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:
For the 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:
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.

4.3 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.

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.
Use of 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.

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

People with known hypersensitivity to florfenicol or any of the excipients 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 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 the 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 dyspnoea 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.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals treated in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, 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.

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.

Pigs:
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 interactions

None known.

4.9 Amounts to be administered and administration route

Cattle: Intramuscular or subcutaneous injection
Pigs: 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.

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

Pig:
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 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 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: Antibacterials for systemic use, amphenicols.
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 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*.

5.2 Pharmacokinetic particulars

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 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 mg/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 mg/ml are reached after 1.8 hours. Plasma concentrations drop below 1 mg/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 Major 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:
- plastic vial: 2 years
- glass vial: 30 months
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

Store below 25 °C.
Keep the vial in the outer carton in order to protect from light.

6.5 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.

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

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

Dopharma Research B.V.
Zalmweg 24
4941 VX Raamsdonksveer
Netherlands

8 MARKETING AUTHORISATION NUMBER(S)

VPA10791/006/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14th February 2014
Date of last renewal: 21st September 2018

10 DATE OF REVISION OF THE TEXT

September 2018