IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Amatib 800 mg/g oral powder for pigs and chickens

PRODUCT SUMMARY

EU Procedure number	IE/V/0346/001/DC
Name, strength and pharmaceutical form	Amatib 800 mg/g oral powder for pigs and chickens
Active substance(s)	Amoxicillin Trihydrate
Applicant	Krka d.d., Novo mesto Šmarješka cesta 6 8501 Novo mesto Slovenia
Legal basis of application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of procedure	17 June 2015
Target species	Pigs and chickens (chicks, broilers, pullets, breeders).
Indication for use	Pigs: Treatment of respiratory tract infections, gastro-intestinal tract infections, meningitis, arthritis and secondary infections caused by micro-organisms susceptible to amoxicillin. Chickens: Treatment of respiratory tract infections and gastro-intestinal tract infections (other than salmonella infections) caused by micro-organisms susceptible to amoxicillin.
ATCvet code	QJ01CA04
Concerned Member States	BE, BG, CZ, DE, EE, ES, FR, HR, HU, LV, LT, NL, PL, PT, RO, SI, SK, 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 possibility for hypersensivity/allergic reactions is indicated in the SPC.

The product is considered to be 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 amoxicillin 697 mg/g (as amoxicillin trihydrate 800 mg/g) and the excipients sodium carbonate monohydrate, sodium citrate and silica, colloidal anhydrous.
The container/closure system consists of thermosealed bags of PET/Al/PE containing 100 g, 250 g or 500 g powder.

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 for the manufacturing process has 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 has 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 has 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 has 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 application was submitted in accordance with Article 13.1 of Directive 2001/82/EC, as amended (a generic application).

The reference product cited was Paracillin SP 800 mg/g prašek za peroralno raztopino za perutnino in prašiče as authorised in Slovenia (i.e. a European reference product).

The formulation was accepted as being qualitatively and quantitatively identical to the reference product in terms of the active substance (amoxicillin trihydrate) but includes different excipients.

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

III.A Safety Testing

Pharmacological Studies

Essential similarity with the reference product was claimed and an exemption from the requirement to demonstrate *in-vivo* bioequivalence with the reference product was accepted. While the candidate formulation differs to that of the reference product in terms of the excipients, it was accepted that the excipients will not affect the rate of gastric transit of, or gastrointestinal permeability to the active substance amoxicillin trihydrate. Accordingly, bioequivalence between candidate and reference products could be accepted.

Toxicological Studies

Given that essential similarity with a reference product could be accepted, the results of toxicological studies were not required.

Microbiological Studies

Given that essential similarity with a reference product could be accepted, the results of microbial studies were not required.

User Safety

The applicant provided a user safety assessment. Given that essential similarity with the reference product was demonstrated, the candidate formulation is not expected to present any new or greater risk for the user when compared with that of the reference product when handled, stored, administered and disposed of in accordance with the proposed SPC.

Warnings and precautions as listed on the product literature are considered to be adequate to ensure safety to users of the product.

Environmental Risk Assessment

Phase I
The Phase I assessment showed that $PEC_{soil\ initial}$ values exceed the trigger value of 100 µg/kg for pigs and for broiler chickens and that a phase II assessment was required.

Phase II
A phase II assessment was conducted in accordance with relevant guidance.For phase II studies and the phase II ERA, the applicant focussed on parent compound amoxicillin trihydrate, rather than considering transformation/degradation products. This was appropriately justified.

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

III.B Residues Documentation

Residue Studies

No residue data was provided. Given that essential similarity with the reference product was claimed and an exemption from the requirement to demonstrate *in-vivo* bioequivalence with the reference product was accepted, it was concluded that the rate of depletion of residues from the candidate formulation following oral ingestion will be the same as that for the reference product.

MRLs

The active substance (amoxicillin) is included in Table I of the Annex to Commission Regulation (EU) No 37/2010 as follows:

Pharmacologically active substance	***Marker residue***	***Animal species***	***MRL***	***Target tissues***	***Other provisions***
Amoxicillin	*Amoxicillin*	*Al food producing species.*	*50 µg/kg* *50 µg/kg* *50 µg/kg* *50 µg/kg* *4 µg/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.*

Withdrawal Periods

Given that essential similarity with a reference product was demonstrated, it was concluded that the withdrawal periods approved for the reference product are also applicable for the candidate formulation.

Withdrawal periods of 1 day for chickens and 2 days for pigs were accepted.

IV. CLINICAL ASSESSMENT

As this was a generic application according to Article 13.1, and bioequivalence with a reference product has been demonstrated, efficacy studies were not required. The efficacy claims for this product are in line with those approved for the reference product and other similar products recently authorised via European procedures.

IV.APre-Clinical Studies

Pharmacology

Essential similarity with the reference product was claimed and consequently, an exemption from the requirement to demonstrate *in-vivo* bioequivalence with the reference product was accepted. While the candidate formulation differs to that of the reference product in terms of the excipients, it was accepted that the excipients will not affect the rate of gastric transit of, or gastrointestinal permeability to the active substance amoxicillin trihydrate. Accordingly, bioequivalence between candidate and reference products could be accepted.

Tolerance in the Target Species of Animals

Given that the candidate formulation includes the same concentration of amoxicillin trihydrate as the reference product and is intended for administration to the same target species using the same posologies and route of administration (drinking water), it was accepted that tolerance to the active substance does not present a concern.

Further, it was accepted that the excipients do not present a risk in terms of target animal tolerance.

The product literature accurately reflects the type and incidence of adverse effects which might be expected (hypersensitivity/allergic-type reactions).

Resistance

Bioequivalence with the reference product has been satisfactorily justified. In addition, the candidate formulation will be administered to the same target species using the same posologies and route of administration already approved for the reference product. Consequently, it could be accepted that no difference in the risk of resistance development is to be expected between the candidate and reference product formulations.

Appropriate prudent use statements and warnings are included in the SPC and product literature.

IV.B Clinical Studies

Laboratory Trials

Field Trials

Essential similarity with the reference product was claimed and an exemption from the requirement to demonstrate *in-vivo* bioequivalence with the reference product was accepted.

Given that the candidate formulation includes the same concentration of amoxicillin trihydrate as the reference product and will be administered to the same target species using the same posologies and route of administration (drinking water), it was accepted that the effectiveness of the product should be the same as that for the reference product.

The proposed indications and posologies are in line with those approved for the reference product and other similar products recently authorised via European procedures.

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.