[Version 8, 10/2012]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

KEFLORIL 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.
Light yellow to yellow, clear viscous liquid.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs and cattle.

4.2 Indications for use, specifying the target species

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

Cattle: diseases caused by florfenicol susceptible bacteria.
Preventive and therapeutic treatment of respiratory tract infections in cattle due to *Mannheimia haemolytica, Pasteurella multocida* and *Histophilus somni*. The presence of the disease in the herd should be established before preventive treatment.

4.3 Contraindications

Do not administer to boars and adult bulls intended for breeding purposes.
Do not use in cases of known hypersensitivity to the active ingredient or to 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
Swab the stopper before removing each dose. Use a dry, sterile syringe and needle.
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 the florfenicol and may decrease the effectiveness of treatment with other antimicrobials, due to the potential for cross-resistance.

Use a suitable draw-off needle or automatic dosing syringe to avoid excessive puncturing of the closure.

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.'
Do not use the product in known cases of sensitivity to propylene glycol and polyethylene glycols.
Avoid direct contact with skin, eyes or mouth.
In case of accidental spillage of the solution onto skin, wash off immediately with soap and water.
In case of accidental contact with eyes, rinse immediately with plenty of water.

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)

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.

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 swelling at the injection site which may persist for 14 days. Inflammation at the injection site may persist up to 32 days after administration.
Administration of the product by the subcutaneous route may cause swelling and inflammation at the injection site which may persist at least for 41 days.

4.7 Use during pregnancy, lactation or lay

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

Pigs: the safety of the product in sows during pregnancy and lactation has not been demonstrated. Use of the product during pregnancy and lactation is therefore not recommended.

Cattle: the effect of florfenicol on bovine reproductive performance and pregnancy has not been assessed. Use only accordingly 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

Pigs
15 mg/kg bodyweight (1 ml per 20 kg) by intramuscular injection into the neck muscle twice at

48-hour intervals using a dry, sterile 16-gauge needle.
The volume administered per injection site should not exceed 3 ml.
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.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.

Cattle
For treatment:
IM route: 20 mg/kg bodyweight (1 ml/15 kg) to be administered twice 48 hours apart using a 16 gauge needle.

SC route: 40 mg/kg bodyweight (2 ml/15 kg) to be administered once only using a 16 gauge needle. The dose volume given at any one injection site should not exceed 10 ml.

The injection should only be given in the neck.

For prevention:
SC route: 40 mg/kg bodyweight (2 ml/15 kg) to be administered once only using a 16 gauge needle. The dose volume given at any one injection site should not exceed 10 ml.

The injection should only be given in the neck.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.

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

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.

Cattle
No other symptoms than those mentioned in section 4.6 are expected.

4.11 Withdrawal period(s)

Pigs
Meat and offal: 18 days

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.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use
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. However, bactericidal activity has been demonstrated in-vitro against *Actinobacillus pleuropneumoniae, Pasteurella multocida, Mannheimia haemolytica and Histophilus somni.*

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.*

Acquired resistance to florfenicol is mediated by efflux pump resistance associated with a floR 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-borne pathogen *Salmonella typhimurium.*

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 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.

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 18.8 hours.

Pigs
After single intramuscular administration of the recommended dose of 15mg/kg to pigs maximum mean plasma concentration (Cmax) of 2.8 µg/ml occurs at 2 hours (Tmax) after dosing.

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dimethyl sulfoxide
Propylene glycol
Macrogol 400

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

50, 100 and 250 ml Type I amber glass bottle closed with a bromobutyl rubber stopper and aluminium seal.
1 bottle (50 ml) in cardboard box.
1 bottle (100 ml) in cardboard box.
1 bottle (250 ml) in cardboard box.

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 product should be disposed of in accordance with local requirements.
The veterinary medicinal product should not enter water courses as florfenicol may be dangerous for fish and other aquatic organisms.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: DD month YYYY.
Date of last renewal: DD month YYYY.

10 DATE OF REVISION OF THE TEXT

MM/YYYY

PROHIBITION OF SALE, SUPPLY AND/OR USE

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

KEFLORIL 300 mg/ml Solution for injection for cattle and pigs
Florfenicol

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Florfenicol……300 mg/ml

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

50 ml
100 ml
250 ml

5. TARGET SPECIES

Already mentioned in the name.

6. INDICATION(S)

Not included

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Pigs: Intramuscular route 1 ml/20kg (15 mg/kg bodyweight) into the neck muscle twice at 48-hour intervals. The volume administered per injection site should not exceed 3 ml.

Cattle:
For treatment:
IM route: 20 mg/kg bodyweight (1 ml/15 kg) to be administered twice 48 hours
SC route: 40 mg/kg bodyweight (2 ml/15 kg) to be administered once
The dose volume given at any one injection site should not exceed 10 ml.

For prevention:
SC route: 40 mg/kg bodyweight (2 ml/15 kg) to be administered once

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

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Pigs
Meat and offal: 18 days

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.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening the immediate packaging: 28 days.

Once broached, use by

11. SPECIAL STORAGE CONDITIONS

Not applicable.

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

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

MINIMUM PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Label of 100 and 250 ml vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

KEFLORIL 300 mg/ml Solution for injection for cattle and pigs
Florfenicol

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Florfenicol……300 mg/ml

3. PHARMACEUTICAL FORM

Not requested

4. PACKAGE SIZE

100 ml
250 ml

5. TARGET SPECIES

Already mentioned in the name.

6. INDICATION(S)

Not included

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Pigs: Intramuscular route 1 ml/20kg (15 mg/kg bodyweight) into the neck muscle twice at 48-hour intervals. The volume administered per injection site should not exceed 3 ml.

Cattle: Intramuscular or Subcutaneous route
For treatment:
IM route: 20 mg/kg bodyweight (1 ml/15 kg) to be administered twice 48 hours
SC route: 40 mg/kg bodyweight (2 ml/15 kg) to be administered once
The dose volume given at any one injection site should not exceed 10 ml.

For prevention:
SC route: 40 mg/kg bodyweight (2 ml/15 kg) to be administered once

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

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Pigs
Meat and offal: 18 days

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.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening the immediate packaging: 28 days.

Once broached, use by

11. SPECIAL STORAGE CONDITIONS

Not applicable.

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

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
Label of 50 ml vials

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

KEFLORIL 300 mg/ml Solution for injection for cattle and pigs
Florfenicol

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Florfenicol……300 mg/ml

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

50 ml.

4. ROUTE OF ADMINISTRATION

Pigs: IM

Cattle: IM or SC

5. WITHDRAWAL PERIOD

Pigs
Meat and offal: 18 days

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.

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {month/year}

Shelf-life after first broaching the vial: 28 days.

Once broached, use by

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:

KEFLORIL 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 <and manufacturer responsible for batch release>:
To be adapted according to countries

Manufacturer responsible for batch release:
Vetoquinol S.A.
Magny-Vernois
70200 Lure
France

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

KEFLORIL 300 mg/ml Solution for injection for cattle and pigs

Florfenicol

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each ml contains:

Active substance: Florfenicol 300 mg/ml

Solution for injection.
Light yellow to yellow, clear viscous liquid

4. INDICATION(S)

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

Cattle: diseases caused by florfenicol susceptible bacteria.
Preventive and therapeutic treatment of respiratory tract infections in cattle due to Mannheimia haemolytica, Pasteurella multocida and Histophilus somni. The presence of the disease in the herd should be established before preventive treatment.

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

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.

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 swelling at the injection site which may persist for 14 days. Inflammation at the injection site may persist up to 32 days after administration.
Administration of the product by the subcutaneous route may cause swelling and inflammation at the injection site which may persist at least for 41 days.

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

7. TARGET SPECIES

Cattle and pigs.

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

Pigs
15 mg/kg bodyweight (1 ml per 20 kg) by intramuscular injection into the neck muscle twice at 48-hour intervals using a dry, sterile 16-gauge needle.
The volume administered per injection site should not exceed 3 ml.
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.

Cattle
For treatment:
IM route: 20 mg/kg bodyweight (1 ml/15 kg) to be administered twice 48 hours apart using a 16 gauge needle.

SC route: 40 mg/kg bodyweight (2 ml/15 kg) to be administered once only using a 16 gauge needle. The dose volume given at any one injection site should not exceed 10 ml.

The injection should only be given in the neck.

For prevention:
SC route: 40 mg/kg bodyweight (2 ml/15 kg) to be administered once only using a 16 gauge needle. The dose volume given at any one injection site should not exceed 10 ml.

The injection should only be given in the neck.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing.

9. ADVICE ON CORRECT ADMINISTRATION

None

10. WITHDRAWAL PERIOD

Pigs
Meat and offal: 18 days

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.

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 blister and carton after 'EXP'. The expiry date refers to the last day of that month.
Shelf-life after first-opening the container: 28 days.

12. SPECIAL WARNING(S)

Special warnings for each target species:
None

Special precautions for use in animals:
Swab the stopper before removing each dose. Use a dry, sterile syringe and needle.
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 the florfenicol and may decrease the effectiveness of treatment with other antimicrobials, due to the potential for cross-resistance.
Use a suitable draw-off needle or automatic dosing syringe to avoid excessive puncturing of the closure.

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.
Do not use the product in known cases of sensitivity to propylene glycol and polyethylene glycols.
Avoid direct contact with skin, eyes or mouth.
In case of accidental spillage of the solution onto skin, wash off immediately with soap and water.
In case of accidental contact with eyes, rinse immediately with plenty of water.

Use during pregnancy, lactation or lay:
Studies in laboratory animals have not revealed any evidence of embryo- or foetotoxic potential for florfenicol.

Pigs: the safety of the product in sows during pregnancy and lactation has not been demonstrated. Use of the product during pregnancy and lactation is therefore not recommended.

Cattle: the effect of florfenicol on bovine reproductive performance and pregnancy has not been assessed. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
None Known

Overdose (symptoms, emergency procedures, antidotes):
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.

Cattle
No other symptoms than those mentioned in section 4.6 are expected.

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.
The veterinary medicinal product should not enter water courses as florfenicol may be dangerous for fish and other aquatic organisms.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Presentation
50, 100 and 250 ml Type I amber glass bottle closed with a bromobutyl rubber stopper and aluminium seal.
1 bottle (50 ml) in cardboard box.
1 bottle (100 ml) in cardboard box.
1 bottle (250 ml) in cardboard box.

Not all pack sizes may be marketed.

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