Livsin-LS Injection
(Lincomycin Hydrochloride & Spectinomycin Hydrochloride)

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Livsin-LS Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains per ml:
Active substances:

Spectinomycin hydrochloride	149,010mg	eq. 100mg Spectinomycin
Lincomycin hydrochloride	56,700 mg	eq. 50mg Lincomycin

Excipients:
Benzyl alcohol 9mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Injectable solution.

4. CLINICAL INFORMATION:

4.1 Target species:

Calves.

4.2 Indications for use, specifying the target species:

Treatment of infections caused by organisms susceptible to lincomycin/spectinomycin provided that effective concentrations are achieved at the site of infection.

4.3 Contraindications:

Do not use in case of hypersensitivity to lincomycin or spectinomycin.
Lincomycin is toxic to rabbits, hamsters and horses. Do not administer the veterinary medicinal product to animals other than calves.
Do not administer concomitantly with macrolides or clindamycin.

4.4 Special warnings for each target species:

A significant proportion of *E. coli* strains exhibit high MICs (minimal inhibitory concentrations) to the lincomycin-spectinomycin combination and may be clinically resistant, although no critical concentration is defined.

4.5 Special precautions for use:

Special precautions for use in animals:
Some microorganisms develop antibiotic resistance. It is recommended to administer the veterinary medicinal product after carrying out an antibiogram.

The veterinary medicinal product cannot be administered intravenously in order to avoid cardiovascular depression.

The risk of nephrotoxicity and ototoxicity from aminoglycosides may increase in cases of administration of diuretics such as furosemide (functional renal failure due to dehydration following administration of diuretics).
Aminoglycoside dosage should be reduced in cases of obesity, dehydration or in animals with reduced renal function.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to lincomycin or spectinomycin should avoid contact with the veterinary medicinal product.

4.6 Adverse reactions (frequency and severity):

During post-marketing surveillance, allergic reactions have been reported very rarely. The frequency of adverse reactions is defined as follows:
- very common (adverse effects in more than 1 in 10 animals treated)
- common (between 1 and 10 animals out of 100 animals treated)
- uncommon (between 1 and 10 animals out of 1000 animals treated)
- rare (between 1 and 10 animals out of 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated cases)

4.7 Use during pregnancy, lactation or laying:

The veterinary medicinal product is only indicated in calves. Do not administer to pregnant or lactating cows.
Administration to pregnant or lactating sows will be done only on the basis of the benefit/risk analysis carried
out by the attending veterinarian.

4.8 Drug interactions and other forms of interaction:

Aminoglycosides enhance the activity of neuromuscular blocking agents such as gaseous anesthetics, magnesium salts and muscle relaxants, resulting in possible paralysis and apnea. Neuromuscular blockade with post-anesthetic paralysis may occur.
In combination with injectable colistin, the risks of nephrotoxic effects are increased.
Antagonism with erythromycin or tetracyclines may be observed.

4.9 Dosage and route of administration:

Intramuscular injection:

-	Calves:	1 ml per 10 kg of body weight (= 15 mg/kg). This dosage can be administered twice on the first day, Subsequently, only one injection per day is given, for 1 to 4 days. Do not administer more than 20 ml per injection site.

The weight of the animal must be assessed as best as possible in order to ensure correct dosage and to avoid any underdosage.

Bacterial sensitivity should be reassessed by antibiogram if clinical improvement does not occur within 3 days. If necessary, change treatment.

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

Rapidly administered intravenously, aminoglycosides slow heart rate, decrease cardiac output, and decrease blood pressure due to their effect on calcium metabolism.
Aminoglycosides can cause competitive (nondepolarizing) neuromuscular blockade, resulting in acute muscle paralysis and apnea.
Lincomycin is also a potential neuromuscular blocker.
Prolonged administration of aminoglycosides may cause ototoxic or nephrotoxic effects. The ototoxicity and nephrotoxicity of spectinomycin is low.

4.11 Waiting times:

Claves: meat and offal: 24 days

5. PHARMACOLOGICAL PROPERTIES:

This injectable solution contains 2 active antimicrobial substances: lincomycin is an antibiotic from the lincosamide family and spectinomycin is an antibiotic from the aminocyclitol family.

Pharmacotherapeutic group: Antibiotics for systemic use

5.1 Pharmacodynamic properties:

Lincomycin binds to the 50S subunit of bacterial ribosomes, while spectinomycin binds to the 30S subunit of bacterial ribosomes. This results in translation erroneous interpretation of genetic information carried by messenger RNA and inhibition of bacterial protein synthesis.

Lincomycin is mainly active against Gram-positive germs, anaerobic germs and mycoplasmas.

Chromosomal resistance to lincomycin evolves in several successive steps. The most important mechanisms of acquired resistance to lincosamides are encoded on bacterial genes. These are rRNA methylation with modification of the antibiotic binding capacity to the ribosome, enzymatic inactivation of the antibiotic and increased efflux of the antibiotic out of the bacterial cell by means of specific transport mechanisms. Resistance encoded by plasmid genes
is quite stable.

Cross-resistance between lincomycin and other lincosamides (e.g. clindamycin) is complete. Cross-resistance between lincomycin and macrolides and type B streptogramins is partial.

Spectinomycin is mainly active against aerobic Gram-negative microorganisms, some aerobic Gram-positive germs and mycoplasmas.
Chromosomal resistance results mainly from a single chromosomal mutation and occurs mainly in Enterobacteriaceae (e.g. *E. coli).*
Acquired resistance to aminocyclitol antibiotics is mainly due to the production of enzymes that inactivate the antibiotic. This resistance is encoded on bacterial genes. Genetic elements such as plasmids, transposons or genetic cassettes can ensure the transfer of resistance from one bacterium to another.

Due to the complementarity of the antimicrobial spectra of lincomycin and spectinomycin the combination has a broad spectrum of activity.

Arcanobacterium pyogenes strains from cattle, *Fusobacterium necrophorum* from cattle and mycoplasma strains *(M. hyopneumoniae, M. hyorhinis, M. hyosynoviae)* and *Erysipelothrix rusiopathiae* from generally highly susceptible. The distribution of MICs (minimum inhibitory concentrations) for *E. coli* appears bimodal with a significant
portion showing high MICs, which may partly correspond to natural (intrinsic) resistance. Most *E. coli* strains

are resistant. A high degree of resistance is observed for the following germs: *Staphylococcus aureus, Staphylococcus*
hyicus, Streptococcus suis and *Bordetella bronchiseptica* of *Mycoplasma bovis* of cattle.

5.2 Pharmacokinetic characteristics:

Lincomycin and spectinomycin are rapidly absorbed after intramuscular injection.
An intramuscular injection of the veterinary product in calves (dose: 1 ml/10 kg BW = 5 mg lincomycin and 10 mg spectinomycin / kg BW) results in mean values of the pharmacokinetic parameters as follows:

	Cmax (µg/ml)	Tmax (h)	T1/2el (h)	AUC (h.µg/ml)
Lincomycin	5.75	0.25	2.42	11,524
Spectinomycin	21.89	0.25	1.08	41,562
		CALF		
Lincomycin	4.20	0.41	4.51	16,199
Spectinomycin	23.66	0.82	2.85	97,930

Lincomycin has a marked lipophilic character, hence its good tissue penetration with tissue levels (e.g. in the lung) exceeding plasma levels.

Spectinomycin, on the other hand, is highly ionized and has difficulty penetrating tissues; it is therefore mainly found at the extracellular level.

6. PHARMACEUTICAL INFORMATION:

6.1 List of excipients:

Benzyl alcohol
Sodium metabisulfite
Sodium citrate
Citric acid (for Ph adjustment)
Water for injection

6.2 Major incompatibilities:

Do not mix in the same syringe with other veterinary medicinal products.

6.3 Retention period:

Shelf life of the veterinary medicinal product as packaged for sale: 2 years. Shelf life after first opening of the primary packaging: 28 days.

6.4 Special precautions for storage:

Store below 25°C.
Do not store in the refrigerator. Do not freeze. Protect from light.

6.5 Nature and composition of primary packaging:

50ml & 100ml Type II vials sealed with a bromobutyl rubber stopper and capped with an aluminium flip off seal and packed in carton box.

6.6 Special precautions for disposal of unused veterinary medicinal products or waste derived from the use of these medicines:
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:
Nawan Laboratories (Pvt.) Ltd.
Plots No. 136-138, Sector-15,
Korangi Industrial Area, Karachi-74900, Pakistan.

8. MARKETING AUTHORISATION NUMBER(S):
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