NATIONAL AGENCY FOR FOOD & DRUG ADMINISTRATION & CONTROL (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

Product Name

LINCOBUL CAPSULES
(Lincomycin Capsules 500 mg)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the Medicinal Product

LINCOBUL CAPSULES
(Lincomycin Capsules 500 mg)

2. Qualitative and Quantitative Composition

Each capsule contains:
Lincomycin Hydrochloride 500mg

3. Pharmaceutical Form

Capsule

4. Clinical Particular

4.1 Therapeutic indications

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

1. Upper respiratory tract infections including tonsillitis, Otitis media, sinusitis, scarlet fever and as adjuvant therapy for diphtheria, effectiveness in
2. Lower respiratory tract infections including cellulitis, furuncles, abscesses.
3. Skin and soft tissue infections including cellulites, furuncles, abscesses impetigo, acne and wound infections including cellulitis, furuncles, abscesses, mastitis and cutaneous gangrene should, if caused by susceptible organisms, respond to lincomycin therapy.
4. Bone and joint infections including osteomyelitis and septicarthritis.
5. 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.
6. Bacilary dysentery-although, Shigella is resistant to lincomycin in vitro (MIC approximately 200-4ug/m). Lincomycin has been effective in its treatment due to the very high levels of lincomycin attained in the bowel (approximately) 3000-7000 ug/mL of stool).

4.2 Posology and method of administration

ADULTS
1. Serious infections due to susceptible organisms 500mg t.i.d
2. More severe infections 500mg t.l.d or q.i.d
CHILDREN: Over one month of age
30mg/kg body weight every 6 to 8 hours depending on the severity of the infection.

4.3 Contraindications

Lincomycin is contraindicated in patients previously found to be sensitive to Lincomycin or clindamycin.

4.4 Special warnings and precautions for use

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

4.5 Interaction with other medicinal products and other forms of interaction

Cross resistance has been demonstrated between clindamycin and lincomycin.

4.6 Fertility, pregnancy and lactation

Safety for use in pregnancy has not been established.

Lincomycin has been reported to appear in breast milk in ranges from 0.5 to 2.4ug/ml.

4.7 Undesirable effects

1. Gastroin testinal-Nausea, vomiting abdominal distress and persistent diarrhea.

2. Hematopoietic-Neatropenia, leukopenia, agranulocutois and thrombocytoopenic purpura have been reported. There have been rare reports of aplastic anemia in which lincomycin could not be ruled out as the causative agent.

3. Hypersensitivity reactions-Hypersensitivity. reactions such as angioneurotic edema, serum sickness and an aphvlaxis have been reported, some of these in patients sensitive to penicillin, rare instance of erythema mutiforme, some resembling Stevens-Johnson syndrome have been associated with lincomycin administration.

4. Skin and mucos membranes-Pruritis, skin rashes urticaria, vaginitis and rare instances of exforliative and vesiculobullousdermatitis.

5. Liver jaundice and abnormal liver function tests(particularly elevation of serum transaminase) have been observed during lincomycin theraphy. As is the case for almost all amtiblotic therapies, the lincomycin therapy has been associated with severe colitis, which may end fatally. The clinical spectrum varies from mild watery diarrhea to severe, persistent diarrhea, leukocytosis, fever, severe abdominal cramps which may be associated with the passage of blood and mucus which, if allowed to progress, may produce peritonitis, shock and toxic megacolon. The diagnosis of antibiotic-associated colitis is usually made by the recognition of the clinical sumptoms. It can be substantiated by endoscopic demonstration of pseudomembranous colitis and may be further confirmed by culture of the stool for Clostridium difficile on selective media and assay of the stool specimen for the toxin(s) of the C. difficile. Onset of antiblotic-associated colitis has occurred during the administration of even two or three week following administration of the antiblotic. The disease is likely to take a more severe course in older patient or in patients who are debilitated.

In case of occurrence of mild associated colitis, discontinuance of lincomycin is recommend. Treatment with cholestyramine and colestipol resins is recommended as these products have been shown to bind the toxins in vitro. The recommended dose of cholestyramire is 4 grams given 3 to 4 times daily and for colestipol, 5 grams given 3 times daily. When severe antibiotic-associated colitis occurs, this has to be treated with appropriate fluid electrolyte and protein supplementation. Studies have also indicated that a toxin(s) produced by Clostridium (especially C.difficile) is/(are) the principal direct cause of antibiotic-associated colitis.

These studies also indicate that this toxigenic Cistridium is usually sensitive in vitro to vancomycin. When 125 to 500 mg vancomycin 4 times daily is administered for 7 to 10 days. There is a rapid observed disappearance of the toxin from feacal samples and a coincident clinical recovery from the diarrhea. In some cases colitis may reoccur after cessation of vancomycin treatment.

Cholestyramine 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.

As an alternative therapy oral bacitracin 25.000 units q.i.d. for 7-10 days could be considered.

Drugs which cause bowel stasis should be avoided.

Caution should be exercised in prescribing lincomycin and erthromycin in vitro. Because of possible clinical significance, these two drugs should not be administered concurrently. If lincomycin antibiotic therapy is prolonged, liver and kidney function tests should be performed.

The use of lincomycin may result in overgrowth of non-susceptible organisms particularly yeast. Lincomycin should not be injected intravenously undiluted as a bolus, but should be infused over at least 10-60 minutes.

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

patients receiving such agents.
Lincomycin should be administered with caution in atopic individuals. Patients with very severe renal disease and/or very severe hepatic disease accompanied by severe metabolic aberration should be dosed with caution, and serum lincomycin levels monitored during high-dose therapy.

4.8 Overdose
Gastric lavage, emetic medicine and fluid replacement

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ANTIINFECTIVES FOR SYSTEMIC USE

Depending on the sensitivity of the micro-organism and the concentration of the antibiotic, lincomycin. May be either bactericidal or bacteriostaic. The in vitro spectrum includes following micro-organisms:
1. Sensitive micro-organisms (MIC-2ug/ml)
-anaerobic non-sporulating gram-positive bacteria such as Peptococis, peptostreptococcis spp and micro-aerofilic streptococci, except S. facealis) and pneumococci.
2. Moderately sensitive micro-organisms (MIC between 2 and 4ug/ ml) which are likely to respond to high dosages.
-anaerobic non-sprulating gram-negative bacteria such as
Clostridium spp and Fusobacterium spp.
-anaerobic sporulating gram-positive bacteria eg. Clostridium spp.
3. Resistant mirco-organisms showing low sensitivity (MIC>8ug/ ml) eg. Streptococcus feacalis, Neisseria, most Heamophilus unfluenza strains, Pseudomonas and other gram-native mirco-organisms.
Cross resistance of the dissociated type has been observed in vitro between clindamycin and lincomycin on the one side and the macrolides (erythromycin, oleandomycin and spiramycin) on the other side. Absolute cross resistance exists between lincomycin and clindamycin. Micro-organisms have not developed resistance to Lincomycin rapidly when tested by in vitro or in vivo methods.
Staphylococci develops in vitro resistance to lincomycin or clindamycin in a slow step wise manner.

5.2 Pharmacokinetic properties

Absorption

Resorption of orally, on an empty stomach, administered lincomycin is 20-30%. After an oral 500mg dose peak levels of circa 3µg/ml are reached in 2 to 4 hours. This value is diminished with about 50% in case the drug is administered with meals. For most gram-positive micro-organisms serum levels are maintained.
above the MIC (between 1 and 2 µg/ml) for 6 to 8 hours.
Intramuscular administration of a single dose of 600mg produces a serum level of 12-20µg/ml ar 1/2 1 hour with detectable concentration as long as 24 hours. The intravenous infusion over a 2-hours interval of 600mg of Lincomycin results in a maximum serum. Concentration of 20µg/ml at 30 minutes, yielding concentrations of 1 to 3 µg/ml at 14 hours.

Distribution

Direct and indirect evidence suggests that protein decreases with high serum concentration 5.471 (saturable plasma protein binding).
In the footal blood, the peritoneal and the pleural liquid concentrations of 25-50% of the blood levels can be reached, in the mother milk 50-100% in the bone tissues about 40% and

lincomycin penetrate slowly in the cerebrospinal fluid(1-18% of the blood level): in case of meningitis, liquor levels up to 40% of the blood levels have been observed.

Excretion

The relatively strong metabolism is mainly taking place through the liver, the normal serum half-life time is 5.4±1 hour. However, this time can be prolonged in case of disturbed liver and/or renal function.

Therefore consideration should be given to decreasing the frequency of administration of lincomycin in patients with impaired hepatic or renal function. After a single oral dose of 500mg the excretion in microbiologically active form in the urine varies from 1 to 31%(average 4%) and in the feaces amounts to about30%.

Apparently the bile in an important route of excretion after oral administration, giving bile level which are about 10 times higher than blood levels. After a 600 mg intramuscular dose the excretion of microbiologically active product in the urine is 1.8 to 24.8% (average 17.3%), in the feaces 4 to 14%. After intravenous administration of 600 mg over a 2 hours period, the excretion of microbiologically active product in the urine is 4.3 to 30.3%(average 13.8%. The remainder is being excreted as microbiological non-active metabolites. There is no influence of hemodialysis and peritioneal dialysis on the excretion of lincomycin from the blood.

5.3 Preclinical safetydata

None

6. Pharmaceutical particulars

6.1 List of excipients

Magnesium Stearate
Talcum Powder

6.2 Incompatibilities

The following drugs are physically incompatible with lincomycin:novbiocin, kanamycin

6.3 Shelf life

36 months

6.4 Special precaution for storage

Store in well-closed container, protected from heat and light. Keep all medicines out of reach of children.

6.5 Nature contents of container

PVC/Aluminum foils blister packs.

6.6 Instruction for use handling and disposal

No special requirements

7. Manufacturer name

Jiangsu Ruinian Qianjin Pharmaceutical Co., Ltd

Chuanbu Village, Yixing Economic Development Zone, Jiangsu Province, China

8. Marketing Authority

MEDNORAL PHARMACEUTICAL LIMITED

Lagos, Nigeria.