SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

OCNIL 400 mg/g powder for use in drinking water *(ES, CY, EL, IE, IT, PT, UK, HU)*
DOPHALIN 400 mg/g powder for use in drinking water *(AT, EE, FR, LT, LV, RO, PL)*

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substance:

Lincomycin .....400 mg
(equivalent to 450 mg of lincomycin hydrochloride)

Excipients:

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Powder for use in drinking water.
White powder, inodorous and without lumps.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs and Chickens.

4.2 Indications for use, specifying the target species

Pigs
Treatment and metaphylaxis of enzootic pneumonia caused by *Mycoplasma hyopneumoniae*.
The presence of the disease in the group must be established before the product is used.

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.

4.3 Contraindications

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

4.4 Special warnings for target species

Medicated drinking water uptake can be affected by the severity of the disease. In case of insufficient uptake of water, pigs should be treated parenterally.

The susceptibility of *Mycoplasma hyopneumoniae* to antimicrobial agents is difficult to test *in vitro* owing to technical constraints. In addition, there is a lack of clinical breakpoints for both *M. hyopneumoniae* and *C. perfringens*. Where possible, therapy should be based on local (regional, farm level) epidemiological information concerning the response of enzootic pneumonia/necrotic enteritis to treatment with lincomycin

4.5 Special precautions for use

Special precautions for use in animals

Use of the veterinary medicinal product preferably should be based on identification of the target pathogen and susceptibility testing of the bacteria isolated from the animal. However, also see text under section 4.4.
Official, national and regional antimicrobial policies should be taken into account when the veterinary medicinal product is used.
Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to lincomycin and may decrease the effectiveness of treatment with other lincosamides, macrolides or streptogramin B due to 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 and lactose monohydrate, either of which can cause allergic reactions in some people. People with known hypersensitivity to lincomycin or any other lincosamide, or to lactose monohydrate, should avoid contact with the veterinary medicinal product.
Care should be taken not to raise and inhale any dust.
Contact with skin and eyes should be avoided.
Personal protective equipment consisting of approved dust masks (either a disposable half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator conforming to European Standard EN 140 with a

filter to EN 143), gloves and safety glasses should be worn when handling and mixing the product. If respiratory symptoms develop following exposure, seek medical advice and show this warning to the physician.
In case of accidental exposure to the skin, eyes or mucous membranes, wash the affected area thoroughly with plenty of water. If symptoms such as skin rash or persistent eye irritation appear 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, cyanobacteria and groundwater bacteria.

4.6 Adverse reactions (frequency and seriousness)

Pigs given lincomycin-medicated water may develop diarrhoea/soft stools and/or mild swelling of the anus within the first 2 days after onset of treatment on rare occasions. Some pigs may show reddening of the skin and mild irritable behaviour on rare occasions. These conditions are usually self-correcting within 5-8 days without discontinuing the lincomycin treatment.
Allergic/hypersensitive reactions occur on rare occasions.
The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reactions)
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or 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 pregnancy, lactation or lay in the target species. Use only according to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction 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 anaesthetic and muscle relaxants.

4.9 Amounts to be administered and administration route

In drinking water use

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:

Pigs:
Enzootic pneumonia: 10 mg lincomycin per kg of body weight (corresponding to 25 mg product per kg bodyweight) for 21 consecutive days.

Chickens:
Necrotic enteritis: 5 mg of lincomycin per kg body weight (corresponding to 12.5 mg product per kg body weight) for 7 consecutive days.

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:

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

The use of suitably calibrated weighing 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.

The maximum solubility of finished product is 50 g/l in soft and hard water. For stock solutions and when using a dosing pump, take care not to exceed the maximum solubility which can be achieved under the given conditions. Adjust flow rate settings of the dosing pump according to concentration of the stock solution and water intake of the animals to be treated.

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

A dosage greater than 10 mg lincomycin per kg of body weight may cause diarrhoea and loose stools in pigs.
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.

4.11 Withdrawal periods

Pigs
Meat and offal: 1 day.

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

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterial for systemic use, Lincosamides.
ATC Vet Code: QJ01FF02

5.1 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)* and mycoplasmas *(Mycoplasma hyopneumoniae)*.

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. However, the most prevalent mechanism in mycoplasmas is the alteration of the binding site through mutational events (chromosomal resistance). Lincomycin resistance

mediated by efflux pumps, or by inactivating enzymes, has also been described. There is often complete cross-resistance between lincomycin and clindamycin.

5.2 Pharmacokinetic particulars

In pigs, lincomycin is rapidly absorbed following oral administration. A single oral administration of lincomycin hydrochloride, at dose levels of approximately 22, 55 and 100 mg/kg body weight in pigs, resulted in dose related lincomycin serum levels, detected for 24-36 hours after administration. Peak serum levels were observed at 4 hours after dosing. Similar results were observed following single oral doses of 4.4 and 11.0 mg/kg body weight in pigs. Levels were detectable for 12 to 16 hours, with peak concentrations occurring at 4 hours. A single oral dose of 10 mg/kg body weight was administered to pigs to determine the bioavailability. The oral absorption of lincomycin was found to be 53% +/- 19%.
Repeated dosing of pigs with daily oral doses of 22 mg lincomycin/kg body weight for 3 days indicated no accumulation of lincomycin in the species, with no detectable serum levels of antibiotic after 24 hours post administration.
Crossing the intestinal barrier, lincomycin is widely distributed to all tissues, especially the lungs and joint cavities; the volume of distribution is about 1 litre. The elimination half-life of lincomycin is greater than 3 hours. Approximately 50% of lincomycin is metabolised in the liver. Lincomycin undergoes enterohepatic circulation. Lincomycin is eliminated unchanged or in the form of various metabolites in bile and urine. High concentrations of the active form are observed in the intestine.
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.

Environmental properties

Lincomycin is known to be toxic to terrestrial plants, cyanobacteria and groundwater bacteria.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silica colloidal anhydrous
Lactose monohydrate

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 as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging: 6 months.
Shelf-life after reconstitution according to directions: 24 hours.

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

Thermosealed bags made of polypropylene/metallized polyester/low density polyethylene.

Pack size:
Bag of 150g
Bag of 1Kg

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

Dangerous to aquatic life (cyanobacteria). 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.

7. MARKETING AUTHORISATION HOLDER

VETPHARMA ANIMAL HEALTH, S.L.
Les Corts, 23
08028 – BARCELONA
Spain

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE