SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Florfenicol ..... 300 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Colourless to yellow clear solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and pigs.

4.2 Indications for use, specifying the target species

Cattle:
Treatment of respiratory tract infections due to *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* susceptible to florfenicol.

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

4.3 Contraindications

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

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
Wipe the stopper before removing each dose. Use a dry, sterile needle and syringe.
Do not use in piglets of less than 2 kg.
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.

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 the florfenicol and may decrease the effectiveness of treatment with other antimicrobials, due to the potential for cross-resistance. Particular attention should be paid to improving farming practices to avoid any stress condition (improving management practices and by cleaning and disinfection).

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Care should be taken when handling the product to avoid accidental self-injection. In case of accidental self-injection, seek medical advice, and show the package leaflet or the label to the physician.
People with known hypersensitivity to the components of the formulation should avoid contact with the product.
Wash hands after handling the product.

4.6 Adverse reactions (frequency and seriousness)

Cattle:
A decrease in food consumption and transient softening of the faeces may occur during the treatment period. Treated animals recover quickly and completely upon termination of treatment.
Administration of the product by the intramuscular route may cause inflammatory lesions at the injection site which may persist for up to 28 days.

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 may be observed for up to one week.
Administration of the product by the intramuscular route may cause inflammatory lesions at injection site which disappear within 28 days.

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals have not revealed any evidence of embryo- or foeto-toxic potential for florfenicol. However, the safety of florfenicol on bovine and porcine reproductive performance and pregnancy has not been assessed. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Intramuscular use.
The injection should be given in the neck.

Cattle:
20 mg florfenicol per kg bodyweight, i.e. 1 ml of solution per 15 kg bodyweight, twice 48 hours apart.

Pigs:
15 mg florfenicol per kg bodyweight, i.e. 1 ml of solution per 20 kg bodyweight, twice 48 hours apart.

The dose volume given at any one injection site should not exceed 10 ml in cattle and 3 ml in pigs.
To ensure a correct dosage body weight 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, treatment should be changed using another formulation or another antibiotic and continued until clinical signs have resolved.

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

In swine after intramuscular 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: 37 days
Milk: Not permitted for use in lactating animals producing milk for human consumption.

Pigs:
Meat and offal: 18 days

5. PHARMACOLOGICAL 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 bacteria proteins synthesis at the ribosomal level, thus is bacteriostatic. However, i*n vitro* tests have shown that florfenicol has a bactericidal activity against the most commonly isolated bacterial pathogens involved in respiratory diseases:

- *Histophilus somni, Mannheimia haemolytica* and *Pasteurella multocida* isolated from cattle
- *Actinobacillus pleuropneumonia,* and *Pasteurella multocida* isolated from pigs.

Acquired resistance to florfenicol is mediated by efflux pump resistance associated with a *flo*R gene. Such resistance has not yet been identified in the target pathogens except for *Pasteurella multocida*. Cross resistance with chloramphenicol can occur. Resistance to florfenicol and other antimicrobials has been identified in the food-born pathogen *Salmonella typhimurium* and co-resistance with the third-generation cephalosporins has been observed in respiratory and digestive *Escherichia coli*.
For *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni* the following breakpoints have been determined for florfenicol in bovine respiratory disease; susceptible: ≤2 µg/ml, intermediate: 4 µg/ml, resistant: ≥8 µg/ml.

In bovine, 99% of *P. multocida* isolates (n=156) and 98% of *M. haemolytica*isolates (n=109) were susceptible to florfenicol (strains isolated in France in 2012).
In swine, 99% of *P. multocida* isolates (n=150) were susceptible to florfenicol (strains isolated in France in 2012).

The following Minimum Inhibitory Concentrations (MIC) have been determined for florfenicol in European isolates collected from diseased animals between 2009 to 2012:

Bacteria species	**Origin**	**Nb of strains**	**CMI of florfenicol (µg/mL)**	
			CMI_{50}	**CMI_{90}**
Mannheimia haemolytica	Cattle	147	0.7	1.0
Pasteurella multocida	Cattle	134	0.3	0.5
Histophilus somni	Cattle	64	0.2	0.2
Pasteurella multocida	Swine	151	0.4	0.5
Actinobacillus pleuropneumoniae	Swine	158	0.2	0.4

5.2 Pharmacokinetic particulars

In cattle
Intramuscular administration of the formulation at the recommended dose of 20 mg/kg maintains efficacious blood levels for 48 hours. Maximum mean serum concentration (Cmax) of 3.8 µg/ml occurred 5.7 hours (Tmax) after dosing. The mean serum concentration 24 hours after dosing was 1.95 µg/ml. The mean elimination half life was 15.3 hours.

In pigs
After intramuscular administration of florfenicol, maximum serum concentration of 4.7 µg/ml is reached after 1.8 hours and the concentrations deplete with a terminal mean half-life of 14.8 hours. Serum concentrations drop below 1 µg/ml, the MIC90 for the target porcine pathogens, 12-24 hours following IM administration Florfenicol concentrations achieved in lung tissue reflect plasma concentration, 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

Dimethylacetamide
Diethylene glycol monoethyl ether
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: 3 years
Shelf-life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Material of the primary container
Colourless glass vial type II (20 – 50 – 100 – 250 - 500 ml).
Translucent multi-layer plastic vials (50 – 100 – 250 – 500 ml).
Chlorobutyl stopper type II.

Pack size
Box containing one vial of 20, 50, 100, 250 or 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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Ceva Animal Health Ltd
Explorer House
Mercury Park
Wycombe Lane
Wooburn Green
High Wycombe
Buckinghamshire
HP10 0HH
United Kingdom

8. MARKETING AUTHORISATION NUMBER

Vm 15052/4046

9. DATE OF FIRST AUTHORISATION

25 August 2009

10. DATE OF REVISION OF THE TEXT

September 2022

Approved 26 September 2022