Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Shotaflor 300 mg/ml solution for injection for pigs
Florfenicol

PuAR correct as of 17/04/2018 when RMS was transferred to DE. Please contact the RMS for future update

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0316/001/MR
Name, strength and pharmaceutical form	Shotaflor 300 mg/ml solution for injection for pigs Florfenicol
Applicant	Virbac S.A. 1ère avenue 2065 m L.I.D. 06516 Carros Cedex France
Active substance(s)	Florfenicol
ATC Vetcode	QJ01BA90
Target species	Pigs
Indication for use	Treatment of acute outbreaks of respiratory disease caused by strains of *Actinoba cillus pleuropneumoniae* and *Pasteurella multocida* susceptible to florfenicol.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	17 October 2008
Date product first authorised in the Reference Member State	05 February 2008
Concerned Member States for original procedure	Austria Belgium Denmark France Germany Greece Ireland Italy Netherlands Portugal Spain

I. SCIENTIFIC OVERVIEW

Shotaflor 300 mg/ml solution for injection for pigs florfenicol contains the active substance florfenicol. The product is authorised to be used in pigs, for the treatment of acute outbreaks of respiratory disease caused by strains of *Actinoba cillus pleuropneumoniae* and *Pasteurella multocida* susceptible to florfenicol. The product is administered intramuscularly and the recommended dose is 15 mg/kg.

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 slight reactions observed are indicated in the SPC (Summary of Product Characteristics).

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. Composition

The product contains florfenicol as an active substance and excipients dimethyl sulfoxide, propylene glycol and macrogol 400.

The container/closure system consists of amber glass (Type I) bottles of normal capacity 50, 100 or 250 ml, closed with bromobutyl rubber stopper and aluminium seal.

The choice of the formulation is justified.

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 from 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 florfenicol is an established active substance and supporting data have been provided in the form of a European Drug Master File (EDMF). It is considered that the manufacturing process is adequately controlled and the active substance specification has been suitably justified.

D. 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.

E. Control on intermediate products

There are no intermediate products.

F. 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.

G. 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 2 year shelf life.

In-use stability testing has been carried out on fresh and aged samples. This is adequate to justify a 28 day in-use shelf life.

H. Genetically Modified Organisms

Not applicable

J. Other Information

Special precautions for storage:
No special warnings for storage

Shelf life
Shelf-life of the veterinary medicinal product as packaged for sale: 2 years

Shelf-life after first opening the immediate container: 28 days

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

Pharmacological Studies

As this is a generic application according to Article 13.1, and bioequivalence with a reference product has been demonstrated, results of pharmacological tests are not required. The pharmacological aspects of this product are identical to the reference product. Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users.

Toxicological Studies

As this is a generic application according to Article 13.1, and bioequivalence with a reference product has been demonstrated, results of toxicological tests are not required.

The toxicological aspects of this product are identical to the reference product. Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users.

User Safety

As bioequivalence has been demonstrated with the reference product and the two products are of the same pharmaceutical form and the active ingredients are of the same qualitative and quantitative composition, there is no requirement to submit any additional safety data.

The following operator warnings are included in the SPC and product literature: Care should be taken to avoid accidental self-injection.

Ecotoxicity

The environmental risk assessment was carried out in accordance with VICH Phase 1 guidelines. The product is indicated for use in pigs to treat respiratory disease. The product is administered by parenteral injection and residues of florfenicol will reach the soil environment either when manure from treated animals is spread onto land or when animals on pasture excrete the residues in urine and faeces. The PEC_{soil} values for fattening animals and sows were below 100 μg/kg using a default of 50% for the proportion of animals treated. For weaner pigs the PEC_{soil} value were below 100 μg/kg when 30 % of animals were treated. These values indicate that exposure is not considered extensive and a Phase II assessment is not required. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

As the formulations of the reference product and Shotaflor 300 mg/ml solution for injection for pigs florfenicol, are not identical and neither are they aqueous solutions, differences in residues at the injection site could occur. As a result, the applicant submitted one residue depletion studies in pigs. This residue depletion study was conducted in pigs following intramuscular injection. The animals were divided into different groups and the product was injected by deep intramuscular injection in the neck. The study concluded that after 4 days withdrawal period, all core injection site samples had residues above the muscle MRL but residues were below the LOQ (Limit of Quantification) from 8 days onwards. Residues in all other tissues including the surrounding injection sites were below their respective MRLs at all time points.

MRLs

Florfenicol is listed in Annex I of Council Regulation 2377/90. The marker substance is florfenicol-amine.

MRLs are listed below:

Muscle	300 µg/kg
Liver	2000 µg/kg
Kidney	500 µg/kg
Fat+skin	500 µg/kg

Withdrawal Periods

Based on the data provided, the following withdrawal periods are included on the SPC:
Pigs: Meat and offal: 18 days

IV CLINICAL ASSESSMENT (EFFICACY)

Pharmacology

As this is a generic application according to Article 13.1, and bioequivalence with a reference product has been demonstrated, results of toxicological tests and pharmacological tests are not required.

Tolerance in the Target Species of Animals

Since the application is made in accordance with Article 13 (1) of Directive 2001/82/EC, no systemic tolerance data was submitted. However, the applicant submitted tolerance data in pigs as part of the residue depletion study. The GLP study was conducted in pigs injected intramuscularly with the product as described in the SPC (administered twice 48 hours apart). The rectal temperature was measured and the injection sites were examined for signs of changes in behaviour or locomotion or appearance of the site (erythema, oedema, scaling, pigmentation). The study concluded that there were no alterations of general health with the exception of a sporadic occurrence of non-serious diarrhoea during the post treatment observation period. Diarrhoea as a prolonged adverse effect was recorded in 12.5 % of animals treated with the test product. Diarrhoea due to administration lasted 1-2 days. No visible lesions or changes of tissue of the injection sites were found during gross pathology. Small changes of skeletal muscle necrosis, proliferation of fibroblasts and inflammatory infiltration were recorded at 5 out of 8 injection sites examined histologically on day 4 after the first administration of the test product, at 2 out of 8 injection sites on day 8 after the first injection and 1 out of 8 injection sites on day 12 after first injection. No changes were recorded on day 18, 16 days after the second injection. Histological findings were related to the physical injection rather than irritability of the test product. No statistical differences were found between treated groups and / or the effects of the test or reference products for the physical examination of the injection site. The effect of the administered products was evaluated as negligible irritation.

IV.B Clinical Studies

Since the application is made in accordance with Article 13 (1) of Directive 2001/82/EC as amended by Directive 2004/28/EC, on the basis of being a generic of a reference medicinal product, there is no requirement to provide results of toxicological or pharmacological tests and clinical trials as it has already been presented for 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.

MODULE 4

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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