GECOMYCIN CAPSULES
(Vardhman Exports),

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

GECOMYCIN 500 CAPSULES

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Capsule contains:

Lincomycin Hydrochloride BP eq. to Lincomycin 500 mg

Excipients with known effects:

Each capsule contains 6.000mg of Magnesium Stearate

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Light blue/dark blue hard gelatin capsule of size '0' having 'LINCOMYCIN' and '500' printed on cap & body alternatively in white ink containing white powder. .

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Gecomycin is indicated 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.
Upper respiratory infections including tonsillitis, pharyngitis, otitis media, sinusitis, scarlet fever and as adjuvant therapy for diphtheria. Effectiveness in the treatment of mastoiditis would be anticipated.
Lower respiratory infections including acute and chronic bronchitis and pneumonia.
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. Bone and joint infections including osteomyelitis and septic arthritis.
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.
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 Posology and method of administration

Posology

Dosage in Adults

Dosage in Adults Oral Administration Infections due to susceptible organisms, 500 mg t.i.d. (q8h).
More severe infections: 500 mg q.i.d. (q6h).
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)

30 mg/kg/day divided into 3 or 4 equal doses.
More severe infections: 60 mg/kg/day divided into 3 or 4 equal doses.
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.

Method of Administration

Capsule should be swallowed whole with adequate fluids (at least 100ml of water) and should be taken in an upright sitting or standing position.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

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 LINCOCIN therapy. If an anaphylactic reaction or severe skin reaction occurs, LINCOCIN should be discontinued and appropriate therapy should be initiated. (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 antibacterial 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 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 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.

4.5 Interaction with other medicinal products and other forms of interaction

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. Fertility, Pregnancy and lactation

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 limited data on the use of lincomycin in pregnant women. 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.
Lincomycin has been reported to appear in human breast milk in concentrations of 0.5 to 2.4 mcg/mL.44

4.7 Effects on ability to drive and use machines

No studies were conducted to determine the effect of Lincomycin on ability to drive and use machines.

4.8 Undesirable effects

Adverse Drug Reactions

Adverse Drug Reaction Table	
System Organ Class	Adverse Drug Reactions
Infections and infestations	Pseudomembranous colitis, Clostridium difficile colitis, vaginal infection
Blood and lymphatic system disorders	Pancytopenia, agranulocytosis, aplastic anaemia, neutropenia, leukopenia, thrombocytopenic purpura
Immune system disorders	Anaphylactic reaction, angioedema, serum sickness
Cardiac disorders	Cardio-respiratory arrest
Vascular disorders	Hypotension, thrombophlebitis
Gastrointestinal disorders	Oesophagitis, diarrhoea, nausea, vomiting, abdominal discomfort
Hepatobiliary disorders	Jaundice, liver function test abnormal
Skin and subcutaneous tissue disorders	Toxic epidermal necrolysis, Stevens-Johnson syndrome, acute generalised exanthematous pustulosis, dermatitis bullous, dermatitis exfoliative, erythema multiforme, rash, urticaria, pruritus
General disorders and administration site conditions	Injection site abscess sterile, injection site induration, injection site pain, injection site irritation
Rare instances have been reported after too rapid intravenous administration. Following parenteral administration, particularly after too rapid administration. Event has been reported with intravenous injection. Event has been reported with oral preparations. Reported with intramuscular injection.	

4.9 Overdose

Hemodialysis or peritoneal dialysis does not effectively remove Lincomycin from the blood.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties.

Pharmacotherapeutic group: Used as Antibacterial,

ATC code: J01FF02

Mode of Action: Lincomycin is an antibiotic produced by fermentation of Streptomyces lincolnensis. Lincomycin inhibits bacterial protein synthesis by binding to the 50S subunit of the bacterial ribosome. Lincomycin is predominantly bacteriostatic in vitro. The antibacterial activity of lincomycin appears to best correlate with the length of time the concentration of active ingredient remains above the MIC of the infecting organism.

Mechanism of Resistance Cross resistance between lincomycin and clindamycin is complete. Resistance in staphylococci and streptococci 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.

Methodology for determining in vitro susceptibility to lincomycin Susceptibility testing should be conducted using standardized laboratory methods, such as those described by the Clinical and Laboratory Standards Institute (CLSI) or the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Because CLSI and EUCAST have not established susceptibility breakpoints for lincomycin, clindamycin should be tested instead. Resistance to lincosamides may be inducible by macrolides in macrolide-resistant staphylococci, Streptococcus pneumoniae, and betahemolytic streptococci. Macrolide-resistant isolates of these organisms should be screened for inducible clindamycin resistance using the D-zone test or other standard methodology.

CLSI dilution and disk diffusion susceptibility interpretive criteria for clindamycin

Organism	**Susceptibility Interpretive Criteria**					
	Minimal Inhibitory Concentrations (MIC in µg/mL) Disk Diffusion (Zone Diameters in mm)			**Minimal Inhibitory Concentrations (MIC in µg/mL) Disk Diffusion (Zone Diameters in mm)**		
	S	**I**	**R**	**S**	**I**	**R**
Staphylococcus spp.	≤0.5	1–2	≥4	≥21	15–20	≤14
Streptococcus pneumoniae, βhemolytic streptococci and viridans group streptococci	≤0.25	0.5	≥1	≥19	16–18	≤15
Anaerobic Bacteria	≤2	4	≥8	NA	NA	NA
Disk content 2 µg. MIC interpretive criteria for anaerobes are based on agar dilution. NA=not applicable.						

The validity of both the dilution and disk diffusion test methods should be verified using quality control (QC) strains, as indicated by CLSI. Acceptable limits when testing clindamycin against these organisms are listed in the table below.
Quality control ranges for clindamycin susceptibility tests (CLSI)

Organism	**Minimum Inhibitory Concentration Range (MIC in µg/mL)**	**Disk Diffusion Range (Zone Diameters in mm)**
Staphylococcus aureus ATCC 29213	0.06–0.25	NA
Staphylococcus aureus ATCC 25923	NA	24–30
Streptococcus pneumoniae ATCC 49619	0.03–0.12	19–25
Bacteroides fragilis ATCC 25285	0.5–2	NA
Bacteroides thetaiotaomicron ATCC 29741	2–8	NA
Eggerthella lenta ATCC 43055	0.06–0.25	NA
MIC ranges for anaerobic bacteria are based on agar dilution.		
NA=Not applicable		
ATCC is a registered trademark of the American Type Culture Collection		

EUCAST dilution and disk diffusion susceptibility interpretive criteria for clindamycin

Organism	Susceptibility Interpretive Criteria			
	Minimal Inhibitory Concentrations (MIC in µg/mL) Disk Diffusion (Zone Diameters in mm)		Minimal Inhibitory Concentrations (MIC in µg/mL) Disk Diffusion (Zone Diameters in mm)	
	S	R	S	R
Staphylococcus spp.	≤0.25	>0.5	≥22	<19
Streptococcus groups A, B, C, G	≤0.5	>0.5	≥17	<17
Streptococcus pneumoniae	≤0.5	>0.5	≥19	<19
Viridans group streptococci	≤0.5	>0.5	≥19	<19
Gram-positive anaerobes (except Clostridium difficile)	≤4	--	NA	NA
Gram-negative anaerobes	≤4	--	NA	NA
Disk content 2 µg. MIC interpretive criteria for anaerobes are based on agar dilution. NA=not applicable.				

Quality control ranges for clindamycin susceptibility tests (EUCAST)

Organism	Minimum Inhibitory Concentration Range (MIC in µg/mL)	Disk Diffusion Range (Zone Diameters in mm)
Staphylococcus aureus ATCC 29213	0.06–0.25	23-29
Streptococcus pneumoniae ATCC 49619	0.03–0.12	22-28
NA=Not applicable		
ATCC is a registered trademark of the American Type Culture Collection		

Antibacterial Spectrum

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Lincomycin is cross-resistant with clindamycin. A decrease in clindamycin/lincomycin susceptibility over time has been noted in particular among methicillin-resistant Staphylococcus aureus and in some species of Clostridium.

Organisms that are commonly susceptible to Lincomycin include:

Aerobic and facultative gram-positive bacteria:

Staphylococcus aureus (methicillin-susceptible strains only); Streptococcus pneumonia, Streptococcus pyogenes; viridans group streptococci; Corynebacterium diphtheriae.

Clostridium perfringens; Clostridium tetani; Propionibacterium acnes

5.2 Pharmacokinetic properties

Oral administration of a single 500 mg dose of Lincomycin in the fasting state produces an average peak serum level of 5.3 µg/mL at 2 hours post-dose. Administration immediately after a meal reduces oral absorption.

5.3 Preclinical safety data

Nonclinical data from conventional studies on repeated administration toxicity, genotoxicity, carcinogenesis, and reproductive and developmental toxicity have not identified any particular risks to humans. No developmental toxicity was observed when doses greater than 6x the maximum recommended human dose (MRHD) were administered to pregnant rats during the organogenesis period. No effects on fertility were observed in rats administered lincomycin at 1.2x the MRHD.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium Stearate,
Colloidal Silicon Dioxide,
Purified Talc,
Hard Geletin Capsule shell.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store at controlled room temperature (15°-30°C). Keep all medicines out of reach of children.

6.5 Nature and contents of container

4 capsules are packed in a blister using printed aluminium foil with clear PVC.

3 such Blisters of 4 capsules are packed in a carton with one literature.

6.6 Special precautions for disposal and other handling

No special requirements.

7. APPLICANT/MANUFACTURER

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