IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Redymox 150 mg/ml suspension for injection for cattle, sheep, pigs, dogs and cats

PRODUCT SUMMARY

EU Procedure number	IE/V/0566/001/DC
Name, strength and pharmaceutical form	Redymox
Active substances(s)	Amoxicillin trihydrate
Applicant	Univet Limited Tullyvin Cootehill Co. Cavan. Ireland
Legal basis of application	Generic application (Article 18 of Regulation (EU) 2019/6)
Date of completion of procedure	02/07/2025
Target species	Cattle,Sheep,Pigs,Cats,Dogs
Indication for use	For the treatment of infections caused by a wide range of Gram-positive and Gram-negative pathogenic bacteria including: *Bacillus anthracis* *Bacillus cereus* *Bordetella bronchiseptica* *Clostridium* spp. *Corynebacterium* spp. *Erysipelothrix rhusiopathiae* *Escherichia coli* *Fusiformis* spp. *Haemophilus* spp. *Pasteurella* spp. *Proteus mirabilis* *Salmonella* spp. Non-penicillinase producing Staphylococci Non-penicillinase producing Streptococci.
ATCvet code	QJ01CA04
Concerned Member States	N/A
Withdrawn CMS during decentralised procedure	NL

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (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 relevant articles of Regulation (EU) 2019/6. 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), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

I. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.
It has been shown that the VMP can be safely used in the target species; the reactions observed are indicated in the SPC.

The VMP 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 VMP 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. Qualitative and Quantitative Particulars
The product contains amoxicillin 150 mg (equivalent to amoxicillin trihydrate 172 mg) and the excipients aluminium distearate and propylene glycol dicaprylocaprate. The container/closures are standard for this pharmaceutical form and are detailed in the SPC. 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.

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 of 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 has been submitted in accordance with Article 18 of Regulation (EU) 2019/6 (generic veterinary medicinal product).
The applicant has cited a suitable reference product, '*Betamox 150 mg/ml suspension for injection*'which has been authorised for in excess of ten years and can be accepted as a valid reference product in this generic application. The applicant claimed a waiver from the requirement to provide *in vivo* bioequivalence data based on compliance with conditions set out in section 7.1d of the CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products. This waiver was accepted.
As bioequivalence with a suitable reference product has been accepted, the results of safety tests are not required. The safety aspects of this product are considered to be the same as the reference product.
Warnings and precautions as listed on the product literature are similar to those of the reference product and are adequate to ensure safety of the product to users, consumers and the environment.

III. SAFETY ASSESSMENT

III.A Safety Testing

Pharmacological Studies

No pharmacodynamic or pharmacokinetic data were presented. Given the legal basis of this application, and accepted bioequivalence with the reference product, omission of these data was accepted.

Toxicological Studies

No toxicological study data were presented. Given the legal basis of this application, and accepted bioequivalence with the reference product, omission of these data was accepted.

User Safety

The formulations of the product and reference product are the same in terms of active substance and excipients. The candidate product is intended to be administered by the same routes of administration at the same dosage and for the same indications for use in the same species as the reference product.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product, as follows:

"*Penicillin and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillin may lead to cross sensitivity to cephalosporins and vice versa. Allergic reaction to these substances can occasionally be serious.*

People with known hypersensitivity to amoxicillin trihydrate should avoid contact with the veterinary medicinal product. Administer the veterinary medicinal product with caution.

Handle this product with great care to avoid exposure, taking all recommended precautions. If you develop symptoms following exposure, such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips and eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

In case of accidental self-administration/ self-injection ingestion/ spillage onto skin, seek medical advice immediately and show the package leaflet or the label to the physician."

Environmental Risk Assessment

A Phase I and Phase II environmental risk assessment has been provided by the applicant.

Phase I

A Phase II ERA is required as the Phase I assessment showed that PECsoil initial exceeds the trigger value of 100 µg/kg soil for cattle (>2 years) weaner pigs and fattening pigs. The highest PEC_{soil} initial value of 152.05 µg/kg for amoxicillin was determined for weaner pigs. Based upon the PEC_{soil} initial values presented, a phase II risk assessment was required.

Phase II

A Phase II Tier A assessment was conducted the results of which are summarised below.

Note: The transformation product amoxicillin penicilloic acid is the principal degradation product of amoxicillin and is formed first on the degradation pathway, with subsequent degradation to other degradation products. Consequently, it was concluded that amoxicillin penicilloic acid provides a summative representation of all subsequent amoxicillin trihydrate degradation products and is appropriate for the purpose of characterising fate and effects of environmental exposure to amoxicillin trihydrate in a phase II ERA.

Physico-chemical properties	
Study type	**Result**
Vapour pressure	3.6×10^{-16} Pa (calculated)
Water solubility	79.9 g/l
Dissociation constants in water (pKa)	$pKa_1 = 8$ $pKa_2 = 10.1$
n-Octanol/Water Partition Coefficient ($logP_{ow}$)	$logP_{ow} = -2.2$ (main component) $logP_{ow} = -0.51$-0.46 (minor components/impurities)

Environmental fate	
Soil Adsorption/Desorption	Koc (mean) = 66.7 cm^3/g
Aerobic and Anaerobic Transformation in Soil	DT_{50} (geometric mean) = 1.6 days

Effect studies			

Study type	Endpoint	Result	Unit
Algae growth inhibition test/ *Anabaena flos-aquae*	EC50 (72 h)	172	mg/l
Daphnia sp. immobilisation	EC50 (48 h)	>1,000	mg/l
Fish, acute toxicity/ *Danio rerio* (zebra fish)	LC50	1,000	mg/l
Soil microorganisms: Nitrogen transformation test (28 days)	% effect	<25%	
Terrestrial Plants, growth test	EC50	1,152	mg/kg
Earthworm/*Eisenia foetida* reproduction	NOEC	≥2,000	mg/kg

Risk characterisation
The Predicted Environmental Concentration (PEC) for each compartment was calculated in accordance with guideline requirements. Using the relevant assessment factors, predicted no effect concentrations (PNECs) were calculated and compared with the PEC values to determine a risk quotient (RQ) for each compartment.

Risk quotients were determined for the most susceptible organisms in each environmental compartment. The risk characterisation for amoxicillin penicilloic acid resulted in risk quotients below 1 for the surface water and soil compartments indicating that the product will not pose a risk to those compartments when used as recommended. As the refined $PEC_{groundwater}$ values were below the trigger value of 0.1 µg/L (drinking water standard established in the EU) and as the most sensitive taxa in the surface water compartment were daphnids/fish with $PNEC_{surfacewaters}$ of 1,000 µg/L, an assessment of the risk to groundwater ecosystems and human health was not required. The risk for drinking water and groundwater organisms was considered to be acceptable.

PBT Assessment
An assessment of the main degradation product, amoxicillin penicilloic acid, in terms of potential for Persistence, Bioaccumulation and Toxicity (PBT) for the environment or whether it may be considered as being very Persistent and very Bioaccumulative (vPvB) was performed. Amoxicillin penicilloic acid is not considered to be either PBT or vPvB.

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.

III.B Residues Documentation

Residue Studies
No residue depletion studies were conducted because no difference in residue depletion between the candidate and reference products was anticipated.

MRLs
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 provision
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	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'

Withdrawal Periods
Based on the data provided, the following withdrawal periods are justified:
Cattle
Meat and offal: 18 days.
Milk: 48 hours.
Sheep
Meat and offal: 7 days.
Do not use in sheep producing milk for human consumption.

Pigs
Meat and offal: 14 days.

IV. CLINICAL ASSESSMENT

IV.A Pre-Clinical Studies
Tolerance in the Target Species of Animals
The product literature accurately reflects the type and incidence of adverse effects which might be expected.

Resistance
Adequate warnings and precautions appear on the product literature.

IV.B Clinical Studies
As this is a generic application according to Article 18 of Regulation (EU) 2019/6, and bioequivalence with a reference product has been accepted, 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 VMP 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 VMP 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 VMP. The current SPC is available in the Union Product Database (UPD).
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 VMP.