unacceptable risk for the environment when stored, handled, administered and disposed of in accordance with the recommendations included in the SPC.

Conclusion

The product is not expected to pose an unacceptable risk for the environment when stored, handled, administered and disposed of in accordance with the recommendations included in the SPC.

III.B Residues Documentation

Residue Studies

No residue study data was provided. Given that bioequivalence between candidate and reference product formulations was satisfactorily demonstrated, the absence of residue depletion studies conducted with the candidate formulation could be accepted, as the depletion of residues is not expected to differ between candidate and reference formulations.

It was concluded that the candidate formulation will not present an unacceptable risk for the consumer of products derived from animals administered the product.

MRLs

Amoxicillin is listed in Table I of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance	**Marker residue**	**Animal species**	**MRL**	**Target tissue**
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

Withdrawal Periods

The candidate formulation was accepted as being bioequivalent to the reference product. Both products are to be administered using the same posology and route of administration in the same target species. It was therefore concluded that no difference in depletion of residues in the target animal is to be expected.

Consequently, it was accepted that the withdrawal periods for meat and offal approved for the reference product, are also applicable to this generic product and are considered adequate to ensure consumer safety.
The product is not authorised for use in laying birds producing eggs for human consumption and within 3 weeks before the onset of the laying period.

IV. CLINICAL ASSESSMENT

As this was a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies were not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Resistance

Amoxicillin is a time-dependent bactericidal antibiotic which acts by inhibiting the synthesis of bacterial cell walls during bacterial replication. There are three main mechanisms of resistance to beta-lactams: beta-lactamase production, altered expression and/or modification of penicillin binding proteins (PBP), and decreased penetration of the outer membrane.

Given that bioequivalence with the reference product has been demonstrated and the candidate formulation is intended for administration to the same target species, using the same posology and route of administration as the reference product, it was accepted that any risk for the development of antimicrobial resistance will be the same for the candidate formulation as already exists for the reference product.

The SPC includes appropriate prudent use advice and information on possible mechanisms of resistance development.

Tolerance in the Target Species of Animals
No target animal tolerance studies were conducted. Given that this was a generic application and the candidate formulation will be administered to the same target species using the same posology and route of administration already approved for the reference product, it was concluded that no difference in tolerance in the target species is to be expected between candidate and reference product formulations. The omission of target animal tolerance data was therefore accepted.

IV.B Clinical Studies

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

Changes:
None.