Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Nuflor Swine Once 450 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each ml contains
Florfenicol 450.00 mg

Excipients:

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection
Clear colourless to yellow solution

4 CLINICAL PARTICULARS

4.1 Target Species

Pigs.

4.2 Indications for use, specifying the target species

For the treatment of respiratory infections in pigs caused by strains of *Actinobacillus pleuropneumoniae*, *Haemophilus parasuis* and *Pasteurella multocida* susceptible to florfenicol.

4.3 Contraindications

Do not use in boars intended for breeding.
Do not use in cases of hypersensitivity to florfenicol.
See section 4.7.

4.4 Special warnings for each target species

Do not use in case of resistance.

4.5 Special precautions for use

Special precautions for use in animals
Do not use in piglets of less than 2kg.
The product should be used in conjunction with susceptibility testing and take into account official and local antimicrobial policies.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Care should be taken to avoid accidental self-injection.
In case of self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Avoid direct contact with skin, mouth and eyes. Wash hands after treatment. People with known hypersensitivity to florfenicol should avoid contact with the veterinary medicinal product.
Do not use the product in known cases of sensitivity to any of the excipients.

4.6 Adverse reactions (frequency and seriousness)

A very commonly* observed adverse effect under field conditions is diarrhoea which is transient and self-recovering. Additionally, peri-anal inflammation and rectal eversion are very common*. These effects can be observed for 1 to 7 days. Diarrhoea may be severe as may be rectal inflammation. Rectal prolapses are uncommon*.
Pain on injection is very common*. Transient swelling is commonly* observed at the site of injection. At necropsy tissue reactions at the injection site have been observed up to 28 days post-dosing. Full resolution has been observed by 21 to 35 days post-injection. Field study data are not available for pigs younger than 11 weeks of age. For this age group, pre-clinical data indicate that the frequency of diarrhoea / peri-anal irritation may be higher than observed in the field study in older animals.

*Explanatory note:
- Very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- Common (more than 1 but less than 10 animals in 100 animals)
- Uncommon (more than 1 but less than 10 animals in 1,000 animals)

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals have not revealed any evidence of embryo- or foetotoxic potential for florfenicol. However, the safety of the product in sows during pregnancy and lactation has not been demonstrated. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

30 mg/kg bodyweight (1 ml per 15 kg) by intramuscular injection into the neck muscle once. The volume administered at the injection site should not exceed 5 ml.
It is recommended to treat animals in early stages of disease and to evaluate the response to treatment. If, after 2 or 3 days, clinical signs of respiratory disease persist or increase, or if relapse occurs thereafter, treatment should be changed using another formulation or another antibiotic and continued until clinical signs have resolved.

Wipe the stopper before removing each dose. Use a dry, sterile syringe and needle.

Do not broach the vial more than 25 times. When treating large numbers of animals, use a suitable draw-off needle or automatic dosing syringe to avoid excessive puncturing of the closure.

To ensure a correct dosage the bodyweight should be determined as accurately as possible to avoid underdosing. Do not exceed the recommended dose.

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

In swine after administration of 1.5 times the recommended dose repeated 5 times at 48 hour intervals, a reduction in feeding, hydration and weight gain has been observed. After administration of 2.5 times the recommended dose repeated 5 times at 48 hour intervals, vomiting has also been noted.
After administration of a florfenicol dose corresponding to 5 times the recommended dose twice at 48 hour intervals, no more adverse effects were observed than at 1.5 times the recommended dose.

4.11 Withdrawal Period(s)

Meat and offal: 23 days

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterial for systemic use (Amphenicols)
ATC Vet Code: QJ01BA90

5.1 Pharmacodynamic properties

Florfenicol is a broad-spectrum synthetic antibiotic active against most Gram positive and Gram negative bacteria isolated from domestic animals. Florfenicol acts bactericidally by inhibition of protein synthesis at the ribosomal level.
In vitro testing has shown that florfenicol is active against the bacterial pathogens most commonly isolated in respiratory diseases in pigs, including *Actinobacillus pleuropneumoniae*, *Haemophilus parasuis* and *Pasteurella multocida*. Bactericidal activity has been demonstrated in vitro against *Actinobacillus pleuropneumoniae*, *Pasteurella multocida* and *Haemophilus parasuis.*
Florfenicol resistance in Gram-negative bacteria has been detected and is related to plasmid transfer of the *flo* gene. This gene codes for a membrane-associated exporter protein that promotes efflux of chloramphenicol and florfenicol. Because of the substitution of a hydroxyl group with a fluorine molecule, florfenicol is less susceptible to resistance from bacteria expressing chloramphenicol acetyl transferase enzymes.
Co-resistance towards other classes of antimicrobials and cross-resistance to chloramphenicol has been described in rare occasions.
Surveillance data collected between 2005-2010 for the target pathogens show no to very low florfenicol resistance rates. The same is observed for the food borne pathogens (*E. coli*, *E. faecium* and *E. faecalis*) according to surveillance data collected in 2001-2009. Depending on the European country resistance in Salmonella is low to moderate.
Using CLSI breakpoints (≤2 µg/ml: susceptible; 2-4 µg/ml: intermediate; ≥ 8 µg/ml: resistant) all target pathogens tested are susceptible.
MIC data for the recent target pathogens are presented in the table below:

Species	**Range (µg/ml)**	**MIC_{50} (µg/ml)**	**MIC_{90} (µg/ml)**
Actinobacillus pleuropneumoniae	0.06 - 1	0.25	0.5
Haemophilus parasuis	0.12 - 0.5	0.5	0.5
Pasteurella multocida	0.06- 1	0.5	0.5

5.2 Pharmacokinetic properties

After intramuscular administration of Nuflor Swine Once at the single dose of 30 mg/kg, florfenicol rapidly reached the blood stream. Maximum plasma concentrations of 3.1 µg/ml are reached after 6 hours. Then, florfenicol concentrations decreased continuously over time. Florfenicol might be still quantified in the plasma of the animals by 96 to 120 hours post-dosing. Half-life was approximately 22 hours. Florfenicol is primarily excreted in urine and extensively metabolised.
Florfenicol concentrations achieved in lung tissue reflect plasma concentrations, with a lung:plasma concentration ratio of approximately 1.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

N-Methylpyrrolidone
Diethylene glycol monoethyl ether

6.2 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: 2 years
Shelf life after first opening the immediate packaging: 28 days

6.4 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions.
Keep the vial in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

50, 100 and 250 ml colourless type II glass multiple dose vials, sealed with bromobutyl rubber stoppers and packed into carton boxes.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

7 MARKETING AUTHORISATION HOLDER

Intervet International BV
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

8 MARKETING AUTHORISATION NUMBER(S)

VPA: 10847/005/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

8th February 2013

10 DATE OF REVISION OF THE TEXT