

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT:

Florgane 300 mg/ml Suspension for Injection for Cattle and Pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each ml contains:

Active substance:

Florfenicol 300 mg

Excipients:

n-Butanol 10 mg

Potassium metabisulfite (E 224) 0.2 mg

For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM:

Suspension for injection.

White to yellowish-white suspension.

4. CLINICAL PARTICULARS:

4.1. Target species:

Cattle, pigs.

4.2. Indications for use:

Cattle:

Preventive and therapeutic treatment of respiratory tract infections in cattle caused by florfenicol susceptible *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni*. The presence of the disease in the herd should be established before treatment.

Pigs:

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

4.3. Contra-indications:

Do not use in adult bulls and boars intended for breeding purposes.

Do not use in animals in cases of hypersensitivity to the active substance or to any of the excipients.

4.4. Special warnings for each target species:

None.

4.5. Special precautions for use:

i) Special precautions for use in animals:

Do not use in piglets of less than 2 kg.

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Official national and regional antimicrobial policies should be taken into account when the product is used.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to florfenicol and may decrease the effectiveness of treatment with other antimicrobials, due to the potential for cross-resistance.

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

People with a history of hypersensitivity to florfenicol or to one of the ingredients of the product should avoid any contact with this veterinary medicinal product.

Avoid contact with skin and eyes. In case of dermal contact, wash the exposed area immediately with water.

Do not smoke, eat or drink while handling this product.

Take care to avoid accidental self-injection.

If such symptoms as skin rash appear after being exposed to this product, seek for medical advice. Face, lip or eye swelling, as well as difficult breathing, are serious signs requiring urgent medical assistance.

4.6. Adverse reactions (frequency and seriousness):

Allergic reactions may occur in animals that are hypersensitive to one of the ingredients of the product.

Cattle:

Intramuscular injection of the product may cause clinically obvious swelling at the injection site. Injection site swellings usually resolve within 5 days but may persist for more than 5 days up to beyond 21 days. Inflammatory lesions at the injection site may persist for 18 days after administration.

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.

Pigs:

Very commonly observed adverse effects are transient diarrhoea and/or peri-anal and rectal erythema/oedema. Symptoms of diarrhoea disappear without treatment within 6 days, while symptoms of peri-anal and rectal erythema/oedema may persist up to between 1 to 2 weeks after treatment.

Intramuscular injection of the product may cause mild swelling at the injection site. Injection site swelling usually resolves within 6 days but may persist up to beyond 12 days. Macroscopic inflammatory lesions at the injection site resolve between 12 and 20 days after administration.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reactions 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)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

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 effect of florfenicol on bovine reproductive performance and pregnancy has not been assessed. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

The safety of the product in sows during pregnancy and lactation has not been demonstrated. Use of the product during pregnancy and lactation is therefore not recommended.

4.8. Interaction with other medicinal products and other forms of interaction:

None known.

4.9. Amounts to be administered and administration route:

Cattle: by one single intramuscular administration in the neck musculature:

30 mg of florfenicol per kg body weight (eq. to 1 ml of the product per 10 kg body weight).

Do not inject more than 15 ml per injection site in cattle.

Pigs: by one single intramuscular administration behind the ears: 22.5 mg of florfenicol per kg body weight (eq. to 0.75 ml of the product per 10 kg body weight).

Do not inject more than 5 ml per injection site in pigs.

In cattle over 150 kg and in pigs over 65 kg the total injection volume must be divided over two or more injections sites while always respecting the maximum injection volume of 15 ml per injection site in cattle and of 5 ml per injection site in pigs. Injections may be given in alternate sides of the neck.

In case injections are given in cattle at the same side of the neck, the minimum distance between injection sites always must be 15 to 20 cm.

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

Shake before use.

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

For 50 and 100 ml bottles, do not broach the vial more than 25 times. For 250 and 500 ml bottles, do not broach the vial more than 50 times.

Another type of treatment needs to be considered if response to treatment is inadequate.

4.10. Overdose (symptoms, emergency procedures, antidotes):

Cattle: None.

Pigs: Parenteral overdoses of florfenicol in swine may cause a reduction in feeding, hydration and weight gain, and vomiting.

4.11. Withdrawal periods:

Cattle:

Meat and offal: 37 days.

Milk: Do not use in cattle producing milk for human consumption.

Pigs:

Meat and offal: 22 days.

5. PHARMACOLOGICAL PROPERTIES:

Pharmacotherapeutic group: Antiinfectives for systemic use, antibacterial for systemic use, amphenicols, florfenicol

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 of protein synthesis at the ribosomal level.

Florfenicol is considered to be a bacteriostatic agent, but *in vitro* studies of florfenicol demonstrate bactericidal activity against bovine strains of *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* 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 | MIC₉₀ (µg/ml) |
|--|---------------------------------|
| Cattle | |
| <i>Mannheimia haemolytica</i> | 1 |
| <i>Pasteurella multocida</i> | 0.5 |
| <i>Histophilus somni</i> | 0.5 |
| Pigs | |
| <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 2009.
 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 particulars:

Cattle:

Following the intramuscular administration of the product, florfenicol absolute bioavailability is 76% in cattle.

Following one single intramuscular administration of the product at the recommended dose of 30 mg of florfenicol per kg body weight, maximum plasma concentrations ($C_{max} = 3.1 \mu\text{g/ml}$

in young cattle and $2.5 \mu\text{g/ml}$ in calves) are attained 12 hours after administration ($T_{max} = 12 \text{ h}$). Thereafter, there is a slow decline of florfenicol plasma levels with an average terminal half-life of about 39 h in young cattle and 47 h in calves.

Plasma concentrations above $1 \mu\text{g/ml}$ are maintained with one single intramuscular injection of 30 mg/kg body weight for on the average 45 hours in young cattle and 52 hours in calves.

Florfenicol is mainly excreted in unchanged form with urine.

Pigs:

Following one single intramuscular administration of the product at the recommended dose of 22.5 mg of florfenicol per kg body weight, mean pharmacokinetic parameters are: $C_{max} = 2.2 \mu\text{g/ml}$, $T_{max} = 8 \text{ h}$ and $T_{1/2\beta} = 15.5 \text{ h}$. Plasma concentrations above $1 \mu\text{g/ml}$ are maintained with one single intramuscular injection of 22.5 mg/kg body weight for on the average 36 hours.

Florfenicol concentrations achieved in lung tissue reflect plasma concentration, with a lung: plasma concentration ration of approximately 1, when measured in homogenised lung tissue. 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-Butanol
Potassium metabisulfite (E224)
Carmellose sodium
Povidone K12
Lecithin (Soybean origin)
Sodium citrate

Potassium dihydrogen phosphate
Magnesium gluconate
Water for injection

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: 3 years.
Shelf-life after first opening the immediate packaging: 28 days.

6.4. Special precautions for storage:

Protect from light. Do not refrigerate or freeze.

6.5. Nature and composition of immediate packaging:

50 ml, 100 ml, 250 ml or 500 ml partially transparent, polypropylene, multidose bottle closed with a fluorinated bromobutyl stopper and aluminium overseal.

Carton containing either

- 1 or 12 x 50 ml,
- 1 or 12 x 100 ml,
- 1 or 12 x 250 ml,
- 1 or 12 x 500 ml,

Not all pack sizes may be marketed.

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

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:

EMDOKA bvba
John Lijssenstraat
16, B-2321 Hoogstraten
Belgium.

8. MARKETING AUTHORISATION NUMBER:

Vm 34534/4000

9. DATE OF FIRST AUTHORISATION:

07 July 2010

10. DATE OF REVISION OF TEXT:

November 2015

DISTRIBUTED BY

Animalcare Ltd
10 Great North Way
York Business Park
Nether Poppleton
York
YO26 6RB

PROHIBITION OF SALE, SUPPLY AND/OR USE:

To be supplied only on veterinary prescription.