

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

FLORFENIKEL 300 mg/ml solution for injection for cattle and pigs (BE, BG, CY, CZ, DE, FR, HU, IE, IT, LU, NL, PT, RO, SK, UK)

KELAFLO 300 mg/ml solution for injection for cattle and pigs (DK, ES, PL)

FLORIKEL 300 mg/ml solution for injection for cattle and pigs (EL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains

Active substance:

Florfenicol 300 mg

Excipient:

N-methyl pyrrolidone 200 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection.

Clear, light yellow to yellow solution.

4. CLINICAL PARTICULARS

4.1 Target Species

Cattle, pigs.

4.2 Indications for use, specifying the target species

Cattle: Treatment of respiratory tract infections due to strains of *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 and boars intended for breeding purposes.

Do not use in piglets of less than 2 kg.

Do not use in case of hypersensitivity to florfenicol or to any of the excipients.

Do not use in case of resistance to the active substance.

Do not administer intravenously.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

The stopper must be cleaned before removing each dose. Use a dry, sterile syringe and needle.

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 amfenicols and other antimicrobials due to the potential for cross-resistance.

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

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 direct contact with skin, mouth and eyes. If eye exposure occurs, flush eyes immediately with clean water. If skin exposure occurs, wash the affected area with clean water. If accidental ingestion occurs, rinse the mouth with plenty of water and seek medical advice immediately.

Wash hands after use.

People with known hypersensitivity to florfenicol should avoid contact with the veterinary medicinal product.

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

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.

Other precautions

The use of this veterinary medicinal product may pose a risk for terrestrial plants, cyanobacteria and groundwater organisms.

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. The treated animals recover quickly and completely upon termination of treatment.

Administration of the product by the intramuscular route may cause inflammatory lesions at injection site which persist for 14 days.

In very rare occasions, anaphylactic reactions were observed.

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).

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.

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.

Under field conditions, approximately 30% of treated pigs may present pyrexia (40°C) associated with either moderate depression or moderate dyspnoea a week or more after administration of the second dose.

4.7 Use during pregnancy and lactation

The safety of the veterinary medicinal product has not been established in cattle and pigs during pregnancy and lactation or in animals intended for breeding. 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.

4.8 Interaction with other medicinal products and other forms of interaction

No data available.

4.9 Amounts to be administered and administration route

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing. The vial cannot be broached more than 25 times.

Ensure that the injection site is clean before administration of the product.

Cattle: IM injection of 20 mg/kg BW (1ml/15kg) into the neck muscle twice 48 hours apart. The volume administered per injection site should not exceed 10 ml. Subsequent injections must be given at different sites.

Pigs: IM injection of 15 mg/kg BW (1 ml/20 kg) into the neck muscle, twice, 48 hours apart. The volume administered per injection site should not exceed 3 ml. Subsequent injections must be given at different sites.

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 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 periods

Cattle:

Meat and offal: 34 days

Milk: Not authorised for use in animals producing milk for human consumption.

Pigs:

Meat and offal: 18 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, amphenicols, Florfenicol

ATC vet 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.

However, bactericidal activity has been demonstrated *in vitro* against most common bacterial pathogens involved in respiratory disease: *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Actinobacillus pleuropneumonia*.

Acquired resistance to florfenicol is mediated by efflux pump resistance associated with a *flo* gene. Cross resistance with chloramphenicol can occur.

The following Minimal Inhibitory Concentrations (MIC) have been determined for florfenicol in European isolates collected from cattle and pigs with respiratory tract infections. For florfenicol in bovine and swine respiratory disease, CLSI breakpoints are: susceptible ≤ 2 µg/ml, intermediate 4 µg/ml and resistant ≥ 8 µg/ml.

Species	Bacterial pathogen	MIC ₅₀ (µg/ml)	MIC ₉₀ (µg/ml)
Cattle	<i>Mannheimia haemolytica</i>	0.5 - 1	1
	<i>Pasteurella multocida</i>	0.5	0.5 - 1
	<i>Histophilus somni</i>	0.25	0.25
Pigs	<i>Actinobacillus pleuropneumonia</i>	0.25 – 0.5	0.5
	<i>Pasteurella multocida</i>	0.5	0.5

5.2 Pharmacokinetic particulars

Cattle:

Intramuscular administration at the recommended dose of 20 mg/kg maintains efficacious blood levels in cattle for 48 hours. Maximum mean serum concentration (C_{max}) of 4.02 µg/ml occurs at 7.0 hours (T_{max}) after dosing.

The mean serum concentration 24 hours after dosing was 1.57 µg/ml. The terminal half-life was 15.1 hours.

Pigs:

After intramuscular administration of the recommended dose of 15 mg/kg, maximum serum concentration of 2.48 µg/ml is reached after 2.0 hours and the concentrations deplete with a terminal half-life of 14.9 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

N-Methylpyrrolidone
Glycerol formal

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 packaged in polypropylene vials for sale: 2 years.
Shelf life of the veterinary medicinal product packaged in colourless glass vials 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 temperature storage conditions.
Keep the bottle in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Vial sizes: 100 and 250 ml

- Colourless Type II glass vials closed with bromobutyl rubber closures and an aluminium cap.
- Polypropylene vials closed with bromobutyl rubber closures and an aluminium cap.

Vials are individually packed in carton box.

Six, ten or twelve of these are grouped as clinical pack.

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

The veterinary medicinal product should not enter water courses as florfenicol may be dangerous for fish and other aquatic organisms.

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

KELA N.V.
Sint Lenaartseweg 48
2320 Hoogstraten
Belgium

8. MARKETING AUTHORISATION NUMBER

XXXX

9. DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

Date of last renewal: {DD/MM/YYYY}

10. DATE OF REVISION OF THE TEXT

<{DD/MM/YYYY}>

PROHIBITION OF SALE, SUPPLY AND/OR USE

For animal treatment only.

To be supplied only on veterinary prescription.

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE**CARTON BOX****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

FLORFENIKEL 300 mg/ml solution for injection for cattle and pigs (BE, BG, CY, CZ, DE, FR, HU, IE, IT, LU, NL, PT, RO, SK, UK)

KELAFLO 300 mg/ml solution for injection for cattle and pigs (DK, ES, PL)

FLORIKEL 300 mg/ml solution for injection for cattle and pigs (EL)

Florfenicol

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Florfenicol 300 mg/ml

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

1 x 100 ml, 6 x 100 ml, 10 x 100 ml, 12 x 100 ml

1 x 250 ml, 6 x 250 ml, 10 x 250 ml, 12 x 250 ml

5. TARGET SPECIES

Cattle, pigs

6. INDICATIONS

Read the package leaflet before use.

7. METHOD, ROUTE OF ADMINISTRATION AND SPECIAL WARNINGS

Intramuscular injection.

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:

Cattle:

Meat and offal: 34 days

Milk: Not authorised for use in animals producing milk for human consumption.

Pigs:

Meat and offal: 18 days

9.

10. EXPIRY DATE

EXP:

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

Once broached, use by...

11. SPECIAL STORAGE CONDITIONS

This veterinary medicinal product does not require any special temperature storage conditions.
Keep the bottle in the outer carton in order to protect from light.

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

The veterinary medicinal product should not enter water courses as florfenicol may be dangerous for fish and other aquatic organisms.

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

KELA N.V.
St. Lenaartseweg 48
2320 Hoogstraten
Belgium

16. MARKETING AUTHORISATION NUMBER

XXXX

17. MANUFACTURER’S BATCH NUMBER

Lot:

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**LABEL****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

FLORFENIKEL 300 mg/ml solution for injection for cattle and pigs (BE, BG, CY, CZ, DE, FR, HU, IE, IT, LU, NL, PT, RO, SK, UK)

KELAFLO 300 mg/ml solution for injection for cattle and pigs (DK, ES, PL)

FLORIKEL 300 mg/ml solution for injection for cattle and pigs (EL)

Florfenicol

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Florfenicol 300 mg/ml

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

100 ml – 250 ml

5. TARGET SPECIES

Cattle, pigs

6. INDICATIONS

Read the package leaflet before use.

7. METHOD, ROUTE OF ADMINISTRATION AND SPECIAL WARNINGS

Intramuscular injection.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:

Cattle:

Meat and offal: 34 days

Milk: Not authorised for use in animals producing milk for human consumption.

Pigs:

Meat and offal: 18 days

9.

10. EXPIRY DATE

EXP:

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

Once broached, use by...

11. SPECIAL STORAGE CONDITIONS

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

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

12. 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.

13. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

14. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

KELA N.V.
St. Lenaartseweg 48
2320 Hoogstraten
Belgium

15. MARKETING AUTHORISATION NUMBER

XXXX

16. MANUFACTURER'S BATCH NUMBER

Lot:

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:

FLORFENIKEL 300 mg/ml solution for injection for cattle and pigs (BE, BG, CY, CZ, DE, FR, HU, IE, IT, LU, NL, PT, RO, SK, UK)

KELAFLOR 300 mg/ml solution for injection for cattle and pigs (DK, ES, PL)

FLORIKEL 300 mg/ml solution for injection for cattle and pigs (EL)

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

Marketing authorisation holder:

KELA N.V., St. Lenaartseweg 48, 2320 Hoogstraten, Belgium

Manufacturer responsible for batch release:

Glass vials: KELA N.V., St. Lenaartseweg 48, 2320 Hoogstraten, Belgium

PP vials: SP VETERINARIA, Ctra. Reus-Vinyols, Km. 4,1, 43330 Riudoms, Tarragona, Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

FLORFENIKEL 300 mg/ml solution for injection for cattle and pigs (BE, BG, CY, CZ, DE, FR, HU, IE, IT, LU, NL, PT, RO, SK, UK)

KELAFLOR 300 mg/ml solution for injection for cattle and pigs (DK, ES, PL)

FLORIKEL 300 mg/ml solution for injection for cattle and pigs (EL)

Florfenicol

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

Florfenicol 300 mg – Excipients: N-methyl pyrrolidone 200 mg, glycerol formal up to 1 ml.
Clear, light yellow to yellow solution.

4. INDICATIONS

Cattle: treatment of respiratory tract infections due to strains of *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 and boars intended for breeding purposes.

Do not use in piglets of less than 2 kg.

Do not use in case of hypersensitivity to florfenicol or to any of the excipients.

Do not use in case of resistance to the active substance.

Do not administer intravenously.

6. ADVERSE REACTIONS

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 route may cause inflammatory lesions at injection site which persist for 14 days.

In very rare occasions, anaphylactic reactions were observed.

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).

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.

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.

Under field conditions, approximately 30% of treated pigs may present pyrexia (40°C) associated with either moderate depression or moderate dyspnoea a week or more after administration of the second dose.

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

7. TARGET SPECIES

Cattle, pigs

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

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing. The vial cannot be broached more than 25 times.

Ensure that the injection site is clean before administration of the product.

Cattle

IM injection of 20 mg/kg BW (1 ml/15kg) into the neck muscle twice 48 hours apart. The volume administered per injection site should not exceed 10 ml. Subsequent injections must be given at different sites.

Pigs

IM injection of 15 mg/kg BW (1 ml/20 kg) into the neck muscle, twice, 48 hours apart. The volume administered per injection site should not exceed 3 ml. Subsequent injections must be given at different sites.

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.

9. ADVICE ON CORRECT ADMINISTRATION

Wipe the stopper before removing each dose. Use a dry, sterile syringe and needle.

10. WITHDRAWAL PERIOD

Cattle:

Meat and offal: 34 days

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

Pigs:

Meat and offal: 18 days

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

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

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

Do not use this veterinary medicinal product after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

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

When the container is broached (opened) for the first time, using the in-use shelf life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.

12. SPECIAL WARNINGS

Special precautions for use in animals:

The stopper must be cleaned before removing each dose. Use a dry, sterile syringe and needle.

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 this leaflet may increase the prevalence of bacteria resistant to florfenicol and may decrease the effectiveness of treatment with other amfenicols and other antimicrobials due to the potential for cross-resistance.

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

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 direct contact with skin, mouth and eyes. If eye exposure occurs, flush eyes immediately with clean water. If skin exposure occurs, wash the affected area with clean water. If accidental ingestion occurs, rinse the mouth with plenty of water and seek medical advice immediately.

Wash hands after use.

People with known hypersensitivity to florfenicol should avoid contact with the veterinary medicinal product.

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

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.

Pregnancy and lactation:

The safety of the veterinary medicinal product has not been established in cattle and pigs during pregnancy and lactation or in animals intended for breeding. 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.

Overdose (symptoms, emergency procedures, 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.

Interaction with other medicinal products and other forms of interaction:

No data available.

Incompatibilities:

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

Other precautions

The use of this veterinary medicinal product may pose a risk for terrestrial plants, cyanobacteria and groundwater organisms.

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

The veterinary medicinal product should not enter water courses as florfenicol may be dangerous for fish and other aquatic organisms.

Medicines should not be disposed of via wastewater.

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

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

DD month YYYY

15. OTHER INFORMATION

Pack sizes: 100 and 250 ml

Clinical containers of 6, 10 and 12 units of 100 ml or 250 ml.

Not all pack sizes may be marketed.

PROHIBITION OF SALE, SUPPLY AND/OR USE

For animal treatment only.

To be supplied only on veterinary prescription.