ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Floron 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
Propylene glycol
Dimethyl sulfoxide
Macrogol 400

A light yellow to yellow, clear, viscous liquid.

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 metaphylaxis.

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

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Do not use in 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.

Special precautions for the protection of the environment:

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

3.6 Adverse events

Cattle:

Undetermined frequency (cannot be estimated from the available data):	Decreased food intake, loose stool[1] Injection site swelling[2,4] Injection site inflammation[3,4]

[1]May occur during the treatment period. The treated animals recover quickly and completely upon termination of treatment.
[2]When administered by the intramuscular route, may persist for 14 days.
[3]When administered by the intramuscular route, may persist up to 32 days after administration.
[4]When administered by the subcutaneous route, may persist at least for 41 days.

Pig:

Very common (>1 / 10 animals treated):	Diarrhoea[1] Peri-anal and rectal erythema/oedema[1] Pyrexia (40 °C) associated with either moderate depression or moderate dyspnea[2]
Undetermined frequency (cannot be estimated from the available data):	Injection site swelling[3] Injection site inflammation[4]

[1]May affect up to 50% of the animals; can be observed for one week.
[2]Approximately 30% of treated pigs presented with week or more after administration of the second dose.
[3]May last up to 5 days.
[4]May last 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

Studies in laboratory animals have not revealed any evidence of embryo- or foetotoxic potential for florfenicol.

Pregnancy and lactation:
Cattle: the safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only according 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. The use is not recommended during pregnancy and lactation.

Fertility:
Do not use in breeding boars and bulls.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

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.

Pigs:
15 mg florfenicol /kg bodyweight (1 mL of the product/ 20 kg) by intramuscular injection into the neck muscle twice at 48 hour intervals using a dry, sterile 16-gauge needle.

The dose volume given at any one injection site should not exceed 10 ml in cattle and 3 ml in pigs. The injection should only be given in the neck.

For intramuscular route, 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.
Do not broach the vial more than 25 times. Use a suitable draw-off needle or automatic dosing syringe to avoid excessive puncturing of the closure.

To ensure a correct dosage, body weight should be determined as accurately as possible.

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

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.

Pigs
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 (intramuscular route, 20 mg/kg bodyweight, twice): 30 days
Meat and offal (subcutaneous route, 40 mg/kg bodyweight, once): 44 days
Not authorised for use in animals producing milk for human consumption.

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.

In-vitro testing has shown that florfenicol is active against the bacterial pathogens most commonly isolated in respiratory diseases in pigs, including *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*. Laboratory tests have also shown that florfenicol is active against the most commonly isolated bacterial pathogens involved in bovine respiratory disease which include *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni*. *In vitro* bactericidal activity has been demonstrated against these porcine and bovine pathogens.

For *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni* the following florfenicol breakpoints have been determined by CLSI (Clinical and Laboratory Standards institute) for bovine respiratory pathogens: susceptible ≤ 2 µg/ml, intermediate : 4 µg/ml, resistant : ≥ 8 µg/ml (2013).
For *A. pleuropneumoniae* and *P. multocida*, the CLSI breakpoint of resistance for swine respiratory disease is 8 µg/ml (2013).

Resistance to florfenicol is mainly mediated by an efflux system due to a specific (Flo-R) or multidrug transporter (AcrAB-TolC). The genes corresponding to these mechanisms are coded on mobile genetic elements such as plasmids, transposon or genes cassettes.

4.3 Pharmacokinetics

Cattle

Intramuscular administration at the recommended dose of 20 mg/kg maintains efficacious blood levels in cattle for 48 hours. Maximum mean plasma concentration (Cmax) of 3.86 µg/ml occurs at 5 hours (Tmax) after dosing. The mean plasma concentration 24 hours after dosing was 1.56 µg/ml.
The harmonic mean elimination half life was 18.8 hours.

After subcutaneous administration of the recommended dose of 40 mg florfenicol/kg b.w., maximum plasma concentration (Cmax) of approximately 3.5 µg/ml occurs approximately 7.0 hours (Tmax) after dosing. The mean plasma concentration 24 hours after dosing is approximately 2 µg/ml.
The harmonic mean elimination half life was 39.7 hours.

Pigs
After single intramuscular administration of the recommended dose of 15mg/kg to pigs maximum mean plasma concentration (Cmax) of 2.08 µg/ml occurs at 2 hours (Tmax) after dosing.

The harmonic mean elimination half life was 10.37 hours.

After administration to pigs by the intramuscular route, florfenicol is rapidly excreted, primarily in urine. Florfenicol is extensively metabolised.

Serum concentrations persist above 1 µg/ml for 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.

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

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Cardboard box containing one Type I amber glass bottle of 50, 100 or 250 ml closed with a bromobutyl rubber (Type I) stopper and aluminium seal.

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 or household waste.

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

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

KRKA, d.d., Novo mesto

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

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

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).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{CARDBOARD BOX}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Floron 300 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Florfenicol 300 mg/ml

3. PACKAGE SIZE

50 ml
100 ml
250 ml

4. TARGET SPECIES

Cattle and pigs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Pigs: IM use
Cattle: IM and SC use

7. WITHDRAWAL PERIODS

Withdrawal period:

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 permitted for use in lactating animals producing milk for human consumption.
Pigs	
Meat and offal:	18 days

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened, use within 28 days.

9. SPECIAL STORAGE PRECAUTIONS

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

KRKA

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

{GLASS BOTTLE 50, 100, 250 ml}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Floron 300 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Florfenicol 300 mg/ml

50 ml
100 ml
250 ml

3. TARGET SPECIES

Cattle and pigs

4. ROUTES OF ADMINISTRATION

Read the package leaflet before use.

Pigs: IM use
Cattle: IM and SC use

5. WITHDRAWAL PERIODS

Withdrawal period:

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 permitted for use in lactating animals producing milk for human consumption.
Pigs	
Meat and offal:	18 days

6. EXPIRY DATE

Exp. {mm/yyyy}

Once opened, use within 28 days.

7. SPECIAL STORAGE PRECAUTIONS

8. NAME OF THE MARKETING AUTHORISATION HOLDER

KRKA

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

Each ml contains:

Active substance:
Florfenicol 300 mg

A light yellow to yellow, clear, viscous liquid.

3. Target species

Cattle and pigs.

4. Indications for use

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 metaphylaxis.

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

5. Contraindications

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

6. Special warnings

Special precautions for safe use in the target species:
Do not use in 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.

Special precautions for the protection of the environment:
The use of this veterinary medicinal product may pose a risk for terrestrial plants, cyanobacteria and groundwater organisms.

Pregnancy and lactation:
Cattle: the safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only according 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. The use is not recommended during pregnancy and lactation.

Fertility:
Do not use in breeding boars and bulls.

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose:
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.
Pigs: 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.

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

7. Adverse events

Cattle:

Undetermined frequency (cannot be estimated from the available data):	Decreased food intake, loose stool[1] Injection site swelling[2,4] Injection site inflammation[3,4]

[1]May occur during the treatment period. The treated animals recover quickly and completely upon termination of treatment.
[2]When administered by the intramuscular route, may persist for 14 days.
[3]When administered by the intramuscular route, may persist up to 32 days after administration.
[4]When administered by the subcutaneous route, may persist at least for 41 days.

Pig:

Very common (>1 / 10 animals treated):	Diarrhoea[1] Peri-anal and rectal erythema/oedema[1]

	Pyrexia (40 °C) associated with either moderate depression or moderate dyspnea[2]
Undetermined frequency (cannot be estimated from the available data):	Injection site swelling[3] Injection site inflammation[4]

[1]May affect up to 50% of the animals; can be observed for one week.
[2]Approximately 30% of treated pigs presented with week or more after administration of the second dose.
[3]May last up to 5 days.
[4]May last up to 28 days.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

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.

Pigs:
15 mg florfenicol /kg bodyweight (1 mL of the product/ 20 kg) by intramuscular injection into the neck muscle twice at 48 hour intervals using a dry, sterile 16-gauge needle.

The dose volume given at any one injection site should not exceed 10 ml in cattle and 3 ml in pigs. The injection should only be given in the neck.

For intramuscular route, 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.
Do not broach the vial more than 25 times. Use a suitable draw-off needle or automatic dosing syringe to avoid excessive puncturing of the closure.

To ensure a correct dosage, body weight should be determined as accurately as possible.

9. Advice on correct administration

None.

10. Withdrawal periods

Cattle
Meat and offal (intramuscular route, 20 mg/kg bodyweight, twice): 30 days
Meat and offal (subcutaneous route, 40 mg/kg bodyweight, once): 44 days
Not authorised for use in 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 storage conditions.

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

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

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

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

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacisthow to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

1 bottle of 50, 100 or 250 ml in a cardboard box

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

Manufacturer responsible for batch release:
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
TAD Pharma GmbH, Heinz-Lohmann-Straße 5, 27472 Cuxhaven, Germany

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information