# ANNEX III

# LABELLING AND PACKAGE LEAFLET

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**Box with bottle of 1L**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

LINCOPHAR 400 mg/ml solution for use in drinking water for chickens (for all countries except for DK, FI and SE)
LINCOPHAR Vet 400 mg/ml solution for use in drinking water for chickens (FI and SE)
LINCOPHAR Vet (DK)

Lincomycin (as hydrochloride monohydrate)

## 2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

**Active substance:**
Lincomycin (as hydrochloride monohydrate) 400 mg

## 3. PHARMACEUTICAL FORM

Solution for use in drinking water.

## 4. PACKAGE SIZE

1L

## 5. TARGET SPECIES

Chickens.

## 6. INDICATION(S)

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

Administer in drinking water.
Read the package leaflet before use.

## 8. WITHDRAWAL PERIOD

Chickens: Meat and offal: 5 days.
Not authorised for use in laying birds producing eggs 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: 3 months
Shelf life after reconstitution according to directions:: 24 hours
Once opened, use by: …

## 11. SPECIAL STORAGE CONDITIONS

Keep the bottle and barrel tightly closed.

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

Disposal: Read the package leaflet before use.

## 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

Ecuphar Veterinaria S.L.U.
Avenida Río de Janeiro, 60 – 66, planta 13
08016 Barcelona (Spain)

## 16. MARKETING AUTHORISATION NUMBER

Vm 46037/4004

## 17. MANUFACTURER'S BATCH NUMBER

Batch{number}

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING**

Label for the bottle of 1L

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

LINCOPHAR 400 mg/ml solution for use in drinking water for chickens (for all countries except for DK, FI and SE)
LINCOPHAR Vet 400 mg/ml solution for use in drinking water for chickens (FI and SE)
LINCOPHAR Vet (DK)

Lincomycin (as hydrochloride monohydrate)

## 2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

**Active substance:**
Lincomycin (as hydrochloride monohydrate) 400 mg

## 3. PHARMACEUTICAL FORM

Solution for use in drinking water.

## 4. PACKAGE SIZE

1L

## 5. TARGET SPECIES

Chickens.

## 6. INDICATION(S)

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

Administer in drinking water.
Read the package leaflet before use.

## 8. WITHDRAWAL PERIOD

Chickens: Meat and offal: 5 days.
Not authorised for use in laying birds producing eggs 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: 3 months
Shelf life after reconstitution according to directions: 24 hours
Once opened, use by: …

## 11. SPECIAL STORAGE CONDITIONS

Keep the bottle and barrel tightly closed.

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

## 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"

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

Ecuphar Veterinaria S.L.U.
Avenida Río de Janeiro, 60 – 66, planta 13
08016 Barcelona (Spain)

## 16. MARKETING AUTHORISATION NUMBER

Vm 46037/4004

## 17. MANUFACTURER'S BATCH NUMBER

Batch{number}

# B. PACKAGE LEAFLET

# PACKAGE LEAFLET for the Bottle of 1L

LINCOPHAR 400 mg/ml solution for use in drinking water for chickens

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

Marketing authorisation holder:
Ecuphar Veterinaria S.L.U.
Avenida Río de Janeiro, 60 – 66, planta 13
08016 Barcelona (Spain)

Manufacturer for the batch release:
Eurovet Animal Health B.V.
Handelsweg, 25- 5531AE Bladel (Netherlands)

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

LINCOPHAR 400 mg/ml solution for use in drinking water for chickens
Lincomycin (as hydrochloride monohydrate)

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

Each ml contains:

**Active substance:**
Lincomycin (as hydrochloride monohydrate) 400 mg

**Excipient:**
Benzyl alcohol (E1519) 10.0 mg

Colourless to yellow clear solution.

## 4. INDICATIONS

Chickens: Treatment and metaphylaxis of necrotic enteritis caused by *Clostridium perfringens*. The presence of the disease in the group must be established before the product is used.

## 5. CONTRAINDICATIONS

Do not use in cases of known hypersensitivity to the active substance or to any of the excipients.
Do not administer and do not allow access to water containing lincomycin to rabbits, hamsters, guinea pigs, chinchillas, horses or ruminants as this could result in severe gastro-intestinal disturbances.

Do not use in case of known resistance to lincosamides.
Do not use in cases of hepatic dysfunction.

## 6. ADVERSE REACTIONS

None described.
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 inform your veterinary surgeon.

## 7. TARGET SPECIES

Chickens

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

For use in drinking water.

*Dosing guidance and recommended doses:*
To ensure a correct dosage, body weight should be determined as accurately as possible to avoid underdosing.
The intake of medicated water depends on the physiological and clinical condition of the animals. In order to obtain the correct dosage, the concentration of the lincomycin has to be adjusted accordingly.
The uptake of water should be monitored frequently.
The medicated water should be the only source of drinking water for the animals for the entire duration of the treatment period.

After the end of the medication period, the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of the active substance.

*Dosage:*

**Chickens**:
Necrotic enteritis: 5 mg lincomycin per kg of bodyweight per day (corresponding to 1.25 ml product/100 kg bodyweight/day) for 7 consecutive days.

*Administration:*

To be administered orally, in the drinking water.

The concentration to be used depends on the actual body weight and the water consumption of the animals and can be calculated according to the following formula:

$$\frac{\textit{Dose (ml product per kg body weight per day)} \times \textit{mean body weight (kg) of animals to be treated}}{\textit{Average daily water intake (litre/animal)}} = \textit{ml product per litre drinking water}$$

The use of suitably calibrated equipment is recommended if part packs are used. The daily amount is to be added to the drinking water in such a way that all medication will be consumed within 24 hours. Medicated drinking water should be freshly prepared every 24 hours. No other source of drinking water should be available.

## 9. ADVICE ON CORRECT ADMINISTRATION

## 10. WITHDRAWAL PERIOD

Chickens: Meat and offal: 5 days.
Not authorised for use in laying birds producing eggs for human consumption

## 11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Keep the bottle and barrel tightly closed.
Do not use this veterinary medicinal product after the expiry date which is stated on the labels after EXP. The expiry date refers to the last day of that month.

Shelf life after first opening the container: 3 months
Shelf life after reconstitution acording to directions: 24 hours

## 12. SPECIAL WARNING(S)

Special warnings for each target species:
Medicated drinking water uptake can be affected by the severity of the disease.

There is a lack of clinical breakpoints for *C. perfringens*. Where possible, therapy should be based on local (regional, farm level) epidemiological information concerning the response of necrotic enteritis to treatment with lincomycin.

Special precautions for use in animals:
Use of the veterinary medicinal product should be based on identification of the target pathogen (s) and on epidemiological information and knowledge of susceptibility of the target bacteria at farm level, or at local/regional level. However, also see text under section above. Official, national and regional antimicrobial policies should be taken into account when the veterinary medicinal product is used.

Use of the veterinary medicine deviating from the instructions given in the summary product characteristics (SPC) may increase the prevalence of bacteria resistant to the lincomycin and may decrease the effectiveness of treatment with other lincosamides, macrolides and streptogramin B due to the potential for cross-resistance.

Repeated or prolonged use should be avoided by improving the farm management and hygiene practices.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This product contains lincomycin, which can cause allergic reactions in some people.
People with known hypersensitivity (allergy) to lincomycin or any other lincosamide or to any of the excipients should avoid contact with the veterinary medicinal product.
Contact with skin and eyes should be avoided.
Personal protective equipment consisting of impervious gloves should be worn when handling the product.
In case of accidental exposure to the skin, eyes or mucous membranes, wash the affected area thoroughly with plenty of water.
In case of allergic reaction (inflammation of the face, lips or eyes, or respiratory difficulties), or persistent eye irritation occurring after exposure, seek medical advice immediately and show the package leaflet or label to the physician.
Wash hands and any exposed skin with soap and water immediately after use.
Do not eat, drink or smoke while handling the product.

Other precautions
Lincomycin is known to be toxic to terrestrial plants and cyanobacteria.

Lay:
Laboratory studies in rats have not produced any evidence of teratogenic effects, foetotoxicity has been reported. The safety of the veterinary medicinal product has not been established during lay in the target species.

Interactions with other medicinal products and other forms of interaction:
Antagonism may exist between lincomycin and macrolides such as erythromycin and other bactericidal antibiotics; concurrent use is therefore not recommended due to competitive binding at the 50S ribosomal subunit of the bacterial cell.
The bioavailability of lincomycin may decrease in the presence of gastric antacids or activated charcoal, pectin or kaolin.
Lincomycin can potentiate neuromuscular effects of anaesthetics and muscle relaxants.

Overdose (symptoms, emergency procedures, antidotes):

In case of accidental overdose, the treatment must be stopped and restarted at the recommended dose level.

There is no specific antidote, treatment is symptomatic.

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

Do not contaminate surface waters or ditches with product or used container.
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

## 15. OTHER INFORMATION

**Pharmacodynamic properties**
Lincomycin is a lincosamide antibiotic derived from *Streptomyces lincolnensis* which inhibits protein synthesis. Lincomycin binds to the 50S sub-unit of the bacterial ribosome close to the peptidyl transfer centre and interferes with the peptide chain elongation process by causing premature peptidyl-tRNA dissociation from the ribosome.
Lincomycin is active against some gram-positive bacteria (*Clostridium perfringens*).
While the lincosamides are generally considered to be bacteriostatic agents, the activity depends on the sensitivity of the organism and concentration of the antibiotic. Lincomycin may be either bactericidal or bacteriostatic.
Resistance to lincomycin is frequently conferred by plasmid-borne factors (erm genes) coding for methylases modifying the ribosomal binding site and frequently leading to cross-resistance to other antimicrobials of the macrolides, lincosamides and streptogramins group. Lincomycin resistance mediated by efflux pumps, or by inactivating enzymes, has also been described. There is often complete cross-resistance between lincomycin and clindamycin.

**Pharmacokinetic particulars**
Chickens were administered lincomycin hydrochloride in the drinking water at a level of approximately 34 mg/litre (5.1-6.6 mg/kg body weight) for seven days. Metabolites comprised more than 75% of total residues in the liver. Unmetabolised lincomycin declined at a slightly faster half-life (t½ = 5.8 hours) than total residue. Lincomycin and one unknown metabolite comprised >50% of the muscle residue at zero hours. The excreta contained mostly unmetabolised lincomycin (60-85%) during treatment.

Nature of the container:

White opaque high density polyethylene bottle with transparent graduated scale closed with white opaque low density polyethylene screw-cap and white polyethylene tamper-evident ring (1 L).

White opaque high density polyethylene barrel, closed with white opaque high density polyethylene screw-cap and a white polyethylene tamper-evident ring (5L).

Polypropylene measuring device is included in the packaging size of 1L.

Pack sizes:
Box with bottle of 1L
Barrelof 5L
Not all pack sizes may be marketed.
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.
For animal treatment only. To be supplied only on veterinary prescription.

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE - COMBINED LABEL AND PACKAGE LEAFLET**

**{NATURE/TYPE} Barrel of 5L**

## 1. Name and address of the marketing authorisation holder and of the manufacturing authorisation holder responsible for batch release , if different

Marketing authorisation holder:
Ecuphar Veterinaria S.L.U.
Avenida Río de Janeiro, 60 – 66, planta 13
08016 Barcelona (Spain)

Manufacturer responsible for batch release:
Eurovet Animal Health B.V.
Handelsweg, 25- 5531AE Bladel (Netherlands)

## 2. Name of the veterinary medicinal product

LINCOPHAR 400 mg/ml solution for use in drinking water for chickens (for all countries except for DK, FI and SE)
LINCOPHAR Vet 400 mg/ml solution for use in drinking water for chickens (FI and SE)
LINCOPHAR Vet (DK)

Lincomycin (as hydrochloride monohydrate)

## 3. Statement of the active substance (s) and other ingredients

Each ml contains:

**Active substance:**
Lincomycin (as hydrochloride) 400 mg

**Excipient(s):**
Benzyl alcohol (E1519) 10.0 mg

Colourless to yellow clear solution.

## 4. Pharmaceutical form

Solution for use in drinking water.

## 5. Package size

5 L

## 6. Indications

Chickens: Treatment and metaphylaxis of necrotic enteritis caused by *Clostridium perfringens*. The presence of the disease in the group must be established before the product is used.

## 7. Contraindications

Do not use in cases of known hypersensitivity to the active substance or to any of the excipients.
Do not administer and do not allow access to water containing lincomycin to rabbits, hamsters, guinea pigs, chinchillas, horses or ruminants as this could result in severe gastrointestinal disturbances.
Do not use in case of known resistance to lincosamides.
Do not use in cases of hepatic dysfunction.

## 8. Adverse reactions

None described.

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 inform your veterinary surgeon.

## 9. Target species

Chickens

## 10. Dosage for each species, route(s) and method of administration

For use in drinking water.

*Dosing guidance and recommended doses:*
To ensure a correct dosage, body weight should be determined as accurately as possible to avoid underdosing.
The intake of medicated water depends on the physiological and clinical condition of the animals. In order to obtain the correct dosage, the concentration of the lincomycin has to be adjusted accordingly.
The uptake of water should be monitored frequently.
The medicated water should be the only source of drinking water for the animals for the entire duration of the treatment period.

After the end of the medication period, the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of the active substance.

*Dosage:*

**Chickens**: Necrotic enteritis: 5 mg lincomycin per kg of bodyweight per day (corresponding to 1.25 ml product/100 kg bodyweight/day) for 7 consecutive days.

*Administration:*

To be administered orally, in the drinking water.

The concentration to be used depends on the actual body weight and the water consumption of the animals and can be calculated according to the following formula:

$$\frac{\textit{Dose (ml product per kg body weight per day)} \times \textit{mean body weight (kg) of animals to be treated}}{\textit{Average daily water intake (litre/animal) per animal per day}} = \textit{ml product per litre drinking water}$$

The use of suitably calibrated equipment is recommended if part packs are used. The daily amount is to be added to the drinking water in such a way that all medication will be consumed within 24 hours. Medicated drinking water should be freshly prepared every 24 hours. No other source of drinking water should be available.

## 11. Advice on correct administration

## 12. Withdrawal period

Withdrawal period:
Chickens: Meat and offal: 5 days.
Not authorised for use in laying birds producing eggs for human consumption

## 13. Special storage precautions

Keep the bottle and barrel tightly closed.
Do not use this veterinary medicinal product after the expiry date which is stated on the labels after EXP. The expiry date refers to the last day of that month.

Shelf life after first opening the container: 3 months
Shelf life after reconstitution according to directions: 24 hours

## 14. Special warning(s)

Special warnings for each target species:
Medicated drinking water uptake can be affected by the severity of the disease.

There is a lack of clinical breakpoints for *C. perfringens*. Where possible, therapy should be based on local (regional, farm level) epidemiological information concerning the response of necrotic enteritis to treatment with lincomycin.

Special precautions for use in animals:
Use of the veterinary medicinal product should be based on identification of the target pathogen (s) and on epidemiological information and knowledge of susceptibility of the target bacteria at farm level, or at local/regional level. However, also see text under section above. Official, national and regional antimicrobial policies should be taken into account when the veterinary medicine is used.

Use of the veterinary medicinal product deviating from the instructions given in the summary product characteristics (SPC) may increase the prevalence of bacteria resistant to the lincomycin and may decrease the effectiveness of treatment with other lincosamides, macrolides and streptogramin B due to the potential for cross-resistance.

Repeated or prolonged use should be avoided by improving the farm management and hygiene practices.

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This product contains lincomycin, which can cause allergic reactions in some people.
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Contact with skin and eyes should be avoided.
Personal protective equipment consisting of impervious gloves should be worn when handling the product.
In case of accidental exposure to the skin, eyes or mucous membranes, wash the affected area thoroughly with plenty of water.
In case of allergic reaction (inflammation of the face, lips or eyes, or respiratory difficulties), or persistent eye irritation occurring after exposure, seek medical advice immediately and show the package leaflet or label to the physician.
Wash hands and any exposed skin with soap and water immediately after use.
Do not eat, drink or smoke while handling the product.

Other precautions
Lincomycin is known to be toxic to terrestrial plants and cyanobacteria.

Lay:
Laboratory studies in rats have not produced any evidence of teratogenic effects, although foetotoxicity has been reported. The safety of the veterinary medicinal product has not been established during lay in the target species.

Interactions with other medicinal products and other forms of interaction:
Antagonism may exist between lincomycin and macrolides such as erythromycin and other bactericidal antibiotics; concurrent use is therefore not recommended due to competitive binding at the 50S ribosomal subunit of the bacterial cell.
The bioavailability of lincomycin may decrease in the presence of gastric antacids or activated charcoal, pectin or kaolin.
Lincomycin can potentiate neuromuscular effects of anaesthetics and muscle relaxants.

Overdose (symptoms, emergency procedures, antidotes):

In case of accidental overdose, the treatment must be stopped and restarted at the recommended dose level.

There is no specific antidote, treatment is symptomatic.

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

## 15. Special precautions for the disposal of unused product or waste materials, if any

Do not contaminate surface waters or ditches with product or used container.
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

## 16. Date on which the package leaflet was last approved

## 17. Other information

**Pharmacodynamic properties**
Lincomycin is a lincosamide antibiotic derived from Streptomyces lincolnensis which inhibits protein synthesis. Lincomycin binds to the 50S sub-unit of the bacterial ribosome close to the peptidyl transfer centre and interferes with the peptide chain elongation process by causing premature peptidyl-tRNA dissociation from the ribosome.
Lincomycin is active against some gram-positive bacteria (*Clostridium perfringens*).
While the lincosamides are generally considered to be bacteriostatic agents, the activity depends on the sensitivity of the organism and concentration of the antibiotic. Lincomycin may be either bactericidal or bacteriostatic.
Resistance to lincomycin is frequently conferred by plasmid-borne factors (erm genes) coding for methylases modifying the ribosomal binding site and frequently leading to cross-resistance to other antimicrobials of the macrolides, lincosamides and streptogramins group. Lincomycin resistance mediated by efflux pumps, or by inactivating enzymes, has also been described. There is often complete cross-resistance between lincomycin and clindamycin.

**Pharmacokinetic particulars**
Chickens were administered lincomycin hydrochloride in the drinking water at a level of approximately 34 mg/litre (5.1-6.6 mg/kg body weight) for seven days. Metabolites comprised more than 75% of total residues in the liver. Unmetabolised lincomycin declined at a slightly faster half-life ($t_{½}$ = 5.8 hours) than total residue. Lincomycin and one unknown metabolite comprised >50% of the muscle residue at zero hours. The excreta contained mostly unmetabolised lincomycin (60-85%) during treatment.

Nature of the container:
White opaque high density polyethylene bottle with transparent graduated scale closed with white opaque low density polyethylene screw-cap and white polyethylene tamper-evident ring (1 L).
White opaque high density polyethylene barrel, closed with white opaque high density polyethylene screw-cap and a white polyethylene tamper-evident ring (5L).
Polypropylene measuring device is included in the packaging size of 1L.

Pack sizes:
Box with bottle of 1L
Barrel of 5L
Not all pack sizes may be marketed.
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

## 18. 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.

## 19. The words "Keep out of the sight and reach of children"

Keep out of the sight and reach of children

## 20. Expiry date

EXP:
Once opened, use by: ……

## 21. Marketing authorisation number

Vm 46037/4004

## 22. Manufacturer's batch number

Batch {number}

Approved: 15 August 2018