LINCOMYCIN HCl
LINOCIN®

250 mg and 500 mg Capsule

1. THERAPEUTIC CATEGORY

Antibacterial

2. FORMULATION

Each Capsule contains lincomycin hydrochloride monohydrate equivalent to lincomycin 250 mg or 500 mg.

WARNING

Lincomycin therapy has been associated with severe colitis which may end fatally. Therefore, it should be reserved for serious infections where less toxic antimicrobial agents are inappropriate, as described in the Indications Section. It should not be used in patients with nonbacterial infections, such as most upper respiratory tract infections. Studies indicate a toxin(s) produced by Clostridia is one primary cause of antibiotic associated colitis. 1-5 (See WARNINGS section). The colitis is usually characterized by severe persistent diarrhea and severe abdominal cramps and may be associated with the passage of blood and mucus. Endoscopic examination may reveal pseudomembranous colitis.

When significant diarrhea occurs, the drug should be discontinued or, if necessary, continued only with close observation of the patient. Large bowel endoscopy has been recommended.

Antiperistatic agents such as opiates and diphenoxylate with atropine may prolong and or worsen the condition. Vancomycin has been found to be effective in the treatment of antibiotic associated pseudomembranous colitis produced by Clostridium difficile. The usual adult dose is 500 milligrams to 2 grams of vancomycin orally per day in three to four divided doses administered for 7 to 10 days. Cholestramine or colestipol resins bind vancomycin in vitro. If both a resin and vancomycin are to be administered concurrently, it may be advisable to separate the time of administration of each drug.

Diarrhea, colitis and pseudomembranous colitis have been observed to begin up to several weeks following cessation of therapy with linomycin.

3. DESCRIPTION

Lincocin contain lincomycin hydrochloride which is the monohydrated salt of lincomycin, a substance by the growth of a member of the lincolnensis group of Streptomyces lincolnensis (Fam. Streptomycetaceae). Its solutions are acid and are dextrorotatory.
Lincomycin hydrochloride is D-erythro-a-D-galacto-Octopyranoside, methyl 6,8-dideoxy-6-[(1-methylpropyl-2-pyrrolidinyl)carbonyl]amino]-1-thio-,monohydrochloride, monohydrate,(2S-trans). The structural formula is:

![Structural formula of Lincomycin hydrochloride]

Lincomycin hydrochloride is a white or practically white, crystalline powder and is odorless or has a faint odor. Its solutions are acid and are dextrorotatory. Lincomycin hydrochloride is freely soluble in water; soluble in dimethylformamide and very slightly soluble in acetone.

**4. CLINICAL PARTICULARS**

Microbiology – Lincomycin has been shown to be effective against most of the common gram-positive pathogens. Depending on the sensitivity of the organism and concentration of the antibiotic, it may be either bactericidal or bacteriostatic. Cross resistance has not been demonstrated with penicillin, chloramphenicol, ampicillin, cephalosporins or the tetracyclines. Despite chemical differences, lincomycin exhibits antibacterial activity similar but not identical to the macrolide antibiotics (e.g. erythromycin). Some cross resistance (with erythromycin) including a phenomenon known as dissociated cross resistance or macrolide effect has been reported. Microorganisms have not developed resistance to lincomycin rapidly when tested by in vitro or in vivo methods. Staphylococci develop resistance to lincomycin in a slow, stepwise manner based on in vitro, serial subculture experiments. This pattern of resistance development is unlike that shown for streptomycin.

Studies indicate that lincomycin does not share antigenicity with penicillin compounds.

Biological Studies – In vitro studies indicate that the spectrum or activity includes Staphylococcus aureus, Staphylococcus albus, B-hemolytic Streptococcus, Streptococcus viridans, Diplococcus pneumoniae, Clostridium tetani, Clostridium perfringens, Corynebacterium diphtheriae and Corynebacterium diphtheriae and Corynebacterium acnes.

NOTE: This drug is not active against most strains of Streptococcus faecalis, nor against Neisseria gonorrhoeae, Neisseria meningitidis, Hemophilus influenzae, or other gram-negative organisms or yeasts.

Human Pharmacology – Lincomycin is absorbed rapidly after a 500 mg oral dose, reaching peak levels in 2 to 4 hours. Levels are maintained above the MIC (minimum
inhibitory concentration) for most gram-positive organisms for 6 to 8 hours. Urinary recovery of drug in a 24-hour period ranges from 1.0 to 31 percent (mean: 4.0 after a single oral dose of 500 mg of lincomycin. Tissue level studies indicate that bile is an important route of excretion. Significant levels have been demonstrated in the majority of body tissues. Although the drug is not present in significant amounts in the spinal fluid of normal volunteers, it has been demonstrated in the spinal fluid of one patient with pneumococcal meningitis.

Intramuscular administration of a single-dose of 600 mg of lincomycin produces a peak serum level at 30 minutes with detectable levels persisting for 24 hours. Urinary excretion after this dose ranges from 1.8 to 24.8 percent (mean: 17.3).

The intravenous infusion over a 2-hour interval of 600 mg of lincomycin in 500 mL of 5 percent glucose in distilled water yields therapeutic levels for 14 hours. Urinary excretion ranges from 4.9 to 30.3 percent (mean: 13.8).

The biological half-life after oral intramuscular or intravenous administration is 5.4 + 1.0 hour.

Hemodialysis and peritoneal dialysis do not effectively remove lincomycin from the blood.

4.1 INDICATIONS AND USAGE

Lincomycin has been shown to be effective in the treatment of the following infections when caused by susceptible strains of gram positive aerobes such as streptococci, pneumococci, and staphylococci, or by susceptible anaerobic bacteria.

(a) Upper respiratory infections \(^{1-9}\) including tonsillitis, pharyngitis, otitis media, sinusitis, scarlet fever and as adjuvant therapy for diphtheria. Effectiveness in the treatment of mastoiditis would be anticipated.

(b) Lower respiratory infections including acute and chronic bronchitis and pneumonia.

(c) Skin and soft tissue infections including cellulitis, furuncles, abscesses, impetigo, acne and wound infections. Conditions like erysipelas, lymphadenitis, paronychia (panaritium), mastitis and cutaneous gangrene, should, if caused by susceptible organisms, respond to lincomycin therapy.

(d) Bone and joint infections including osteomyelitis and septic arthritis.

(e) Septicemia and endocarditis. Selected cases of septicemia and/or endocarditis due to susceptible organisms have responded well to lincomycin. However, bactericidal drugs are often preferred for these infections.

(f) Bacillary dysentery. Although *Shigella* is resistant to lincomycin in vitro (MIC approximately 200-400 mcg/ml), lincomycin has been effective in its treatment due to the very high levels of lincomycin attained in the bowel (approximately 3000-7000 mcg/gram of stool).
4.2 DOSAGE AND METHOD OF ADMINISTRATION

If significant diarrhea occurs during therapy, this antibiotic should be discontinued. (See WARNING box).

**Dosage in Adults**

**Oral Administration**

1) Infections due to susceptible organisms: 500 mg 3 times per day every 8 hours.
2) More severe infections: 500 mg 4 times per day every 6 hours.
3) For optimal absorption, it is recommended that nothing be given by mouth for a period of 1 to 2 hours before or after oral administration of lincomycin.

**Dosage in Children (over 1 month of age):**

**Oral Administration:**

1) 30 mg/kg/day divided into 3 or 4 equal doses.
2) More severe infections: 60 mg/kg/day divided into 3 or 4 equal doses.
3) For optimal absorption, it is recommended that nothing be given by mouth for a period of 1 to 2 hours before or after oral administration of lincomycin.

**Dosage in Patients with Diminished Hepatic or Renal Function**

In patients with impaired hepatic function or impaired renal function, lincomycin’s serum half-life is increased. Consideration should be given to decreasing the frequency of administration of lincomycin in patients with impaired hepatic or renal function.

When therapy with lincomycin is required in individuals with severe impairment of renal function, an appropriate dose is 25% to 30% of that recommended for patients with normally functioning kidneys.

**With Beta-hemolytic streptococcal infections:**

Treatment should continue for at least 10 days to diminish the likelihood of subsequent rheumatic fever or glumerulonephritis.

**Incompatibilities** (This list may not be all-inclusive due to the multiple factors influencing drug compatibility data).

Note: For optimal absorption it is recommended that nothing be given by mouth except water for a period of one to two hours before and after oral administration of Lincocin preparations (lincomycin).
4.3 CONTRAINDICATIONS

Lincomycin is contraindicated in patients previously found to be sensitive to lincomycin or clindamycin or to any other component of the product.

4.4 WARNINGS & PRECAUTIONS

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including lincomycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider the diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by Clostridium difficile is a primary cause of “antibiotic-associated colitis”. After the primary diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate-to-severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against Clostridium difficile colitis.

Although lincomycin appears to diffuse into cerebrospinal fluid, levels of lincomycin in the CSF may be inadequate for the treatment of meningitis. Thus, the drug should not be used in the treatment of meningitis.

If lincomycin antibiotic therapy is prolonged, liver and kidney function tests should be performed.

The use of antibiotics may result in overgrowth of non-susceptible organisms, particularly yeasts.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including lincomycin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile. 1-14

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. 1-14

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

4.5 INTERACTION WITH OTHER DRUGS AND OTHER FORMS OF INTERACTION

Antagonism has been demonstrated between lincomycin and erythromycin in vitro. Because of possible clinical significance, these two drugs should not be administered concurrently.

Lincomycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, lincomycin should be used with caution in patients receiving such agents.

4.6 PREGNANCY AND LACTATION

Usage in Pregnancy – Safety for use in pregnancy has not been established.

No adverse effects on survival of offspring from birth to weaning were seen in studies performed in rats using oral doses of lincomycin up to 1000 mg/kg (7.5 times the maximum human dose of 8 g/day). No teratogenic effects were seen in study conducted in rats treated with more than 55 times the highest recommended adult human dose of 8 g/day.

In humans, lincomycin crosses the placenta and results in cord serum levels about 25% of the maternal serum levels. No significant accumulation occurs in the amniotic fluid. There are no controlled studies in pregnant women; however, the progeny of 302 patients treated with lincomycin at various stages of pregnancy showed no increases in congenital anomalies or delayed development compared to a control group for up to 7 years after birth. Lincomycin should be used during pregnancy only if clearly needed.

Usage in Newborn – Until further clinical experience is obtained, Licocin preparations (lincomycin) are not indicated in the newborn.

Nursing Mothers – Lincomycin has been reported to appear in breast milk in ranges of 0.5 to 2.4 mcg/mL.

4.7 UNDESIRABLE EFFECTS

Gastrointestinal—Nausea, vomiting, abdominal distress and persistent diarrhea and, with oral preparations, esophagitis.

Hematopoietic—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura. Rare reports of aplastic anemia and pancytopenia.

Hypersensitivity Reactions—Angioneurotic edema, serum sickness and anaphylaxis. Rare instances of erythema multiforme, some resembling Stevens-Johnson syndrome, have been associated with lincomycin administration.
Skin and Mucous Membranes—Pruritus, skin rashes, urticaria, vaginitis, and rarely exfoliative and vesiculobullous dermatitis have been reported.

Liver—Jaundice and abnormal liver function tests.

Cardiovascular—Hypotension following parenteral administration has been reported, particularly after too rapid administration. Rare instances of cardiopulmonary arrest have been reported after too rapid intravenous administration.

4.8 OVERDOSE

Hemodialysis or peritoneal dialysis do not effectively remove lincomycin from the blood.

5. PHARMACEUTICAL PARTICULARS

5.1 Shelf Life

See outer package for the expiry date of the product.

5.2 Special Precaution for Storage

Store at temperature not exceeding 25ºC.

5.3 Availability

250 mg capsule: Hard Gelatin capsule with opaque dark blue cap and opaque light blue cap and body (Box of 100’s)
500 mg capsule: Hard Gelatin capsule with opaque dark blue cap and opaque light blue body imprinted “Pfizer and LIN 500” in white ink on cap and body (Box of 100’s)

REFERENCES


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