

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Nifencol 300 mg/ml solution for injection for cattle and pigs.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance

Florfenicol 300 mg

Excipients

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.

Clear slightly yellowish solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle and pigs.

4.2 Indications for use, specifying the target species

Cattle:

Prevention and treatment of respiratory tract infections in cattle due to *Histophilus somni*, *Mannheimia haemolytica* and *Pasteurella multocida*, susceptible to florfenicol.

The presence of the disease in the herd should be established before preventive treatment.

Pigs:

Treatment of acute outbreaks of respiratory disease caused by strains of *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* susceptible to florfenicol.

4.3 Contraindications

Do not administer to adult bulls and boars intended for breeding purposes.

Do not use in case of hypersensitivity or previous allergic reactions to florfenicol or to any of the excipients.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

This veterinary medicinal product does not contain an antimicrobial preservative.

Special precautions for use in animals

Do not administer to piglets of less than 2 kg.

The veterinary medicinal 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

Take care to avoid accidental self-injection. In case of accidental self-injection, seek medical advice taking the label or package leaflet with you to show the physician.

Avoid skin or eye contact with the product. In case of contact with the skin or eyes, rinse the affected area immediately with plenty of water. Wash the hands after use.

Do not use the product if you know you are sensitive to propylene glycol or polyethylene glycols.

4.6 Adverse reactions (frequency and seriousness)

In cattle, a decrease in food consumption and transient softening of the faeces may occur during the treatment period. The treated animals recover quickly and completely upon termination of treatment.

Administration of the product by the intramuscular and subcutaneous routes may cause inflammatory lesions at injection site which persist for 14 days.

On very rare occasions, anaphylactic reactions have been reported in cattle.

In pigs, commonly observed adverse effects are transient diarrhoea and/or peri-anal and rectal erythema/oedema which may affect 50% of the animals. These effects can be observed for one week. Under field conditions approximately 30% of treated pigs presented with pyrexia (40°C) associated with either moderate depression or moderate dyspnea a week or more after administration of the second dose.

Transient swelling lasting up to 5 days may be observed at the site of injection. Inflammatory lesions at the injection site may be seen up to 28 days.

4.7 Use during pregnancy, lactation or lay

Laboratory studies have not produced any evidence of teratogenic or foetotoxic effects.

Cattle:

The safety of the veterinary medicinal product has not been established during pregnancy.

Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

Pig:

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

It is not recommended to use the veterinary medicinal product in pigs 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

Cattle: Intramuscular or subcutaneous injection

Pig: intramuscular injection

Cattle:

Treatment

IM route: 20 mg florfenicol /kg bodyweight (1ml of the product/15kg) to be administered twice 48 hours apart using a 16 gauge needle.

SC route: 40 mg florfenicol /kg bodyweight (2ml of the product/15kg) to be administered once only using a 16 gauge needle.

Prevention:

SC route: 40 mg florfenicol/kg bodyweight (2ml of the product/15kg) to be administered once only using a 16 gauge needle.

Pigs:

15 mg florfenicol/kg bodyweight (1 ml of the product / 20 kg) by intramuscular injection twice at 48 hour intervals using a 16-gauge needle.

The dose volume given at any one injection site should not exceed 10ml for both routes of administration (intramuscular and subcutaneous) in cattle and 3 ml in pigs. The injection should only be given in the neck in both target species.

To ensure a correct dosage body weight of the animals should be determined as accurately as possible to avoid underdosing.

It is recommended to treat animals in the early stages of disease and to evaluate the response to treatment within 48 hours after the second injection. If clinical signs of respiratory disease persist 48 hours after the last injection or if relapse occurs, treatment should be changed using another formulation or another antibiotic and continued until clinical signs have resolved.

Swab septum before removing each dose. Use a dry sterile needle and syringe.

Do not broach the stopper of vial more than 25 times.

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

In cattle, a decrease in food consumption and transient softening of the faeces may occur during the treatment period. The treated animals recover quickly and completely upon termination of treatment.

In swine, after administration of 3 times the recommended dose or more, a reduction in feeding, hydration and weight gain has been observed.

After administration of 5 times the recommended dose or more, vomiting has also been noted.

4.11 Withdrawal Period(s)

Cattle:

Meat and offal: by IM (at 20 mg/kg bodyweight, twice): 30 days
by SC (at 40 mg/kg bodyweight, once): 44 days

Milk: Not authorised for use in cattle producing milk for human consumption, including during the dry period.

Pigs:

Meat and offal: 18 days

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterial for systemic use
ATCVet code: QJ01BA90

5.1 Pharmacodynamic properties

Florfenicol is a synthetic broad spectrum antibiotic effective against most Gram-positive and Gram-negative bacteria isolated from domestic animals. Florfenicol acts by inhibiting protein synthesis at the ribosomal level.

Florfenicol is considered to be a bacteriostatic agent, but *in vitro* studies of florfenicol demonstrate bactericidal activity against *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Actinobacillus pleuropneumoniae* and porcine strains of *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*, , the most commonly isolated bacterial pathogens involved in bovine and porcine respiratory disease.

MIC₉₀ values of florfenicol against bovine and porcine respiratory pathogens

Microorganism	MIC ₉₀ (µg/ml)
<i>Cattle</i>	
<i>Mannheimia haemolytica</i>	1
<i>Pasteurella multocida</i>	0.5
<i>Histophilus somni</i>	0.5
<i>Pigs</i>	
<i>Actinobacillus pleuropneumoniae</i>	1
<i>Pasteurella multocida</i>	0.5

Organisms were isolated from clinical cases of bovine and porcine respiratory disease in France, Spain, UK, Germany, Ireland, Denmark, Austria, Belgium and The Netherlands during the years 2004 and 2008. CLSI breakpoints: S ≤ 2 µg/ml, I = 4 µg/ml and R ≥ 8 µg/ml.

In contrast to chloramphenicol, florfenicol does not carry the risk of inducing non-dose-related aplastic anemia in man. Organisms resistant to chloramphenicol and thiamphenicol through the common transacetylation resistance mechanisms are less susceptible to resistance of florfenicol. However, cross-resistance to chloramphenicol and florfenicol mediated by a gene (floR) that codes for an efflux protein and is carried on plasmids has been observed in isolated cases of bovine and porcine Pasteurellae. Resistance to florfenicol and other antimicrobials has been identified in the food-borne pathogen *Salmonella typhimurium* and co-resistance to florfenicol and other antimicrobials (e.g. ceftiofur) has been identified in the microorganisms from the family *Enterobacteriaceae*.

5.2 Pharmacokinetic properties

In cattle, intramuscular administration at the recommended dose of 20mg/kg maintains efficacious blood levels in cattle for 48 hours. Maximum mean plasma concentration (C_{\max}) of 3.37µg/ml occurs at 3.3 hours (T_{\max}) after dosing. The mean plasma concentration 24 hours after dosing was 0.77µg/ml.

The administration of the product by subcutaneous route at the recommended dosage of 40mg/kg maintains bovine efficacious blood levels in cattle (ie above the MIC_{90} of the main respiratory pathogens) for 63 hours. Maximum plasma concentration (C_{\max}) of approximately 5 µg/ml occurs approximately 5.3 hours (T_{\max}) after dosing. The mean plasma concentration 24 hours after dosing is approximately 2 µg/ml. The elimination half life was 18.3 hours. In pigs intravenously administered florfenicol had a mean plasma clearance rate of 5.2 ml/min/kg and a mean volume of distribution at equilibrium of 948 ml/kg. The mean terminal half-life is 2.2 hours.

After initial intramuscular administration of florfenicol, maximum plasma concentrations of between 3.8 and 13.6 µg/ml are reached after 1.4 hours and the concentrations deplete with a terminal mean half-life of 3.6 hours. After a second intramuscular administration, maximum plasma concentrations of between 3.7 and 3.8 µg/ml are reached after 1.8 hours. Plasma concentrations drop below 1 µg/mL, the MIC_{90} for the target porcine pathogens, 12 to 24 hours following IM administration. Florfenicol concentrations achieved in lung tissue reflect plasma concentrations, with a lung:plasma concentration ratio of approximately 1. After administration to pigs by the intramuscular route, florfenicol is rapidly excreted, primarily in urine. The florfenicol is extensively metabolised.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

N-methylpyrrolidone
Propylene glycol
Macrogol 300

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

Keep the vial in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Polypropylene vial of 100 ml and 250 ml, closed with bromobutyl stopper secured with flip-off aluminium collar.
One vial of 100 ml or 250 ml is available in a cardboard box.
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 products should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Vetpharma Animal Health S.L
Les Corts, 23
08028 Barcelona
Spain

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10516/007/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18th December 2013

10 DATE OF REVISION OF THE TEXT

August 2014