FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Floron 300 mg/ml solution for injection for cattle and pigs

Date: 29/01/2015

French agency for food, environnemental and occupational health safety– French Agency for Veterinary Medicinal Products
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MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0280/001/DC
Name, strength and pharmaceutical form	Floron 300 mg/ml solution for injection for cattle and pigs
Applicant	KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
Active substance(s)	Florfenicol
ATC Vetcode	QJ01BA90
Target species	Cattle and pigs.
Indication for use	Cattle diseases caused by florfenicol susceptible bacteria: preventive and therapeutic treatment of respiratory tract infections in cattle due to *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni*. The presence of the disease in the herd should be established before preventive treatment. Pigs: treatment of acute outbreaks of respiratory disease caused by strains *of Actinobacillus pleuropneumoniae* and *Pasteurella multocida* susceptible to florfenicol.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website http://www.anmv.anses.fr/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13(1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	14/12/2014
Concerned Member States for original procedure	BE – DE – ES – IT – NL – PT

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 slight 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 of the product 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. Composition

The product contains 300 mg/ml florfenicol as the active substance and excipients propylene glycol, dimethyl sulfoxide and macrogol 400.

The container is a glass bottle closed with a rubber stopper. The particulars of the containers and controls performed are provided and conform to the regulation.
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 is florfenicol, an established active substance. 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.

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

Not applicable.

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 shelf life when stored under the approved conditions.
A shelf-life after first opening the immediate packaging, as detailed on the SPC, has been supported by appropriate data.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

III.A Safety Testing

Pharmacological Studies

The tested product has shown to be bioequivalent to the reference product, NUFLOR 300 MG/ML SOLUTION FOR INJECTION, in three bioequivalence studies: in cattle following intramuscular and subcutaneous injections and in pig following intramuscular injection.

As this is a generic application according to Article 13, 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.

Toxicological Studies

As this is a generic application according to Article 13, 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.

User Safety

The applicant has provided a user safety assessment in regards to the excipient of the tested product formulation that differs from the reference product formulation.

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

Ecotoxicity

The applicant provided a Phase I & II environmental risk assessment in compliance with the relevant guidelines. The predicted no effect concentration (PNEC) values derived from several studies were acceptable and in accordance with VICH guidelines. 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

Residue Studies

The applicant submitted three residue depletion studies: one in cattle after intramuscular administration, one in cattle after subcutaneous administration and one in pigs after intramuscular administration.

MRLs

a. active substances

The active substance, florfenicol, is included in table 1 of the MRL regulation 37/2010, as follows,

Marker residue	Animal Species	MRL	Target Tissues	Other Provisions	Therapeutic Classification	Regulation
Sum of florfenicol and its metabolites measured as florfenicol-amine	Bovine, ovine, caprine	200 µg/kg 3 000 µg/kg 300 µg/kg	Muscle Liver Kidney	Not for animals from which milk is produced for human consumption. Not for animals from which eggs are produced for human consumption	Anti-infectious agents/ Antibiotics	37/2010 of 22.12.2009
	Porcine	300 µg/kg 500 µg/kg 2 000 µg/kg 500 µg/kg	Muscle Skin + Fat Liver Kidney			
	Poultry	100 µg/kg 200 µg/kg 2 500 µg/kg 750 µg/kg	Muscle Skin + Fat Liver Kidney			
	Fin fish	1 000 µg/kg	Muscle and skin in natural proportions			
	All other food producing species	100 µg/kg 200 µg/kg 2 000 µg/kg 300 µg/kg	Muscle Fat Liver Kidney			

b. excipients

The MRL status of excipients of the product FLORON 300 MG/ML SOLUTION FOR INJECTION FOR CATTLE AND PIGS is indicated in the following table:

Excipient	MRL status
Propylene glycol	Table 1, no MRL required
Dimethyl sulfoxide	Table 1, no MRL required
Macrogol 400	Table 1, no MRL required

Temps d'attente

The same meat withdrawal periods as the reference product are considered satisfactory:

Cattle (IM) – 30 days
Cattle (SC) – 44 days
Pigs (IM) – 18 days.
Not permitted for use in lactating animals producing milk for human consumption.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.A Pre-Clinical Studies

Tolerance in the Target Species of Animals

The tolerance of the product was tested in the bioequivalence and residue studies. The slight reactions observed are indicated in the SPC.

Resistance

An overview of the level of resistance to florfenicol in target pathogens and commensal bacteria based on recent bibliographical data has been submitted. Target pathogens: *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Actinobacillus pleuropneumoniae*, isolated from bovine and/ or porcine species remain susceptible to florfenicol.

IV.B Clinical Studies

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, 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 product 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 product for humans and the environment is acceptable.