Office for Registration
of Medicinal Products, Medical Devices and Biocidal Products

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# DECENTRALISED PROCEDURE

# PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

# FLOROLAB 100 mg/ml solution for use in drinking water for pigs

# MODULE 1

## PRODUCT SUMMARY

| | |
|---|---|
| EU Procedure number | PL/V/0107/001/DC |
| Name, strength and pharmaceutical form | FLOROLAB 100 mg/ml solution for use in drinking water for pigs |
| Applicant | Vetpharma Animal Health, S.L.<br>Les Corts 23<br>08028 Barcelona<br>Spain |
| Active substance(s) | Florfenicol |
| ATCvet code | QJ01BA90 |
| Target species | pig |
| Indication for use | Treatment and metaphylaxis at the group level where clinical signs are present of swine respiratory disease associated with *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* susceptible to florfenicol. The presence of the disease should be established in the herd before initiating metaphylactic treatment. |

# 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).

# MODULE 3

## PUBLIC ASSESSMENT REPORT

| | |
|---|---|
| Legal basis of original application | Application in accordance with Article 13 (3) of Directive 2001/82/EC as amended. |
| Date of completion of the original decentralised procedure | 03/07/2019 |
| Date product first authorised in the Reference Member State (MRP only) | Not applicable. |
| Concerned Member States for original procedure | ES, IE, PT, 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 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 100 mg/ml as the active substance and the excipient: macrogol 300.

The container/closure system are white high density polyethylene containers of 500 ml, 1L and 5L capacity. Containers are closed with a white screw cap of the same material, with induction disc.

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.

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 not described in the European/British Veterinary 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 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 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 24-hour stability after dilution in drinking water is based on the demonstration of stability for a batch diluted as described in the posology and stored over a period of 24 hours.

The claim of a 3 months stability after broaching is based on the demonstration of stability for a batch broached and stored 3 months at +25°C.

### *G. Other Information*

None

## III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a "This product was originally authorised under an EU procedure prior to 1st January 2021 where the UK participated as a Concerned Member State. Therefore, the contents of this Public Assessment Report are not owned by the Veterinary Medicines Directorate. Please contact the original Reference Member State for any queries in relation to this report."

generic hybrid application according to Article 13.3 of Directive 2001/82/EC (as amended by Dir 2004/28/EC), the applicant declared that the product is bioequivalent to the reference product NUFLOR 23 mg/mL Drinking Water Concentrate for Swine and claimed exemption from providing *in vivo* bioequivalence studies.

The product meets the criteria for Waivers from bioequivalence study according to section 7.1.c) of CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2), as it is an aqueous oral solution at time of administration and contains an active substance in the same concentration as an approved reference veterinary medicinal product presented as an aqueous oral solution at time of administration, both products contain the same qualitative composition of excipients, so no differences on the affection of the gastrointestinal transit, absorption or *in vivo* stability of the active substance between both products will occur.

Therefore, the results of pharmacological and toxicological studies are not required.

## *User Safety*

The applicant has provided and updated a user safety assessment in compliance with the relevant guideline which shows all potential routes of accidental administration and confirms that the product is not expected to pose a risk for users when used as recommended. The following warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product:

People with known hypersensitivity to florfenicol or polyethylene glycols should avoid contact with the veterinary medicinal product.

In case of accidental spillage onto skin, rinse with water. In case of contact with eyes, rinse immediately with copious amounts of water.

Personal protective goggles should be worn when handling the veterinary medicinal product.

## *Environmental Risk Assessment*

### *Phase I*

The environmental risk assessment cannot stop in Phase I because $PEC_{soil\text{-}initial}$ for pigs exceed trigger value 100 µg/kg soil (max. for weaner pig < 25 kg, $PEC_{soil\text{-}initial}$ equals 434,44 µg/kg). The applicant provided a phase I environmental risk assessment in compliance with the relevant guidelines, which showed that further assessment was required.

### *Phase II Tier A*

A Phase II Tier A assessment was conducted.

The applicant provided studies which show that using of FLOROLAB could not be safe for aquatic environment (PECground water > 0.1 µg/l) and organisms (algae, RQ>1). In order to further characterise the risk for the environment, a refinement of predicted exposures was undertaken. Based upon the data provided an unacceptable risk for the environment could not be excluded and a Tier B assessment was performed.

### *Phase II Tier B*

A Phase II Tier B assessment was conducted.

The applicant provided studies which showed that recalculated high values of $PEC_{surface\ water}$ and $PEC_{groundwater}$ were reduced in FOCUS application. The applicant presented also the recalculation of risk level on the environment, using the corrected value of DT50 in manure for parent

compound. The results of the tier B assessment indicate that a risk for the environment cannot be excluded and that appropriate risk mitigation advice is required for this product.

**Conclusion**

Based on the data provided in the ERA, a risk to the aquatic environment cannot be excluded. Therefore suitable risk mitigation measures and advice were included in the SPC for this product. Warnings and precautions as listed in the product literature are adequate to ensure safety to the environment when the product is used as recommended.

## *III.B Residues documentation*

### *Residue Studies*

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The results of residues studies are therefore not required. The product has the same withdrawal period as the product being cited for pharmaceutical equivalence. The withdrawal period for meat and offal is 20 days.

### *MRLs*

MRL are listed below:

Florfenicol is listed in Table I of the Annex of Commission Regulation (EU) No. 37/2010 as follows:

| | Porcine |
|---|---|
| Muscle | 300 µg/kg |
| Liver | 2000 µg/kg |
| Kidney | 500 µg/kg |
| Fat / skin | 500 µg/kg |

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|---|---|
| FLOROLAB 100 mg/ml solution for use in drinking water for pigs | PL/V/0107/001/DC |
| Vetpharma Animal Health, S.L. | Decentralised Procedure |
| | Publicly available assessment report |

***Withdrawal Periods***

Based on the data provided above, a withdrawal period of 20 days for meat and offal in pigs is justified.

## IV. CLINICAL ASSESSMENT (EFFICACY)

As this is a generic hybrid application according to Article 13.3 of Directive 2001/82/EC (as amended by Dir 2004/28/EC), the applicant declared that the product is bioequivalent to the reference product NUFLOR 23 mg/mL Drinking Water Concentrate for Swine and claimed exemption from providing *in vivo* bioequivalence studies.

The product meets the criteria for Waivers from bioequivalence study according to section 7.1.c) of CVMP Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2), as it is an aqueous oral solution at time of administration and contains an active substance in the same concentration as an approved reference veterinary medicinal product presented as an aqueous oral solution at time of administration, both products contain the same qualitative composition of excipients, so no differences on the affection of the gastrointestinal transit, absorption or *in vivo* stability of the active substance between both products will occur. Therefore, the results of clinical studies are not required.

## 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 Vetrinary 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. <None>