NUFLOR-S- florfenicol injection
Merck Sharp & Dohme Corp.

Nuflor®-S
(FLORFENICOL)
Injectable Solution
300 mg/mL

PRODUCT INFORMATION

For intramuscular use in swine except for nursing piglets and swine of reproductive age intended for breeding.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Nuflor®-S Injectable Solution is a sterile solution of the synthetic, broad-spectrum antibiotic florfenicol. Each milliliter of sterile Nuflor®-S Injectable Solution contains 300 mg of florfenicol, 250 mg *N*-methyl-2-pyrrolidone (NMP), 150 mg propylene glycol and polyethylene glycol q.s.

INDICATIONS: Nuflor®-S Injectable Solution is indicated for treatment of swine respiratory disease associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella* Choleraesuis*, Streptococcus suis*, *Bordetella bronchiseptica*, and *Glaesserella (Haemophilus) parasuis* in swine except for nursing piglets and swine of reproductive age intended for breeding.

DOSAGE AND ADMINISTRATION: Nuflor®-S Injectable Solution should be administered by intramuscular injection to swine at a dose rate of 15 mg/kg (1 mL/45 lb) body weight. A second dose should be administered 48 hours later. The injection should be given only in the neck musculature. If a positive response is not noted within 24 hours after the second injection, the diagnosis should be re-evaluated, and/or an alternative treatment may be considered. Administered dose volume should not exceed 10 mL per injection site.

Nuflor®-S DOSAGE GUIDE FOR SWINE

ANIMAL WEIGHT (lbs)	IM Nuflor®-S DOSAGE (1 mL/ 45 lb Body Weight) (mL)
22	0.5
45	1
90	2
135	3
180	4
225	5
270	6

WARNINGS: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This

product contains materials that can be irritating to skin and eyes. Avoid direct contact with skin, eyes and clothing. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. Consult a physician if irritation persists. Accidental injection of this product may cause local irritation. Consult a physician immediately. Reproductive and developmental toxicities have been reported in laboratory animals following high, repeated exposures to NMP. Pregnant women should wear gloves and exercise caution or avoid handling this product. The Safety Data Sheet (SDS) contains more detailed occupational safety information.

For customer service, adverse effects reporting and/or a copy of the SDS, call 1-800-211-3573. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

PRECAUTIONS: Not for use in animals intended for breeding purposes. The effects of florfenicol on porcine reproductive performance, pregnancy and lactation have not been determined.

Intramuscular injection in swine may result in local tissue reaction which could persist up to 21 days post-dosing. This may result in trim loss of edible tissue at slaughter.

RESIDUE WARNINGS: Swine intended for human consumption must not be slaughtered within 11 days of the last intramuscular treatment.

ADVERSE REACTIONS: Perianal inflammation, rectal eversion, rectal prolapse and diarrhea may occur transiently following treatment. Decreased feed and water consumption may occur if the labeled dosage regimen is exceeded.

CLINICAL PHARMACOLOGY: The pharmacokinetic disposition of florfenicol was evaluated in 20 pigs following a single IM injection of Nuflor®-S at the labeled dose of 15 mg/kg BW. The mean ± standard deviation maximum plasma concentration (C_{max}) and the time to reach C_{max} (T_{max}) of florfenicol were 3.42 ± 0.82 µg/mL and 4.70 ± 2.15 hours, respectively. The mean ± standard deviation area under the drug concentration-time curve between times 0 and the last quantifiable concentration ($AUC_{0\text{-}LOQ}$) and the terminal half-life ($T_{1/2}$) of florfenicol were 70.34 ± 23.78 µg*hours/mL and 11.21 ± 3.73 hours, respectively.

MICROBIOLOGY: Florfenicol is a synthetic, broad-spectrum antibiotic active against many Gram-negative and Gram-positive bacteria isolated from domestic animals. It acts by binding to the 50S ribosomal subunit and inhibiting bacterial protein synthesis. Florfenicol is generally considered a bacteriostatic drug, but exhibits bactericidal activity against certain bacterial species.

In vitro activity of florfenicol has been demonstrated against commonly isolated pathogens associated with swine respiratory disease. Isolates tested were obtained from pre-treatment lung samples from representative non-enrolled pigs at each study site and post-treatment lung samples from pigs in the florfenicol-treated and saline-treated groups that died or were euthanized during the study, or were classified as treatment failures at the end of the study. The minimum inhibitory concentrations (MICs) of florfenicol for swine respiratory pathogens from clinical studies were determined using dilution methods. These susceptibility test methods were adequately controlled with the inclusion and acceptable performance of appropriate reference strains. The results are presented in Table 1.

Table 1. Florfenicol minimum inhibitory concentration (MIC) values* for indicated target pathogens isolated from a multi-site field study evaluating swine respiratory disease in the U.S. in 2001.

Indicated pathogens	Number of Isolates	MIC_{50}† (µg/mL)	MIC_{90}† (µg/mL)	MIC Range (µg/mL)
Actinobacillus pleuropneumoniae	100	0.25	0.5	0.25-1
Pasteurella multocida	107	0.5	0.5	0.25-0.5
Bordetella bronchiseptica	49	2	2	0.5-4
Glaesserella parasuis	36	0.5	0.5	≤0.12-1.0
Streptococcus suis	62	2	2	1-2
Salmonella Choleraesuis	36	4	4	2-4

* The correlation between *in vitro* susceptibility data and the clinical effectiveness of florfenicol is unknown.
† The lowest MIC to encompass 50% and 90% of the most susceptible isolates, respectively.

EFFECTIVENESS: In a multi-site natural infection field study, a total of 620 growing pigs with clinical signs of SRD (rectal temperature of ≥ 104.5°F, and a depression score (on a scale of 0 [absent] to 3 [severe]) of ≥ 2, and a dyspnea score (on a scale of 0 [absent] to 3 [severe]) of ≥ 2) were treated with either florfenicol (15 mg/kg BW IM given on Days 0 and 2) or an equivalent volume of saline. Treatment success (rectal temperature of < 104°F, and a depression score of 0 or 1, and a dyspnea score of 0 or 1) was evaluated on Day 6. The treatment success rate was statistically significantly different ($p < 0.0001$) and higher in the florfenicol-treated group (72%) than in the saline-treated control group (33.1%).

ANIMAL SAFETY: A safety study was conducted in 40 healthy crossbred growing pigs. Pigs were administered florfenicol by IM injection in the neck at 1X, 3X, or 5X the labeled dose (15, 45, or 75 mg/kg BW, respectively) for 3X the labeled duration of treatment (6 injections at 48-hour intervals), or 10X the labeled dose (150 mg/kg BW) administered as two injections 48 hours apart. Test article-related diarrhea (moderate), anal swelling/erythema (mild to moderate), and injection site swelling (mild to moderate) were seen in all florfenicol-treated groups after dosing, most frequently in the 3X and 5X groups. Although these findings were considered clinically relevant, the incidence and severity in the 1X group was considered within acceptable limits. Test article-related decreases in feed and water consumption and an associated decrease in body weight were seen in the 3X and 5X groups. Test article-related changes in some serum chemistry parameters and decreased numbers of white blood cells were seen in the 3X, 5X, and/or 10X groups; the changes were generally minimal and not considered clinically significant. Most changes in drug-related, in-life parameters did not become apparent until after dosing was extended beyond the labeled duration of two injections, 48 hours

apart.

Injection site irritation was evaluated in a safety study using 20 healthy crossbred growing pigs administered florfenicol at 15 mg/kg BW IM in the neck as two injections 48 hours apart. Mild injection site swelling was seen in up to approximately 32% of the pigs by 4 days post-injection and was resolved by 16 days post-injection. Gross and histopathologic evaluation showed that injection site discoloration and inflammation was present at 7 and 14 days post-injection, and absent at 21, 28, and 42 days post-injection.

STORAGE CONDITIONS: Store between 2-30°C (36-86°F). Do not store above 30°C (86°F). Protect from light when not in use. Use within 30 days of first puncture and puncture a maximum of 30 times. If more than 30 punctures are anticipated, the use of multi-dosing equipment is recommended. When using a draw-off spike or needle with bore diameter larger than 18 gauge, discard any product remaining in the vial immediately after use.

HOW SUPPLIED: Nuflor®-S (florfenicol) Injectable Solution is packaged in 100 mL glass sterile multiple dose vials.

Approved by FDA under NADA # 141-063
Formulated in Germany.

Rev. 06/22

394544 R1

PRINCIPAL DISPLAY PANEL - 100 mL Vial Carton

100 mL
Multiple-Dose Vial
300 mg/mL

NDC 0061-5581-02
Sterile

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MERCK
Animal Health

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MERCK
Animal Health

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385802 R1

385802 R1

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API Made in:
LOT
EXP

(01) 08713184194039

Sterile

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Sterile

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TAKE TIME

OBSERVE LABEL DIRECTIONS

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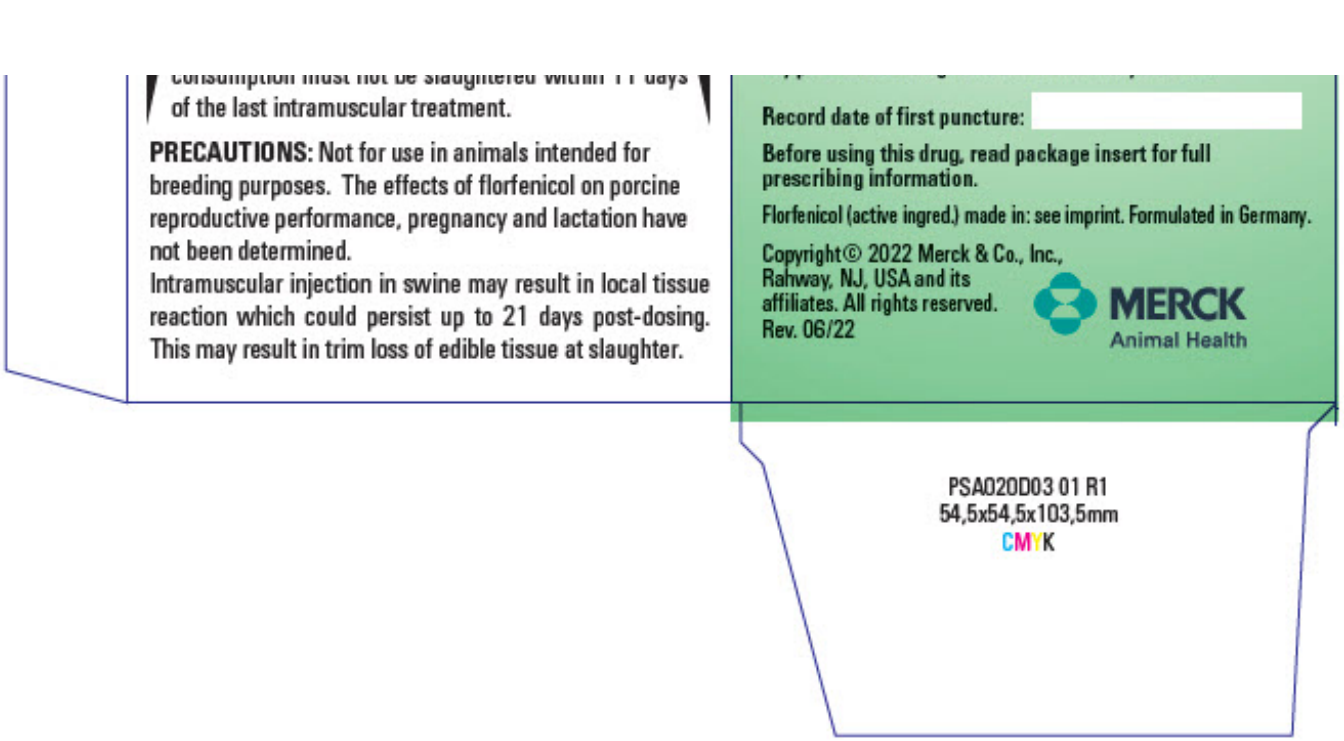

NUFLOR-S

florfenicol injection

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:0061-5581
Route of Administration	INTRAMUSCULAR		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
FLORFENICOL (UNII: 9J97307Y1H) (FLORFENICOL - UNII:9J97307Y1H)	FLORFENICOL	300 mg in 1 mL

Product Characteristics			
Color	YELLOW	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0061-5581-02	6 in 1 CARTON		
1	NDC:0061-5581-01	100 mL in 1 VIAL		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141063	08/19/2021	

Labeler - Merck Sharp & Dohme Corp. (001317601)

Establishment

Name	Address	ID/FEI	Business Operations
Vet Pharma Friesoythe GmbH		341934053	LABEL, ANALYSIS, MANUFACTURE, PACK

Establishment

Name	Address	ID/FEI	Business Operations
MINSHENG GROUP SHAOXING PHARMACEUTICAL CO., LTD.		544607919	API MANUFACTURE

Establishment

Name	Address	ID/FEI	Business Operations
Zhejiang Apeloa Jiayuan Pharmaceutical Co., Ltd.		529047249	API MANUFACTURE

Revised: 3/2023 Merck Sharp & Dohme Corp.