1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Nuflor 40 mg/g Premix for Medicated Feeding Stuff for Swine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition per gram:

Active substance:	**Quantity:**
Florfenicol	40 mg
Excipients:	
Propylene Glycol (E1520)	10 mg
Ground Limestone	qs to 1 g

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Premix for medicated feeding stuff.
White to off-white, free flowing powder with red and/or black grains dispersed throughout.

4 CLINICAL PARTICULARS

4.1 Target Species

Pigs (Fattening pigs).

4.2 Indications for use, specifying the target species

For the treatment and metaphylaxis of swine respiratory disease caused by *Pasteurella multocida* susceptible to florfenicol in infected herds. The presence of the disease in the herd must be established before the product is used.

4.3 Contraindications

Do not administer to boars intended for breeding.
Do not use in case of hypersensivity to the active substance or any of the excipients.

4.4 Special warnings for each target species

Animals showing a decreased appetite and/or a poor general condition should be treated by the parenteral route.

4.5 Special precautions for use

Special precautions for use in animals:

The product should be used in conjunction with susceptibility testing and take into account official and local policy relating to the use of antimicrobials.
This premix is intended for the manufacturing of solid medicated feed and cannot be used as it is; the incorporation rate of the premix in feed cannot be lower than 5 kg/ton.
This premix contains ground limestone, which can lead to a decrease in food consumption and to a phosphorus calcium imbalance in feed intake. Care should therefore be taken to consider the calcium content of the final medicated feed.
Treatment should not exceed 5 days.
In a field clinical study, within a week after the administration of the last dose, the incidence of pigs presenting either mild depression and/or mild dyspnea and/or pyrexia (40°C) was approx. 20 % in the initially severely ill animals.

Special precautions to be taken by the person administering the medicinal product to animals:

Skin sensitisation may occur.
Avoid skin contact.
Do not handle this product in case of known sensitization to active substance or any of the excipients.
Handle this product with care to avoid exposure during incorporation of premix intofeed 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 premix 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.

Other precautions:

Manure from treated swine must be stored for a minimum of one month before being spread and incorporated in fields.

4.6 Adverse reactions (frequency and seriousness)

Commonly observed adverse effects are diarrhoea perianal inflammation and rectal eversion. Increased serum calcium may also be observed. These effects are transient, resolving on cessation of treatment.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Therefore the use is not recommended during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

To be administered orally, in medicated feeding stuff.

Dosage:
10 mg of florfenicol per kg body weight (bw) (equivalent to 250 mg product) per day administered for 5 consecutive days.

Administration:
For a daily feed intake of 50 g/kg bodyweight, this dosage corresponds to a rate of incorporation of 5 kg of premix per ton of feed, i.e. 200 ppm of florfenicol.
The rate of incorporation of the medicated premix in the feed may be increased in order to achieve the required dosage on a mg/kg bodyweight basis and to take into account the actual feed intake. Thus, the inclusion level may need adjusting as follows to give the correct dose.

$$\frac{\text{250 mg product per kg body weight and day} \times \text{Average pig body weight (kg)}}{\text{Average daily feed intake (kg/animal)}} = \text{mg product per kg of feed}$$

The maximum rate of incorporation is 12.5 kg/ton (500 ppm of florfenicol), higher rates of inclusion may lead to poor palatability and decreased food consumption. Under no circumstances should the incorporation rate of the premix be below 5 kg/ton of feed.

In all cases the recommended dose of 10 mg of florfenicol per kg of body weight per day, for 5 consecutive days has to be respected.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing. The required doses should be measured by suitably calibrated weighing equipment.

A horizontal ribbon mixer should be used to incorporate the product into the feeding stuff. It is recommended that the product is added to the mixer containing the feeding stuff ingredients and mixed thoroughly to produce a homogeneous medicated feeding stuff. Medicated feed may also then be pelleted. Pelleting conditions include a pre-conditioning step with steam and then the mixture is passed through a pelleter or extruder under normal conditions.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

In the event of overdose, a reduction in food and water consumption, together with a decrease in bodyweight may be observed. There may be an increase in refused feed and an increase in serum calcium.

4.11 Withdrawal period(s)

Meat and offal: 14 days

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic Group: Antibiotic, member of the phenicol family.
ATC vet code: QJ01BA90.

5.1 Pharmacodynamic properties

Florfenicol is a broad-spectrum synthetic antibiotic in the phenicol group that is active against most Gram-positive and Gram-negative bacteria isolated from domestic animals. Florfenicol acts by inhibition of protein synthesis at the ribosomal level and is bacteriostatic. However, bactericidal activity has been demonstrated *in-vitro* against *Pasteurella multocida* when florfenicol is present at concentrations above the MIC for 4 to 12 hours.

In-vitro testing has shown that florfenicol is active against the bacterial pathogens most commonly isolated in respiratory diseases in pigs, including *Pasteurella multocida*.
A total of 193 *Pasteurella multocida* isolates from the respiratory tract of swine were collected between 2002 and 2003 in France, Spain, Greece, Germany, the United Kingdom and Belgium. The Minimal Inhibitory Concentration (MIC) of florfenicol against the target pathogen ranges from 0.25 to 1 µg/ml with a MIC_{90} of 0.5 µg/ml. The only mechanisms of chloramphenicol resistance that are known to have significant clinical relevance are CAT (Chloramphenicol Acetyl Transferase)-mediated inactivation and efflux-pump resistance. Of these, only some of the efflux mediated resistance would also confer resistance to florfenicol and thus have the potential to be affected by florfenicol use in animals.

5.2 Pharmacokinetic particulars

After administration to pigs by gavage at 10 mg/kg under experimental conditions, absorption of florfenicol was variable but peak serum concentrations of approximately 5 µg/ml were reached approximately 3 hours after dosing. The terminal half-life was between 3 and 4 hours. When pigs were given free access, for 5 days, to feed medicated with Nuflor Premix at the recommended dose of 10 mg/kg serum florfenicol concentrations exceeds 1 µg/ml for more than 16 hours each day of treatment.
Florfenicol is well absorbed when administered orally and following distribution it is rapidly eliminated in the urine and faeces in a ratio of 3:1. A fraction is excreted unchanged and the rest is metabolised into 5 major metabolites.
After parenteral dosing of florfenicol to pigs, it has been shown that lung concentrations are similar to serum concentrations.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene Glycol (E 1520)
Ground Limestone

6.2 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: 28 days.
Shelf life after incorporation into meal or pelleted feed: 3 months.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

LDPE/HDPE/paper sealed bag containing 5 kg premix.
LDPE/paper/paper/paper sealed bag containing 25 kg premix.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste material derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Intervet Ireland Limited
Magna Drive
Magna Business Park, Citywest Road
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA10996/238/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31st August 2007

10 DATE OF REVISION OF THE TEXT

February 2018