SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Linco-Sol 400 mg/g powder for use in drinking water for pigs and chickens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Lincomycin (as hydrochloride) 400 mg/g

Excipient:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for use in drinking water.
White or almost white powder.

4. CLINICAL PARTICULARS

4.1 Target species

Swine and chicken (broiler)

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 use if resistance to lincosamides has been detected.
Do not administer to horses, ruminants, guinea pigs, hamsters, chinchilla and rabbits. Ingestion by these species may result in severe gastrointestinal effects.
Do not use in cases of hepatic dysfunction.

4.4 Special warnings for each target species

Medicated drinking water uptake can be affected by the severity of the disease. In case of insufficient uptake of water, animals 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 summary of product characteristics 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 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. The wearing of approved dust masks (either a disposable half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator to European Standard EN 140 with a filter to EN 143), gloves and safety glasses are recommended whilst reconstituting or administering the solution.
Direct contact of the product with the skin, eyes and mucous membranes should be avoided.
In case of accidental exposure to the skin, eyes or mucous membranes, rinse abundantly with water. In case of allergic reaction (inflammation of the face, lips or eyes or respiratory difficulties) during reconstituting or administering of the product, seek medical advice immediately and show the package leaflet or the label to the physician.
Do not smoke, eat or drink when handling the product.
Wash hands and any exposed skin with soap and water immediately after use.

4.6 Adverse reactions (frequency and seriousness)

On rare occasions Lincomycin may cause transient soft stools and/or mild swelling of the anus within the first two days of treatment in pigs. On rare occasions some pigs may show reddening of skin and mild irritable behaviour. These conditions are usually self-correcting within 5-8 days without discontinuing 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 in accordance with 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 anaesthetics and muscle relaxants.

4.9 Amounts to be administered and administration route

For use in drinking water.

Dosage:
Swine:
Enzootic pneumonia: 10 mg lincomycin per kg of body weight for 21 consecutive days.
Chicken (boiler)
Necrotic enteritis*:* the daily dose is 5 mg lincomycin per kg of body weight for 7 consecutive days.
Administration:
To be administered orally, in the drinking water.
Swine:
The product should be administered continuously in the drinking water. In pigs, administration of 33 mg lincomycin per litre containing to the completion of drinking water by dissolving 100 g of product in 1200 litres of water. When using a water proportioner, prepare a stock solution by dissolving 100 g of product in 12 litres of water. Set the proportioner to deliver 10 ml of stock solution per litre of drinking water.
Chicken (broiler):
The concentration to be used depends on the actual body weight and the water consumption of the animals and can be calculated as follows:

$$\frac{\text{.....mg product per kg body weight and day} \times \text{Average chicken body weight (kg)}}{\text{Average daily water intake (litre/animal)}} = \text{....mg product per litre of drinking water}$$

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

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, throughout the treatment period. Medicated water should be refreshed every 24 hours. 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.

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

Lincomycin has a good margin of safety, but higher levels of dosage than recommended 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 period(s)

Meat and offal of swine: 1 day
Meat and offal of chicken (broiler): 5 days
Not authorised for use in laying birds producing eggs for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use; Lincosamides.
ATC vet code: QJ01FF02

5.1 Pharmacodynamic properties

Lincomycin is a lincosamide antibiotic produced by *Streptomyces lincolensis*. Lincomycin is bacteriostatic in action inhibiting the protein synthesis predominantly by binding to the 50S ribosomal subunits of bacteria.
Depending on the sensitivity of micro-organisms, and on the concentration of the active substance the protein synthesis inhibition antibacterial action can either be bacteriostatic or bactericide.
Lincomycin is active against a wide range of Gram-positive micro-organisms, including also anaerobic bacteria such as *clostridia* and *Brachyspira spp.*, as well as *Mycoplasma spp.*
Lincomycin has no activity against Gram-negative bacteria, such as *Klebsiella spp.*, *Pasteurella spp.* and *Salmonella spp.*
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

Systemic bioavailability of lincomycin is approximately 53% after oral administration in pigs.
Lincomycin is rapidly absorbed orally and reaches therapeutic plasma concentration.
After a single, oral administration of approximately 4.4 mg/kg and 11 mg/kg lincomycin to pigs resulted therapeutic plasma concentration for 12-16 hours, reaching peak plasma concentration after 4 hours. After a single, oral dose of 10 mg/kg lincomycin to pigs the maximum plasma concentration (C_{max}) of 1.45 mg/kg was reached at 3.6 hours (T_{max}). The elimination half life ($T_{1/2\beta}$) is about 3.36 hours. The oral administration of 22 mg/kg lincomycin for 3 days to pigs did not result in drug accumulation after 24 hours of administration and there was no therapeutic plasma concentration.
After oral administration the absorbed lincomycin is eliminated through the bile and faeces in active form or as metabolites.
Lincomycin is also *excreted* in the milk.
Lincomycin reaches the inflammation site by polymorf neutrophil granulocytes that explains its fast absorption and distribution, efficient penetration and targeted activity in difficult to reach tissues.

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.

5.3 Environmental properties

Lincomycin is known to be toxic to terrestrial plants after application of slurry/manure from treated weaner pigs, fattening pigs and broiler.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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: 2 years
Shelf life after first opening the immediate packaging: 3 months
Shelf life after dilution or reconstitution according to directions: 24 hours

6.4 Special precautions for storage

Do not store above 25°C.

Store in the original container tightly closed in order to protect from moisture.

6.5 Nature and composition of immediate packaging

150 g polypropylene container with polypropylene lid and inner bag of LDPE.
1.5 kg polypropylene container with polypropylene lid and inner bag of LDPE.
5 kg polypropylene container with polypropylene lid and inner bag of LDPE.
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.

7. MARKETING AUTHORISATION HOLDER

Lavet Pharmaceuticals Ltd.
2143 Kistarcsa
Batthyány u. 6.
Hungary

8. MARKETING AUTHORISATION NUMBER

Vm 32823/4005

9. DATE OF FIRST AUTHORISATION

11 February 2011

10. DATE OF REVISION OF THE TEXT

July 2021

Approved: 02/07/21