

Lincosamides*

Overview

Lincosamides are derived from an amino acid and a sulfur-containing octose, a synthetic monosaccharide containing eight carbon atoms in a molecule. Lincomycin, the prototypical antimicrobial of this class, was isolated from *Streptomyces lincolnensis* in 1962. The mechanism of action of lincosamides is reversible binding to the 50S ribosomal subunit and resultant suppression of protein synthesis. This site is also targeted by chloramphenicol, macrolides, quinupristin-dalfopristin and linezolid. Due to the shared site of activity, these drugs can be antagonistic to each other and lincosamides should not be administered concurrently with erythromycin, chloramphenicol or most bactericidal agents. The lincosamides can be bacteriostatic or bactericidal depending on concentration and are more stable in hydrochloride and phosphate salts. Activity is enhanced in alkaline environments.

Resistance to lincosamides, likely due to alterations in the 50S subunit by chromosomal mutation, appears to develop slowly. Plasmid mediated resistance has been observed with *Bacteroides fragilis*. Cross resistance with other antimicrobials has been observed in vitro.

Lincosamides are characterized by a fairly broad spectrum of activity against anaerobes, like *Bacteroides* species and a limited spectrum against aerobes. Many Gram-positive cocci are inhibited but most Gram-negative bacteria, mycoplasmas and strains of *Clostridium difficile* are resistant.

Lincosamides do not reach significant levels in the CSF, even in the presence of meningeal inflammation, but are well distributed in many fluids and tissues, including bone. In many species these drugs have the ability to diffuse across the placenta. The unchanged antibiotics and many metabolites are excreted in bile, urine and milk; proportions of which are determined by route of administration. Lincosamides can elevate serum alkaline phosphatase, ALT and AST on laboratory tests. Fecal levels remain high for several days after administration and microorganisms in the colon may be suppressed for up to two weeks. Kaolin-pectin preparations prevent absorption of lincosamides from the gastrointestinal tract.

Use of lincosamides may result in GI disturbances. Pseudomembranous enterocolitis caused by toxigenic *Clostridium difficile* is a serious adverse reaction seen in humans. The possibility of development of fatal colitis precludes the use of lincosamides in horses. Although no serious organ toxicities have been reported, skeletal muscle paralysis is observed with very high concentrations and additive neuromuscular effects are observed with concurrent use of anesthetic agents and skeletal muscle relaxants. Lincosamides are contraindicated in neonates due to decreased capacity to metabolize the chemical.

***References available by request. Call the Infectious Disease Epidemiology Section, Office of Public Health, Louisiana Department of Health and Hospitals (504-219-4563)**