IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Qivitan 25 mg/ml suspension for injection for cattle and pigs

PRODUCT SUMMARY

EU Procedure Number	IE/V/0479/001 (formerly UK/V/0602/001)
Name, Strength, Pharmaceutical Form	Qivitan 25 mg/ml suspension for injection for cattle and pigs
Active Substances(s)	Cefquinome (as sulfate)
Applicant	Industrial Veterinaria S.A., Esmeralda 19, Esplugues De Llobregat, Barcelona, 08950, Spain
Legal Basis of Application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Target Species	Cattle,Pigs
Indication For Use	For the treatment of bacterial infections in cattle and pigs caused by the Gram positive and Gram negative microorganisms sensitive to cefquinome. <u>Cattle:</u> Respiratory disease caused by Pasteurella multocida and Mannheimia haemolytica. Digital dermatitis, infectious bulbar necrosis and acute interdigital necrobacillosis (foul in the foot). Acute E.coli mastitis with signs of systemic involvement. <u>Calves:</u> E.coli septicaemia in calves <u>Pigs:</u> For the treatment of bacterial infections of the lungs and respiratory tract caused by Pasteurella multocida, Haemophilus parasuis, Actinobacillus pleuropneumoniae, Streptococcus suis and other cefquinome-sensitive organisms. Mastitis-Metritis-Agalactia syndrome (MMA) with involvement of E.coli, Staphylococcus spp., Streptococcus spp. and other cefquinome sensitive organisms. <u>Piglets:</u> Reduction of mortality in cases of meningitis caused by Streptococcus suis. For the treatment of: Arthritis caused by Streptococcus spp., E. coli and other cefquinome-sensitive organisms. ***Epidermitis (mild or moderate lesions) caused by Staphylococcus hyicus.***
ATC Code	QJ01DE90
Date of conclusion of the decentralised procedure	23 November 2016 (UK) 27 January 2017 (IE)
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	AT, BE, HR, CY, DE, EL, HU, IE (now RMS), IT, NL, PL, PT, RO, SK, SI, ES UK added via RMS change

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

This was an application for a generic product, in accordance with Article 13(1) of Directive 2001/82/EC, as amended. The reference product is Cobactan 2.5% w/v, Suspension for Injection for Cattle and Pigs authorised in the UK since 1993. The applicant is exempt from providing bioequivalence studies in accordance with paragraph 7.1.d) of the Guideline on the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMA/CVMP/016/00-Rev 2) – the formulation is identical to the reference product.

The product is indicated for use in cattle and pigs for the treatment of bacterial infections caused by the Gram positive and Gram negative microorganisms sensitive to cefquinome. For cattle, this includes respiratory disease caused by *Pasteurella multocida* and *Mannheimia haemolytica*; digital dermatitis, infectious bulbar mecrosis and acute interdigital necrobacilliosis (foul in the foot); and *E.coli* septicaemia in calves. In pigs, the product is used for the treatment of bacterial infections of the lungs and respiratory tract caused by *Pasteurella multocida, Haemophilus parasui, Actinobacillus pleuropneumoniae, Streptococcus suis* and other cefquinome-sensitive organisms. In pigs, it is also indicated for Mastitis-Metritis-Agalactia syndrome (MMA) with involvement of *E.coli, Staphylococcus spp, Streptococcus spp*, and other cefquinome sensitive oragisms. In piglets, it is used for reduction of mortality in cases of meningitis caused by *Streptococcus suis* and for the treatment of arthritis caused by *Streptococcus spp, E.coli*, and other cefquinome-sensitive organisms and for epidermitis (mild or moderate lesions) caused by *Staphylococcus hyicus*. The dosage and frequency of administration varies depending on the species and indication to be used for (refer to the SPC[1] for full dosage details).

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the product can be safely used in the target species, any 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 [1] 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.

[1] Efficacy – The production of a desired or intended result.

II. QUALITY ASPECTS

II.A. Composition

The product contains cefquinome 25 mg (equivalent to 29.64 mg cefquinome sulfate) and the excipient ethyl oleate.

The container/closure system consists of Type II glass vials with a fluro polymer coated rubber stopper and sealed with an aluminium cap. The vials contain 50 ml, 100 ml, or 250 ml and come in cartons containing 1, 6 or 12 vials. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation and the absence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method is a simple process and consists of filtering of the excipient, followed by mixing with the active substance before filling into the primary packaging. The active substance is already sterile and the excipient is heat sterilised prior to mixing.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is cefquinome sulfate, an established active substance. It is manufactured in accordance with the principles of good manufacturing practice in accordance with an Active Substance Master File (ASMF) to the applicant's specification.

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 excipient ethyl oleate is controlled to the specificationin the current Ph. Eur. monograph.

II.C.4. Substances of Biological Origin

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.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 have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control tests on the finished product include those for appearance, density, particle size, identity and content of the active substance and sterility.

II.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.
The claim of a 28 day stability after opening is based on the demonstration of stability for a batch broached and stored as per the SPC. Full shelf-life testing after 14 and 28 days showed that batch fully met the shelf-life specification.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years
Shelf-life after first opening of the immediate packaging: 28 days
Protect from light.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

Due to the nature of the application, pharmacological and toxicological data are not required.

III.A Safety Documentation

User Safety

A user risk assessment was provided in compliance with the relevant guideline. On the basis that generic product is essentially similar to the reference product it is concluded that the hazard, exposure and hence risk to the user will be the same for both products. The same user warnings as authorised for the reference product appear on the SPC. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

Cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross sensitivity to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.

1. Do not handle this veterinary medicinal product if you know you are sensitized, or if you have been advised not to work with such preparation.
2. Handle this veterinary medicinal product with great care to avoid exposure, taking all recommended precautions.
3. 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 or eyes or difficulty with breathing, are more serious symptoms and require urgent medical attention.

Wash hands after use.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:

The assessment stopped at Question 17, where the PEC_{soil} values have been calculated for all categories of indicated target species and scenarios. The initial predicted environmental concentration (PEC) in soil is less than 100 µg/kg. A Phase II ERA was not required. The product is not expected to pose a risk for the environment when used in accordance with the recommendations included in the SPC.

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were conducted because the product is identical in formulation to the reference product. Therefore, the same withdrawal periods as those approved for the reference product apply:

Cattle:
Meat and offal: 5 days
Milk: 24 hours

Pigs:
Meat and offal: 3 days

MRLs

Cefquinome is listed in Table 1 of Regulation 37/2010 and MRLs have been established for edible tissues and milk The marker substance is cefquinome.

MRLs are listed below:

	Bovine	Porcine
Muscle	50 µg/kg	50 µg/kg
Liver	100 µg/kg	100 µg/kg
Kidney	200 µg/kg	200 µg/kg
Fat / skin	50 µg/kg	50 µg/kg
Milk	20 µg/kg	N/A

Withdrawal Periods

Based on the data provided, a withdrawal period of 5 days for meat in cattle and 24 hours for milk are justified. A withdrawal period of 3 days for meat is justified.

IV. CLINICAL ASSESSMENT

On the basis of essential similarity to the reference product in accordance with paragraph d) of Section 7.1 of the 'Guidelines for the conduct of bioequivalence studies for veterinary medicinal products', the applicant was exempt from providing bioequivalence studies or any additional clinical studies.

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 of the product is favourable.