Pharmacology of Lincocin Forte

Lincocin Forte is an intramammary mastitis treatment for lactating cows. It contains two antibiotics which act synergistically; lincomycin and neomycin. Lincomycin is classified as a lincosamide antibiotic whilst neomycin is an aminoglycoside. Different classes of antibiotics have their effect on bacterial cells at various sites and via diverse mechanisms (refer Figure 1).

Lincosamide Antibiotics

Lincosamides are monoglycoside antibiotics. Their mechanism of action is to bind to the 50S sub-unit of bacterial ribosomes and suppress protein synthesis. This is a similar site of action as macrolides, although the two groups are not structurally related. The lincosamides are bacteriostatic or bactericidal depending on the concentration. The efficacy of lincosamides is time-dependent.

Lincosamides are widely distributed in many fluids and tissues. Milk is an important excretory route.

Aminoglycocide Antibiotics

The aminoglycosides are characterised by an aminocyclitol group. They are weak bases which tend to be ionised at physiological pH, and have high aqueous solubility. Aminoglycosides are more effective against rapidly multiplying organisms, and they ultimately destroy bacteria by irreversibly binding to the intracellular 30S subunit of the bacterial ribosome, thus interfering with protein synthesis. They need only a short contact with bacteria to kill them and, as such, are concentration-dependent in action. To reach the ribosome, aminoglycocides must first cross the lipopolysaccharide covering (gram-negative organisms), the bacterial cell wall, and finally the cell membrane. Because of the polarity of these compounds, a specialized active transport process is required.

Aminoglycosides are associated with a post-antibiotic effect in a number of bacteria, principally gram-negative (e.g. *E. coli, Klebsiella pneumoniae, P. aeruginosa*). The effect generally lasts 2 – 8 hours after exposure and allows for dosing intervals longer than the half-lives of the drugs. Efficacy of aminoglycosides is enhanced when drug concentration is very high, and as stated above they are concentration-dependent antibiotics.

Synergism is common when aminoglycosides are used in combination.

Combining a lincosamide with an aminoglycoside means that the bacterial cell is attacked in two important metabolic sites, at two different locations on the ribosome. This double action leads to significantly increased efficacy when combined.

These two antibiotic classes are also effective against non-replicating bacteria, in contrast to the widely used cell wall inhibitors (e.g. all ß-lactam antibiotics) which are mainly effective against rapidly multiplying bacteria.

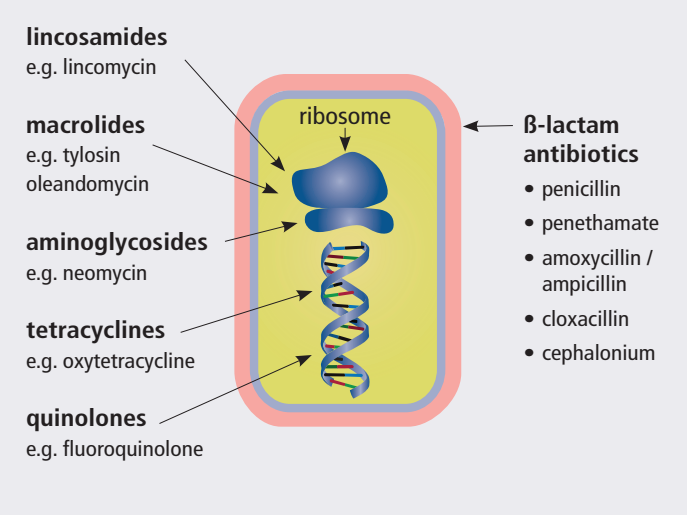

Figure 1. Site of action of different antibiotic classes

Pharmacodynamic properties

Lincomycin is derived from *Streptomyces lincolnensis.* It possesses specific activity against gram-positive organisms, particularly *Staphylococcus* and *Streptococcus* species and has efficacy against anaerobic pathogens. It has little or no activity against gram-negative bacteria such as *E.coli.* Lincomycin has good activity against mycoplasma. Lincomycin binds to the 50S sub-unit of the bacterial ribosome, thereby inhibiting protein synthesis of the cell. It is generally regarded as a bacteriostatic compound.

Neomycin is derived from *Streptomyces fradiae.* It has a broad spectrum of activity against both gram-positive bacteria, including *Staphylococcus* and *Streptococcus* species, and gram-negative aerobic bacteria, including *Escherichia coli, Salmonella, Klebsiella, Enterobacter, Proteus,* and *Acinetobacter* spp. Neomycin is more active against *Staphylococcus* species than against *Streptococcus* species. Neomycin has demonstrated synergistic effects with other antibiotics, especially against *Staphylococcus*. Neomycin binds to the 30S sub-unit of the bacterial ribosome resulting in a malconformation of binding ribosomal protein due to errors in reading the amino acid coding of the mRNA. Neomycin thus compromises translation and hence bacterial protein synthesis.

In vitro studies have demonstrated that lincomycin and neomycin in combination have bactericidal activity against *Staphylococcus aureus* and *Escherichia coli* and bacteriostatic activity against streptococci (De Oliveira 2000).

The two antibiotics combined have also demonstrated synergy against *Staphylococcus aureus* (refer Figure 2). Lincomycin, neomycin and the combination have been shown to be active against both penicillinase and non-penicillinase producing Staphylococci.

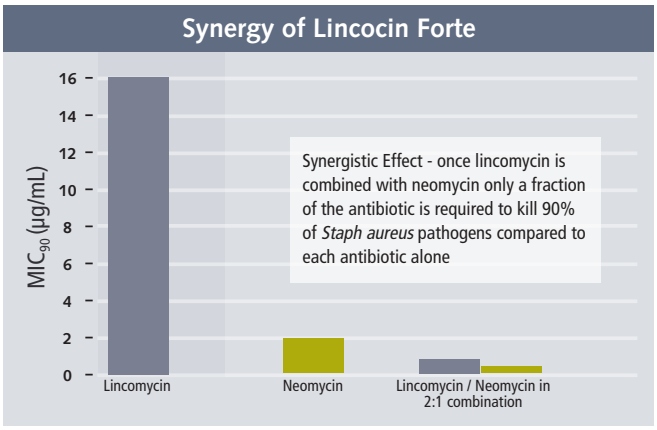

Figure 2. MIC_{90} against Staphylococcus aureus for lincomycin, neomycin and lincomycin + neomycin combination demonstrating the synergy of the combination

Pharmacokinetic properties

Lincocin Forte is an aqueous formulation. This ensures both antibiotics have rapid and complete diffusion throughout the milk duct system of the mammary gland. The lower viscosity of Lincocin Forte means lincomycin and neomycin will generally reach target pathogens more quickly than other intramammary mastitis treatments.

After infusion of the product into the mammary gland, the following mean concentrations of lincomycin and neomycin were measured in individual treated quarters.

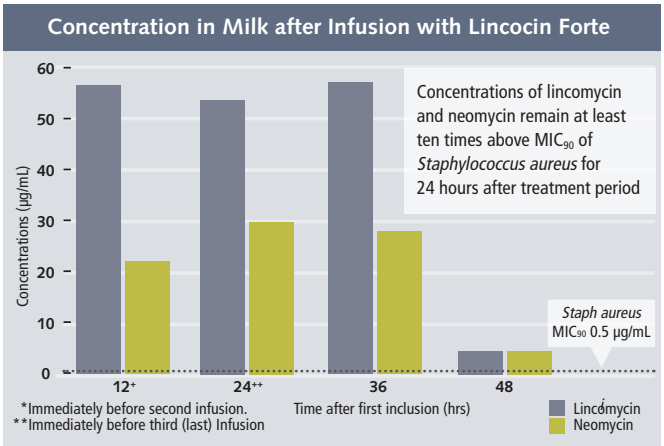

Figure 3. Concentrations of lincocmycin and neomycin in milk compared with MIC_{90} of the combination of antibiotics

Antibiotic levels in milk remain above the MIC - values for target pathogens for the full dosage period up to 24 hours thereafter.

Summary

Lincocin Forte contains two antibiotics from different classes which have a synergistic effect against *Staphylococcus aureus*. The truly broad spectrum nature of this intramammary treatment for lactating cows is ideally suited for treating mastitis cases in New Zealand dairy cattle; having high levels of efficacy against gram positive organisms including *Streptococcus* sp. and *Staphylococcus* sp. as well as gram negative organisms including *E. coli*.

The aqueous base allows rapid and complete diffusion throughout the infected mammary tissue. The antibiotics remain at high concentrations for a significant duration after treatment. In addition the neomycin component provides a post-antibiotic effect, continuing efficacy against target bacteria after drug exposure.

Lincocin Forte's broad spectrum efficacy along with its short treatment and milk withholding periods provides farmers with effective treatment of infected quarters, and return to saleable milk earlier than with other mastitis therapy alternatives.

About Lincocin Forte

Lincocin Forte is for the treatment of bovine mastitis caused by organisms sensitive to lincomycin and neomycin.

Each 10ml syringe of Lincocin Forte contains 330mg lincomycin and 100mg neomycin.

Lincocin Forte is effective against Gram positive cocci, including staphylococcal organisms such as Staphylococcus aureus (penicillinase positive and penicillinase negative), CNS, Streptococcal spp, Streptococcus agalactiae, Streptococcus dysgalactiae and Streptococcus uberis.

Lincocin Forte is also effective against Gram negative organisms including *E. coli* and other enterobacteriaceae.

Dosage

Administer one 10mL syringe per infected quarter.

Treated quarters should not be milked for at least six hours after treatment, but should be milked at regular intervals thereafter.

For twice daily milking: Treatment may be repeated at 12 hourly intervals, up to a total of three doses, if necessary.

For once daily milking: Treatment may be repeated at 24 hourly intervals, up to a total of three doses, if necessary.

Withholding Times

Milk: Twice daily milking: 5 milkings (approx. 60 hours)
Once daily milking: 4 milkings (approx. 96 hours)
Meat: 10 days

References

De Oliveira, et al, 2000 J Dairy Sci 83: 855-862

Lincocin Forte SPC downloaded on 24 January 2017 from http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_10019-089-001_18072014121001.pdf

Merck Veterinary Manual http://www.msdvetmanual.com/

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