Lincomycin Injection USP 600mg/2ml, 3g/10ml

1. Name of the medicinal product

Lincomycin Injection USP 600mg/2mlTaj Pharma

Lincomycin Injection USP 3g/10ml Taj Pharma

2. Qualitative and quantitative composition

a) Lincomycin Injection USP 600mg/2mlTaj Pharma
Each ml contains:
Lincomycin hydrochloride equivalent
Lincomycin 300mg
Benzyl alcohol 9.45

b) Lincomycin Injection USP 3g/10ml Taj Pharma
Each ml contains:
Lincomycin hydrochloride equivalent
Lincomycin 300mg
Benzyl alcohol 9.45

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

3. PHARMACEUTICAL FORM

Liquid Injection

3.1 DESCRIPTION

LINCOMYCIN HYDROCHLORIDE 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-L2-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.

3.2 INDICATIONS

LINCOMYCIN HYDROCHLORIDE 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 CDAD, as described in the List, before selecting lincomycin the physician should consider the nature of the infection and the suitability of other alternatives.

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

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 LINCOMYCIN HYDROCHLORIDE and other antibacterial drugs, LINCOMYCIN HYDROCHLORIDE 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.

3.3 DOSAGE AND ADMINISTRATION

If significant diarrhea occurs during therapy, this antibacterial should be discontinued.

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 LINCOMYCIN HYDROCHLORIDE) 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.

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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 concentrations of antibacterial (lasting for at least 5 hours) sufficient for most susceptible pathogens.

Patients With Diminished Renal Function

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

HOW SUPPLIED

LINCOMYCIN HYDROCHLORIDE Sterile Solution is available in the following strength and package sizes: 300 mg

2 mL Vials
10 mL Vials

Each mL of LINCOMYCIN HYDROCHLORIDE 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)

SIDE EFFECTS

- The following adverse reactions have been reported with the use of lincomycin.
- Gastrointestinal Disorders
- Diarrhea, nausea, vomiting, glossitis, stomatitis, abdominal pain, abdominal discomfort†, anal pruritus
- Skin And Subcutaneous Tissue Disorders
- Toxic epidermal necrolysis, Stevens-Johnson syndrome, acute generalized exanthematous pustulosis, dermatitis bullous, dermatitis exfoliative, erythema multiforme (see WARNINGS), rash, urticaria, pruritus
- Infections And Infestations
- Vaginal infection, pseudomembranous colitis, *Clostridium difficile* colitis (see WARNINGS)
- Blood And lymphatic System Disorders
- Pancytopenia, agranulocytosis, aplast ic anemia, leukopenia, neutropenia, thrombocytopenic purpura
- Immune System
- disorders Anaphylactic reaction (see WARNINGS), angioedema, serum sickness
- Hepatobiliary Disorders
- Jaundice, liver function test abnormal, transaminases increased
- Renal And Urinary Disorders
- Renal impairment, oliguria, proteinuria, azo temia
- Cardiac Disorders
- Cardio-respiratory arrest (see DOSAGE AND ADMINISTRATION)
- Vascular Disorders

- Hypotension (see DOSAGE AND ADMINISTRATION), thrombophle bitis†
- Ear And Labyrinth Disorders
- Vertigo, tinnitus
- Neurologic Disorders
- Headache, dizziness, somnolence
- General Disorders And Administration Site Conditions
- Injection site abscess sterile‡, injection site induration‡, injection site pain‡, injection site irritation‡

†Event has been reported with intravenous injection.
‡Reported with intramuscular injection.

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.

WARNINGS

Clostridium Difficile Associated Diarrhea

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*.

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 antibacterial use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibacterial use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

Hypersensitivity

Severe hypersensitivity reactions, including anaphylactic reactions and severe cutaneous adverse reactions (SCAR) such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), acute generalized exanthematous pustulosis (AGEP), and erythema multiforme (EM) have been reported in patients receiving LINCOMYCIN HYDROCHLORIDE therapy. If an anaphylactic reaction or severe skin reaction occurs, LINCOMYCIN HYDROCHLORIDE should be discontinued and appropriate therapy should be initiated. (see ADVERSE REACTIONS)

Benzyl Alcohol Toxicity In Pediatric Patients (Gasping Syndrome)

This product contains benzyl alcohol as a preservative. The preservative benzyl alcohol has been associated with serious adverse events, including the “gasping syndrome”, and death in pediatric patients. Although normal therapeutic doses of this

product ordinarily deliver amounts of benzyl alcohol that are substantially lower than those reported in association with the "gasping syndrome", the minimum amount of benzyl alcohol at which toxicity may occur is not known. The risk of benzyl alcohol toxicity depends on the quantity administered and the liver and kidneys' capacity to detoxify the chemical. Premature and low-birth weight infants may be more likely to develop toxicity.

Use In Meningitis

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

PRECAUTIONS

General

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

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

LINCOMYCIN HYDROCHLORIDE 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 antibacterial therapy.

The use of LINCOMYCIN HYDROCHLORIDE 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 LINCOMYCIN HYDROCHLORIDE, concomitant antimonilial treatment should be given.

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

Patients with severe renal impairment and/or hepatic impairment should be dosed with caution and serum lincomycin concentrations monitored during high-dose therapy. (see DOSAGE AND ADMINISTRATION)

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 LINCOMYCIN HYDROCHLORIDE 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.

Laboratory Tests

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

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

There are no adequate and well-controlled studies in pregnant women. LINCOMYCIN HYDROCHLORIDE Sterile Solution contains benzyl alcohol as a preservative. Benzyl alcohol can cross the placenta. See WARNINGS. LINCOMYCIN HYDROCHLORIDE should be used during pregnancy only if clearly needed.

Teratogenic Effects

In a study with 60 pregnant women, cord serum concentrations were approximately 25% of the maternal serum concentrations, indicating that lincomycin crosses the placenta, and no substantial accumulation occurred in the amniotic fluid. Experience with 345 obstetrical patients receiving LINCOMYCIN HYDROCHLORIDE revealed no ill effects related to pregnancy.

There was no evidence of teratogenicity when lincomycin was administered in diet or via oral gavage to pregnant Sprague Dawley rats during the period of major organogenesis at doses up to 5000 mg/kg and 100 mg/kg (approximately 6 times and 0.12 times the maximum recommended human dose [MRHD], respectively, based on body surface area comparison).

Nonteratogenic Effects

However, reproduction studies performed in rats administered oral lincomycin in diet for 2 weeks prior to mating, throughout pregnancy and lactation, revealed no adverse effects on survival of offspring from birth to weaning at doses up to 1000 mg/kg (1.2 times the MRHD based on body surface area comparison) up to 2 generations.

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 LINCOMYCIN HYDROCHLORIDE, 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

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

OVERDOSAGE & CONTRAINDICATIONS

OVERDOSE

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

CONTRAINDICATIONS

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

4. CLINICAL PHARMACOLOGY

Intramuscular administration of a single dose of 600 mg of lincomycin produces average peak serum concentrations of 11.6 mcg/mL at 60 minutes and maintains therapeutic concentrations 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 concentrations of 15.9 mcg/mL and maintains therapeutic concentrations 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 renal impairment compared to patients with normal renal function. In patients with hepatic impairment, 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 distribution studies indicate that bile is an important route of excretion. Significant concentrations have been demonstrated in most body tissues. Although lincomycin appears to diffuse into cerebrospinal fluid (CSF), concentrations of lincomycin in the CSF appear inadequate for the treatment of meningitis.

Microbiology

Mechanism Of Action

Lincomycin inhibits bacterial protein synthesis by binding to the 23S RNA of the 50S subunit of the bacterial ribosome. Lincomycin is predominantly bacteriostatic *in vitro*.

Resistance

Cross resistance has been demonstrated between clindamycin and lincomycin. Resistance is most often due to methylation of specific nucleotides in the

23S RNA of the 50S ribosomal subunit, which can determine cross resistance to macrolides and streptogramins B (MLSB phenotype). Macrolide-resistant isolates of these organisms should be tested for inducible resistance to lincomycin/clindamycin using the D-zone test or other appropriate method.

Antimicrobial Activity

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

Staphylococcus aureus
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 LINCOMYCIN HYDROCHLORIDE in treating clinical infections due to these organisms have not been established in adequate and well controlled trials.

Gram-positive Bacteria

Corynebacterium diphtheriae
Streptococcus pyogenes
Viridans group streptococci

Anaerobic Bacteria

Clostridium tetani
Clostridium perfringens

Susceptibility Testing

For specific information regarding susceptibility test interpretive criteria and associated test methods and quality control standards recognized by FDA for this drug, please see: https://www.fda.gov/STIC.

Animal Pharmacology

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

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

Antibacterial 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

7.Manufactured in India by:
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Maharashtra chambers of Commerce Lane,
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