ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Floron 40mg/g Oral Powder for Swine

PuAR correct as of 03/07/18 when RMS was transferred to CZ. Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0344/002/DX/001
Name, strength and pharmaceutical form	Floron 40mg/g Oral Powder for Swine
Applicant	KRKA, d.d., Novo mesto Šmarješka cesta 6 8501 Novo mesto Slovenia
Active substance(s)	Florfenicol
ATC Vetcode	QJ01BA90
Target species	Pigs
Indication for use	In fattening pigs: For the treatment of swine respiratory disease in individual pigs due to *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	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	23rd January 2013
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Czech Republic, Poland, Romania, Slovenia.

I. SCIENTIFIC OVERVIEW

This was an application for a generic product, submitted in accordance with Article 13 (1) of Directive 2001/82/EC as amended. The reference product was Nuflor 40 mg/g Oral Powder for Pigs, authorised in the UK since June 2009. This falls under the global marketing authorisation for Nuflor 300 mg/ml Solution for Injection, authorised since December 1994.

The product is intended for use in fattening pigs, at a dose rate of 10 mg florfenicol per kg bodyweight, equivalent to 250 mg of the product given per day, mixed in the feed ration for five consecutive days. Refer to the SPC for a feeding guide.

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 and to be 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[1]. The efficacy of the product was demonstrated according to the claims made in the SPC and so the overall risk/benefit analysis is in favour of granting a marketing authorisation.

[1] SPC – Summary of Product Characteristics.

II. QUALITY ASPECTS

A. Composition

The product contains florfenicol (40mg/g) and excipients propylene glycol (E1520) and ground limestone.

The container/closure system consists of a 250 g sachet, or 1 kg or 3kg packs formed from a polyethylene terepthalate/aluminium/polyethylene laminate. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation is justified and uses an established pharmaceutical form, the development of which 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 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.

One of the excipients, propylene glycol, is monographed in the Ph. Eur. Calcium carbonate, is not monographed, however, a raw material specification was 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

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. The tests are relevant for the respective pharmaceutical form. 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

Active substance

Stability data on the active substance has been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Finished product

Suitable studies were performed on the finished product, enabling the shelf-life to be established. Tests were performed in order to establish stability in line with that already established for a sister product, Floron 40 mg/g Premix for Medicinal Feeding Stuff for Swine.

H. Genetically Modified Organisms

Not Applicable

J. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 4 years
Shelf life after first opening the immediate packaging: 3 months

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, results of toxicological and pharmacological tests were not required. 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, the environment and consumers.

III.A Safety Testing

User Safety

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. These are essentially similar to those of the reference product.

- Skin sensitisation may occur.
- Avoid skin contact.
- Do not handle this product in case of known sensitisation to propylene glycol.
- Handle this product with care to avoid exposure during incorporation of the powder into feed and administration of feed to animals, taking all recommended precautions.
- Wear either a disposable half-mask respirator conforming to European standard EN 149 or a non-disposable respirator to European Standard EN 140 with a filter to EN 143, chemically resistant gloves, protective coveralls and goggles while incorporating the powder into feed.
- Wear gloves and do not smoke, eat, or drink when handling the product or medicated feed.
- Wash hands thoroughly with soap and water after use of the product or medicated feed.
- Rinse thoroughly with water in case of exposure.
- If you develop symptoms following exposure such as skin rash, you should seek medical advice and take the package leaflet or the label with you.

Ecotoxicity

The applicant provided an environmental risk assessment in compliance with the relevant guideline. The assessments concluded that the product did not pose an unacceptable risk for the environment. 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

No residue depletion studies were conducted because of the claim of bioequivalence with the reference product.

Withdrawal Periods

A withdrawal period of 14 days for meat and offal in pigs is justified.

IV CLINICAL ASSESSMENT (EFFICACY)

As this is a generic application according to Article 13 (1), and bioequivalence with a reference product has been demonstrated, further studies were not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

Pharmacodynamics

No data were required for this section as the product was bioequivalent to the reference product. Florfenicol is described as a broad-spectrum antibiotic from the phenicol group, demonstrating activity against the majority of Gram-positive and Gram-negative bacteria. Inhibition is caused by the cessation of protein synthesis within ribosomes, and the active substance also possesses bactericidal activity. Bactericidal activity has also been demonstrated *in vitro* against *Pasteurella multocida* at a suitable concentration.

Pharmacokinetics

A GLP-compliant, single-dose, two-way, cross-over study was performed to demonstrate the bioequivalence of Floron 40 mg/g Oral Powder for Swine with the reference product, Nuflor 40 mg/g Oral Powder for Pigs. A suitable number of target animals were treated with 250 mg of either Floron 40 mg/g Premix for Medicated Feeding Stuff for Swine or the reference product. The products were given to the animals individually, via a medicated diet, to fasted pigs, at day 0 and day 7. Clinical observations were carried out daily, and blood samples taken at various time points. Statistical analyses were carried out on the products, and bioequivalence was established while the 90% confidence intervals for ratio of the means for pharmacokinetic parameters fell well within acceptable bounds. Therefore, it was concluded from this study that Floron 40 mg/g and Nuflor 40 mg/g were bioequivalent in terms of the extent and rate of absorption of florfenicol.

These data were therefore acceptable for assuring the bioequivalence of Floron 40 mg/g Oral Powder for Swine and Nuflor 40 mg/g Oral Powder for Pigs.

Resistance

Florfenicol is structurally related to older compounds in the phenicol class, chloramphenicol and thiamphenicol. Resistance to chloramphenicol has been identified via four different pathways. Only the efflux pump pathway may have some relevance for florfenicol. The bibliography and information provided suggests that *P. multocida* is susceptible to florfenicol, and that resistance has not been noted in this specific pathogen. Adequate warnings and precautions appear on the product literature.

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.

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