Lincocin®
lincomycin injection, USP

PHARMACIA

To reduce the development of drug-resistant bacteria and maintain the effectiveness of LINCOCIN and other antibacterial drugs, LINCOCIN should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

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WARNING

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 this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Because lincomycin therapy has been associated with severe colitis which may end fatally, it should be reserved for serious infections where less toxic antimicrobial agents are inappropriate, as described in the **INDICATIONS AND USAGE** section. It should not be used in patients with nonbacterial infections such as most upper respiratory tract infections. 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 one primary cause of "antibiotic-associated colitis".

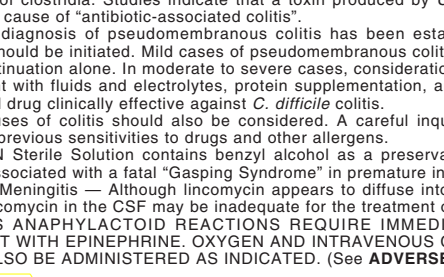
After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

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

DESCRIPTION

LINCOCIN Sterile Solution contains lincomycin hydrochloride which is the monohydrated salt of lincomycin, a substance produced by the growth of a member of the *lincolnensis* group of *Streptomyces lincolnensis* (Fam. *Streptomycetaceae*). The chemical name for lincomycin hydrochloride is Methyl 6,8-dideoxy-6-(1-methyl-trans-4-propyl-L-2-pyrolidinecarboxamido)-1-thio-D-erythro-α-D-galacto-octopyranoside monohydrochloride monohydrate. The molecular formula of lincomycin hydrochloride is $C_{18}H_{34}N_2O_6S.HCl.H_2O$ and the molecular weight is 461.01.

The structural formula is represented below:



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.

CLINICAL PHARMACOLOGY

Intramuscular administration of a single dose of 600 mg of lincomycin produces average peak serum levels of 11.6 µg/mL at 60 minutes and maintains therapeutic levels for 17 to 20 hours for most susceptible gram-positive organisms. Urinary excretion after this dose ranges from 1.8 to 24.8 percent (mean: 17.3 percent).

A two hour intravenous infusion of 600 mg of lincomycin achieves average peak serum levels of 15.9 µg/mL and yields therapeutic levels for 14 hours for most susceptible gram-positive organisms. Urinary excretion ranges from 4.9 to 30.3 percent (mean: 13.8 percent).

The biological half-life after intramuscular or intravenous administration is 5.4 ± 1.0 hours. The serum half-life of lincomycin may be prolonged in patients with severe impairment of renal function compared to patients with normal renal function. In patients with abnormal hepatic function, serum half-life may be twofold longer than in patients with normal hepatic function. Hemodialysis and peritoneal dialysis are not effective in removing lincomycin from the serum.

Tissue level studies indicate that bile is an important route of excretion. Significant levels have been demonstrated in the majority of body tissues. Although lincomycin appears to diffuse into cerebrospinal fluid (CSF), levels of lincomycin in the CSF appear inadequate for the treatment of meningitis.

Microbiology: Lincomycin has been shown to be active against most strains of the following organisms **both *in vitro* and in clinical infections:** (see **INDICATIONS AND USAGE**).

Staphylococcus aureus (penicillinase- and non-penicillinase producing strains)
Streptococcus pneumoniae

The following *in vitro* data are available; **but their clinical significance is unknown.**

Lincomycin has been shown to be active *in vitro* against the following microorganisms; however, the safety and efficacy of LINCOCIN in treating clinical infections due to these organisms have not been established in adequate and well controlled trials.

Aerobic gram-positive cocci:
Streptococcus pyogenes
Viridans group streptococci
Aerobic gram-positive bacilli:
Corynebacterium diphtheriae
Anaerobic gram-positive non-sporeforming bacilli:
Propionibacterium acnes
Anaerobic gram-positive sporeforming bacilli:
Clostridium tetani
Clostridium perfringens

This drug is not active against most strains of *Enterococcus faecalis* nor against *Neisseria gonorrhoeae, Neisseria meningitidis, Haemophilus influenzae* or other gram-negative organisms or yeasts.

Cross resistance has been demonstrated between clindamycin and lincomycin. Some cross resistance with erythromycin including a phenomenon known as dissociated cross resistance or macrolide effect has been reported.

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

INDICATIONS AND USAGE

LINCOCIN Sterile Solution is indicated in the treatment of serious infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Its use should be reserved for penicillin-allergic patients or other patients for whom, in the judgment of the physician, a penicillin is inappropriate. Because of the risk of antibiotic-associated pseudomembranous colitis, as described in the **WARNING** box, before selecting lincomycin the physician should consider the nature of the infection and the suitability of less toxic alternatives (eg, erythromycin).

Bacteriologic studies should be performed to determine the causative organisms and their susceptibility to lincomycin.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy.

Lincomycin has been demonstrated to be effective in the treatment of staphylococcal infections resistant to other antibiotics and susceptible to lincomycin. Staphylococcal strains resistant to LINCOCIN have been recovered; culture and susceptibility studies should be done in conjunction with therapy with LINCOCIN. In the case of macrolides, partial but not complete cross resistance may occur (see **Microbiology**). The drug may be administered concomitantly with other antimicrobial agents when indicated.

Lincomycin is not indicated in the treatment of minor bacterial infections or viral infections.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of LINCOCIN and other antibacterial drugs, LINCOCIN should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

CONTRAINDICATIONS

This drug is contraindicated in patients previously found to be hypersensitive to lincomycin or clindamycin.

WARNINGS

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 this 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 one primary cause of "antibiotic-associated colitis".

After the 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 *C. difficile* colitis.

Other causes of colitis should also be considered. A careful inquiry should be made concerning previous sensitivities to drugs and other allergens.

LINCOCIN Sterile Solution contains benzyl alcohol as a preservative. Benzyl alcohol has been associated with a fatal "Gasping Syndrome" in premature infants.

Usage in Meningitis — Although lincomycin appears to diffuse into cerebrospinal fluid, levels of lincomycin in the CSF may be inadequate for the treatment of meningitis.

SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE. OXYGEN AND INTRAVENOUS CORTICOSTEROIDS SHOULD ALSO BE ADMINISTERED AS INDICATED. (See **ADVERSE REACTIONS**.)

PRECAUTIONS

General

Review of experience to date suggests that a subgroup of older patients with associated severe illness may tolerate diarrhea less well. When LINCOCIN is indicated in these patients, they should be carefully monitored for change in bowel frequency.

LINCOCIN should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

LINCOCIN should be used with caution in patients with a history of asthma or significant allergies.

Certain infections may require incision and drainage or other indicated surgical procedures in addition to antibiotic therapy.

The use of LINCOCIN may result in overgrowth of nonsusceptible organisms—particularly yeasts. Should superinfections occur, appropriate measures should be taken as indicated by the clinical situation. When patients with pre-existing monilial infections require therapy with LINCOCIN, concomitant antimonilial treatment should be given.

The serum half-life of lincomycin may be prolonged in patients with severe impairment of renal function compared to patients with normal renal function. In patients with abnormal hepatic function, serum half-life may be twofold longer than in patients with normal hepatic function.

Patients with severe impairment of renal function and/or abnormal hepatic function should be dosed with caution and serum lincomycin levels monitored during high-dose therapy. (See **DOSAGE AND ADMINISTRATION** Section.)

Lincomycin should not be injected intravenously undiluted as a bolus, but should be infused over at least 60 minutes as directed in the **DOSAGE AND ADMINISTRATION** Section.

Prescribing LINCOCIN in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients

Patients should be counseled that antibacterial drugs including LINCOCIN should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When LINCOCIN is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by LINCOCIN or other antibacterial drugs in the future.

Laboratory Tests

During prolonged therapy with LINCOCIN, periodic liver and kidney function tests and blood counts should be performed.

Drug Interactions

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

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

Carcinogenesis, Mutagenesis, Impairment of Fertility:

The carcinogenic potential of lincomycin has not been evaluated.

Lincomycin was not found to be mutagenic in the Ames *Salmonella* reversion assay or the V79 Chinese hamster lung cells at the HGPRT locus. It did not induce DNA strand breaks in V79 Chinese hamster lung cells as measured by alkaline elution or chromosomal abnormalities in cultured human lymphocytes. *In vivo*, lincomycin was negative in both the rat and mouse micronucleus assays and it did not induce sex-linked recessive lethal mutations in the offspring of male *Drosophila*. However, lincomycin did cause unscheduled DNA syntheses in freshly isolated rat hepatocytes.

Impairment of fertility was not observed in male or female rats given oral 300 mg/kg doses of lincomycin (0.36 times the highest recommended human dose based on mg/m^2).

Pregnancy: Pregnancy Category C

Teratogenic Effects:

There are no studies on the teratogenic potential of lincomycin in animals or adequate and well-controlled studies of pregnant women.

Pfizer

Composition Unit 2566

Black

COMPOSITION ORDER #	PRODUCT		COPY CODE #
22720	LINCOCIN		810 174 315
CCS #	NDC #		EDP #
0555-02	0009-0555-02		691659
ITEM	SIZE	FOLDED SIZE	DRAWING #
Insert	4 x 24"	4 x 1"	PD1726 Rev. 2
ADDITIONAL INFORMATION		DATE	TYPESET BY
Spine 2.875" from top		10/24/03	DHUFF

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Nonteratogenic Effects:
Reproduction studies have been performed in rats using oral doses of lincomycin up to 1000 mg/kg (1.2 times the maximum daily human dose based on mg/m^2) and have revealed no adverse effects on survival of offspring from birth to weaning.

Nursing Mothers
Lincomycin has been reported to appear in human milk in concentrations of 0.5 to 2.4 mcg/mL. Because of the potential for serious adverse reactions in nursing infants from

(continued below)

LINCOCIN, a decision should be made whether to discontinue nursing, or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use
LINCOCIN Sterile Solution contains benzyl alcohol as a preservative. Benzyl alcohol has been associated with a fatal "Gasping Syndrome" in premature infants. Safety and effectiveness in pediatric patients below the age of one month have not been established. (See **DOSAGE AND ADMINISTRATION** Section.)

ADVERSE REACTIONS
The following reactions have been reported with the use of lincomycin:

Gastrointestinal—Glossitis, stomatitis, nausea, vomiting, antibiotic-associated diarrhea and colitis, and pruritus ani. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see **WARNINGS**).

Hematopoietic—Neutropenia, leukopenia, agranulocytosis and thrombocytopenic purpura have been reported. There have been rare reports of aplastic anemia and pancytopenia in which LINCOCIN could not be ruled out as the causative agent.

Hypersensitivity Reactions—Hypersensitivity reactions such as angioneurotic edema, serum sickness and anaphylaxis have been reported. Rare instances of erythema multiforme, some resembling Stevens-Johnson syndrome, have been associated with LINCOCIN. If an allergic reaction to LINCOCIN occurs, discontinue the drug. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.

Skin and Mucous Membranes—Skin rashes, urticaria and vaginitis and rare instances of exfoliative and vesiculobullous dermatitis have been reported.

Liver—Although no direct relationship of LINCOCIN to liver dysfunction has been established, jaundice and abnormal liver function tests (particularly elevations of serum transaminase) have been observed.

Renal—Although no direct relationship of lincomycin to renal damage has been established, renal dysfunction as evidenced by azotemia, oliguria, and/or proteinuria has been observed in rare instances.

Cardiovascular—After too rapid intravenous administration, rare instances of cardiopulmonary arrest and hypotension have been reported. (See **DOSAGE AND ADMINISTRATION**.)

Special Senses—Tinnitus and vertigo have been reported occasionally.

Local Reactions—Patients have demonstrated excellent local tolerance to intramuscularly administered LINCOCIN. Reports of pain following injection have been infrequent. Intravenous administration of LINCOCIN in 250 to 500 mL of 5% dextrose injection or 0.9% sodium chloride injection produced no local irritation or phlebitis.

OVERDOSAGE
Serum levels of lincomycin are not appreciably affected by hemodialysis and peritoneal dialysis.

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

INTRAMUSCULAR—Adults: *Serious infections*—600 mg (2 mL) intramuscularly every 24 hours. *More severe infections*—600 mg (2 mL) intramuscularly every 12 hours or more often. **Pediatric patients over 1 month of age:** *Serious infections*—one intramuscular injection of 10 mg/kg (5 mg/lb) every 24 hours. *More severe infections*—one intramuscular injection of 10 mg/kg (5 mg/lb) every 12 hours or more often.

INTRAVENOUS—Adults: The intravenous dose will be determined by the severity of the infection. For serious infections doses of 600 mg of lincomycin (2 mL of LINCOCIN) to 1 gram are given every 8 to 12 hours. For more severe infections these doses may have to be increased. In life-threatening situations daily intravenous doses of as much as 8 grams have been given. **Intravenous doses are given on the basis of 1 gram of lincomycin diluted in not less than 100 mL of appropriate solution (see PHYSICAL COMPATIBILITIES) and infused over a period of not less than one hour.**

Dose	Vol. Diluent	Time
600 mg	100 mL	1 hr
1 gram	100 mL	1 hr
2 grams	200 mL	2 hr
3 grams	300 mL	3 hr
4 grams	400 mL	4 hr

These doses may be repeated as often as required to the limit of the maximum recommended daily dose of 8 grams of lincomycin.

Pediatric patients over 1 month of age: 10 to 20 mg/kg/day (5 to 10 mg/lb/day) depending on the severity of the infection may be infused in divided doses as described above for adults.

NOTE: Severe cardiopulmonary reactions have occurred when this drug has been given at greater than the recommended concentration and rate.

SUBCONJUNCTIVAL INJECTION—0.25 mL (75 mg) injected subconjunctivally will result in ocular fluid levels of antibiotic (lasting for at least 5 hours) with MICs sufficient for most susceptible pathogens.

Patients with diminished renal function: *When therapy with LINCOCIN 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.*

HOW SUPPLIED
LINCOCIN Sterile Solution is available in the following strength and package sizes:

300 mg
2 mL Vials — NDC 0009-0555-01
10 mL Vials — NDC 0009-0555-02

Each mL of LINCOCIN Sterile Solution contains lincomycin hydrochloride equivalent to lincomycin 300 mg; also benzyl alcohol, 9.45 mg added as preservative.

Store at controlled room temperature 20° to 25°C (68° to 77°F) [see USP].

ANIMAL PHARMACOLOGY
In vivo experimental animal studies demonstrated the effectiveness of LINCOCIN preparations (lincomycin) in protecting animals infected with *Streptococcus viridans, β-hemolytic Streptococcus, Staphylococcus aureus, Diplococcus pneumoniae* and *Leptospira pomona*. It was ineffective in *Klebsiella, Pasteurella, Pseudomonas, Salmonella* and *Shigella* infections.

CLINICAL STUDIES
Experience with 345 obstetrical patients receiving this drug revealed no ill effects related to pregnancy.

PHYSICAL COMPATIBILITIES
Physically compatible for 24 hours at room temperature unless otherwise indicated.

Infusion Solutions
5% Dextrose Injection
10% Dextrose Injection
5% Dextrose and 0.9% Sodium Chloride Injection
10% Dextrose and 0.9% Sodium Chloride Injection
Ringer's Injection

1/6 M Sodium Lactate Injection
Travert 10%-Electrolyte No. 1
Dextran in Saline 6% w/v

Vitamins in Infusion Solutions
B-Complex
B-Complex with Ascorbic Acid

Antibiotics in Infusion Solutions
Penicillin G Sodium (Satisfactory for 4 hours)
Cephalothin
Tetracycline HCl
Cephaloridine
Colistimethate (Satisfactory for 4 hours)
Ampicillin
Methicillin
Chloramphenicol
Polymyxin B Sulfate

Physically Incompatible with:
Novobiocin
Kanamycin

IT SHOULD BE EMPHASIZED THAT THE COMPATIBLE AND INCOMPATIBLE DETERMINATIONS ARE PHYSICAL OBSERVATIONS ONLY, NOT CHEMICAL DETERMINATIONS. ADEQUATE CLINICAL EVALUATION OF THE SAFETY AND EFFICACY OF THESE COMBINATIONS HAS NOT BEEN PERFORMED.

℞ only

LINCOCIN Sterile Solution
Made by
Pharmacia & Upjohn Company
A subsidiary of Pharmacia Corporation
Kalamazoo, MI 49001, USA

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