SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Flordofen 300 mg/ml solution for injection for cattle and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Florfenicol 300 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
N-methyl pyrrolidone	250 mg
Propylene glycol	
Macrogol 300	

Clear, slightly yellowish solution

3. CLINICAL INFORMATION

3.1 Target species

Cattle and pigs

3.2 Indications for use for each target species

Cattle:
Treatment and metaphylaxis of respiratory tract infections in cattle due to *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni*, susceptible to florfenicol.
The presence of the disease in the herd should be established before methaphylaxis.

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

3.3 Contraindications

Do not use in adult bulls and boars intended for breeding purposes.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

This veterinary medicinal product does not contain an antimicrobial preservative.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Do not administer to piglets of less than 2 kg.
Use of the veterinary medicinal 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 veterinary medicinal product is used.
Use of the veterinary medicinal 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.

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

People with known hypersensitivity to florfenicol, propylene glycol or polyethylene glycols should avoid contact with the veterinary medicinal product.

Care should be taken to avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

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

Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. Women of childbearing age, pregnant women or women suspected of being pregnant should use the veterinary medicinal product with serious caution to avoid accidental self-injection.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylactic shock
Undetermined frequency (cannot be estimated from the available data):	Reduced food intake, loose stool[1] Injection site inflammation[2]

[1] Quick and complete recovery upon termination of treatment.
[2] After intramuscular and subcutaneous injection; may persist for 14 days.

Pigs:

Very common (>1 animal / 10 animals treated):	Diarrhoea, Anal and rectal disorder (peri-anal and rectal erythema/oedema)[1] Pyrexia[2,3], Depression[3,4] Dyspnoea[3,4]
Undetermined frequency (cannot be estimated from the available data):	Injection site swelling[5] Injection site lesion[6]

[1] May affect 50% of animals. Can be observed for one week.
[2] 40ºC.
[3] Occurred in approximately 30% of pigs treated under field conditions; presented a week or more after administration of the second dose.
[4] Moderate. Associated with pyrexia.
[5] Lasting up to 5 days.
[6] Lasting up to 28 days.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established in cattle and pigs during pregnancy, lactation or in animals intended for breeding.
Studies in laboratory animals have not revealed any evidence of embryo- or foetotoxic potential for florfenicol.
Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects.
Use only according to the benefit-risk assessment by the responsible veterinarian.

Fertility:
Do not use in adult bulls and boars intended for breeding (see section 3.3).

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Cattle: Intramuscular or subcutaneous use.
Pigs: Intramuscular use.

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

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

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

Pig:
15 mg florfenicol /kg bodyweight (1 ml of the veterinary medicinal 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 10 ml 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 should be determined as accurately as possible.

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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

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 animals producing milk for human consumption, including during the dry period.

Pigs:
Meat and offal: 18 days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01BA90

4.2 Pharmacodynamics

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 and is bacteriostatic. Laboratory tests have shown that florfenicol is active against the most commonly isolated bacterial pathogens involved in bovine respiratory disease which include *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni* and in swine respiratory disease which include *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*.

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*.

In contrast to chloramphenicol, florfenicol does not carry the risk of inducing non-dose-related aplastic anaemia 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 microrganisms from the family *Enterobacteriaceae.*

4.3 Pharmacokinetics

In cattle, intramuscular administration at the recommended dose of 20 mg/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 veterinary medicinal product by subcutaneous route at the recommended dosage of 40 mg/kg maintains bovine efficacious blood levels in cattle (i.e. 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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale:
- plastic vial: 2 years
- glass vial: 30 months

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

5.3 Special precautions for storage

Store below 25 °C.

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

5.4 Nature and composition of immediate packaging

Polypropylene vial of 250 ml, closed with bromobutyl stopper secured with flip off aluminium collar.
Colourless type II glass vial of 50 or 100 ml, closed by a type I bromobutyl stopper and sealed by an aluminium cap with centre hole.
Brown-coloured type II glass vial of 250 ml, closed by a type I bromobutyl stopper and sealed by an aluminium cap with centre hole.
One vial of 50, 100 or 250 ml is available in a cardboard box.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Dopharma Research B.V.

7. MARKETING AUTHORISATION NUMBER(S)

Vm 28365/3005

8. DATE OF FIRST AUTHORISATION

10 February 2014

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

November 2023

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

Gavin Hall
Approved: 20 October 2024