# ANNEX III

# LABELLING AND PACKAGE LEAFLET

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**Cardboard box: 20, 50, 100, 250 & 500 ml**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

## 2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains 300 mg florfenicol.

## 3. PHARMACEUTICAL FORM

Solution for injection

## 4. PACKAGE SIZE

20 ml
50 ml
100 ml
250 ml
500 ml

## 5. TARGET SPECIES

Cattle and pigs

## 6. INDICATION(S)

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.

## 8. WITHDRAWAL PERIOD

Meat and offal:
Cattle: 37 days

Pigs: 18 days
Milk: Not permitted for use in lactating animals producing milk for human consumption.

## 9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

## 10. EXPIRY DATE

EXP: {month/year}
Once broached, use within 28 days, by: ___/___/___.

## 11. SPECIAL STORAGE CONDITIONS

## 12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

## 13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
To be supplied only on veterinary prescription.

## 14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

## 15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

## 16. MARKETING AUTHORISATION NUMBER(S)

Vm 15052/4046

## 17. MANUFACTURER'S BATCH NUMBER

Lot:

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**Label: 20 & 50 ml**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

## 2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

300 mg/ml

## 3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

20 ml
50 ml

## 4. ROUTE(S) OF ADMINISTRATION

I.M.

## 5. WITHDRAWAL PERIOD

Meat and offal:
Cattle: 37 days
Pigs: 18 days
Milk: Not permitted for use in lactating animals producing milk for human consumption.

## 6. BATCH NUMBER

Lot: {number}

## 7. EXPIRY DATE

EXP: {month/year}
Once broached, use within 28 days.

## 8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

**Label: 100, 250 & 500 ml**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

## 2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml contains 300 mg florfenicol.

## 3. PHARMACEUTICAL FORM

Solution for injection

## 4. PACKAGE SIZE

100 ml
250 ml
500 ml

## 5. TARGET SPECIES

Cattle and pigs.

## 6. INDICATION(S)

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

I.M.

## 8. WITHDRAWAL PERIOD

Meat and offal:
Cattle: 37 days
Pigs: 18 days
Milk: Not permitted for use in lactating animals producing milk for human consumption.

## 9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

## 10. EXPIRY DATE

EXP: {month/year}
Once broached, use within 28 days.

## 11. SPECIAL STORAGE CONDITIONS

## 12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

## 13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
To be supplied only on veterinary prescription.

## 14. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

## 15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

## 16. MARKETING AUTHORISATION NUMBER(S)

Vm 15052/4046

## 17. MANUFACTURER'S BATCH NUMBER

Lot:

# B. PACKAGE LEAFLET

# PACKAGE LEAFLET for 20, 50, 100, 250 & 500 ml

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

## 1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

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

Manufacturer responsible for batch release:
Ceva Santé Animale, 10 av. de La Ballastière, 33500 Libourne, France

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

## 3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

Each ml contains 300 mg of florfenicol
Colourless to yellow clear solution.

## 4. INDICATIONS

**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.

## 5. 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.

## 6. ADVERSE REACTIONS

**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.
If you notice any serious effects not mentioned in this package leaflet, please inform your veterinary surgeon.

## 7. TARGET SPECIES

Cattle and pigs.

## 8. DOSAGE FOR EACH SPECIES, ROUTE AND METHOD OF ADMINISTRATION

Intramuscular use. 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.

## 9. ADVICE ON CORRECT ADMINISTRATION

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.

## 10. WITHDRAWAL PERIOD

Meat and offal:
Cattle: 37 days
Pigs: 18 days
Milk: Not permitted for use in lactating animals producing milk for human consumption.

## 11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
This veterinary medicinal product does not require any special storage conditions.
Do not use after the expiry date stated on the carton and vial after EXP.
Shelf-life after first opening the container: 28 days.
When the container is broached for the first time write in the space provided on the label the date on which any product remaining in the container is to be discarded.
Discard any product remaining in the container at this time.

## 12. SPECIAL WARNINGS

**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.

**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.

**Interactions**
None known.

**Overdose**
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.

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

## 13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

## 14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

September 2022

## 15. OTHER INFORMATION

Pack sizes:
Box containing one glass vial of 20, 50, 100, 250 or 500 ml.
Box containing one plastic vial of 50, 100, 250 or 500 ml.

Not all pack sizes may be marketed.

**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 |

**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.