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AGENCY FOR MEDICINAL PRODUCTS AND MEDICAL DEVICES OF THE REPUBLIC OF SLOVENIA

Slovenčeva ulica 22, 1000 Ljubljana, Slovenia
(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

FlorFlu 300/16.5 mg/ml solution for injection for cattle (Florfenicol, Flunixin)

MODULE 1

PRODUCT SUMMARY

EU Procedure number	SI/V/0101/001/DC
Name, strength and pharmaceutical form	FlorFlu 300/16.5 mg/ml solution for injection for cattle
Applicant	KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
Active substance(s)	Florfenicol, flunixin
ATC Vetcode	QJ01BA99
Target species	Cattle
Indication for use	Treatment of respiratory infections caused by *Mannheimia haemolytica*, *Pasteurella multocida*, *Mycoplasma bovis* and *Histophilus somni* associated with pyrexia.

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MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with article 13(1) of Directive No 2001/82/EC as amended (generic)
Date of completion of the original decentralised procedure	18.11.2020
Date product first authorised in the Reference Member State (MRP only)	/
Concerned Member States for original procedure	BG, FR, DE, IT, RO, ES, UK

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. Qualitative and quantitative particulars

The product contains florfenicol (300.0 mg), flunixin (16.5 mg) and the excipients propylene glycol (E1520), N-methylpyrrolidone, citric acid, macrogol 300.

The medicinal product is packaged in type II clear glass bottles of 100 ml and type I clear glass bottles of 250 ml with type I bromobutyl rubber stoppers and aluminium caps with plastic tear/flip-off tabs, in a cardboard box.

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.

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

C. Control of Starting Materials

The active substance flunixin is an established active substance described in the European Pharmacopoeia. The active substance florfenicol is an established active substance which is not described in a pharmacopoeia. The active substances are 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.

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 have been provided.

Batch analytical data from the proposed production sites have been provided demonstrating compliance with the specification.

F. Stability

Stability data on the active substances 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.

Appropriate data have been provided to support the in-use shelf-life of the product.

G. Other Information

Residual solvents that have potential to be present in the final product do not exceed the recommended levels given in VICH GL18(R).

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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” veterinary medicinal product). The reference veterinary medicinal product is RESFLOR 300/16.5 mg/mL Solution for Injection for Cattle. Bioequivalence with a reference product has been demonstrated, results of safety tests are not required.
The safety aspects of this product are identical to the reference product.

III.A Safety Testing

Pharmacological Studies

As this is a generic application according to Article 13 and bioequivalence with the 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 the 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

Although this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, a user safety assessment has been provided. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Environmental Risk Assessment

A Phase I environmental risk assessment (ERA) was provided according to the CVMP/VICH guidelines.

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the initial predicted environmental concentration in soil (PECsoil, initial) is less than 100 µg/kg.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because bioequivalence to the reference product has been demonstrated and there are no differences in the composition of the candidate product when compared to the reference product.

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MRLs

The active substances florfenicol and flunixin are allowed substances as described in table 1 of the annex to Commission Regulation (EU) No 37/2010:

Pharmacologically active substance(s)	Marker residue	Animal species	MRLs (µg/kg)	Target tissues	Other provisions
Florfenicol	Sum of florfenicol and its metabolites measured as florfenicol-amine	Bovine, ovine, caprine	200 µg/kg 3000 µg/kg 300 µg/kg	Muscle Liver Kidney	Not for use in animals producing milk for human consumption
Flunixin	Flunixin	Bovine	20 µg/kg 30 µg/kg 300 µg/kg 100 µg/kg	Muscle Fat Liver Kidney	
	5-Hydroxy Flunixin	Bovine	40 µg/kg	Milk	
The MRL status of the excipients of the product is indicated in the following table:					
Propylene glycol (E1520)	N/A	All food producing species	No MRL required	N/A	No entry
N-methylpyrrolidone	N/A	All food producing species	No MRL required	N/A	No entry
Citric acid (E330)	N/A	All food producing species	No MRL required	N/A	A food additive with a valid E number (E330) approved for use in foodstuffs for human consumption and is therefore covered by the entry for ‘Food additives’ in table 1 of Commission Regulation (EU) No 37/2010.
Macrogol 300	N/A	All food producing species	No MRL required	N/A	No entry

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Withdrawal Periods

The withdrawal periods are identical to those approved for the reference product and are considered adequate to ensure consumer safety:

Meat and offal: 46 days.
Milk: Not authorised for use in animals producing milk for human consumption. Do not use during lactation or drying off periods. Do not use in pregnant animals which are intended to produce milk for human consumption within 2 months of expected parturition.

IV. CLINICAL ASSESSMENT (EFFICACY)

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.

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 Heads of Veterinary Medicines Agencies website (www.HMA.eu).

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