Drugfield PHARMACEUTICALS LIMITED

SUMMARY OF PRODUCT CHARACTERISTICS

Biocine® (Lincomycin 500mg) Capsules

1. Name Of The Medicinal Product

Biocine® (Lincomycin 500mg) Capsules

2. Qualitative And Quantitative Composition

Each capsule contains Lincomycin 500mg

For a full list of excipients, see section 6.1.

3. Pharmaceutical Form

Capsules

4. Clinical particulars

Therapeutic indications

Lincomycin is used for the treatment of infections caused by any of the following micro organisms.

Bacteroides fragilis
Streptococcus pyogenes
Streptococcus pneumoniae
Haemophilus influenzae
Neisseria spp.
Bacteroides spp.

Serious infections due to sensitive gram-positive organism (staphylocci, streptococci, pneumococci) when the patient is intolerant of, or the organism resistant to appropriate antibiotics.

4.1 Posology and method of administration

Posology

Important Dosage and Administration Instructions

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

Initial Dosage

Oral use:
To be adapted according to physiopathologic status.
Do not ingest anything except water for 1 to 2 hours before and after taking Lincomycin.
Adults: 1.5 g to 2 g/24 hours.
Children: 30 to 60 mg/kg/24 hours.

Method of administration

Oral route

4.2 Contraindications

Biocine® Capsule is contraindicated in people that are hypersensitive to Lincomycin or clindamycin, and those that have severe liver or kidney damage.

4.3 Special warnings and precautions foruse

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

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

LINCOMYCIN 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 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.

Prescribing LINCOMYCIN 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, 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 recessivelethal 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

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 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, 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.

4.4 Interaction with other medicinal products and other forms of interaction

- Atracurium

  Lincomycin increases effects of atracurium by pharmacodynamic synergism. Avoid or Use Alternate Drug. Risk of respiratory depression.

- Cholera vaccine

  Lincomycin, cholera vaccine. pharmacodynamic antagonism. Avoid or Use Alternate Drug. Avoid coadministration of cholera vaccine with systemic antibiotics since these agents may be active against the vaccine strain. Do not administer cholera vaccine to patients who have received oral or parenteral antibiotics within 14 days prior to vaccination.

- Cisatracurium

  Lincomycin increases effects of cisatracurium by pharmacodynamic synergism. Avoid or Use Alternate Drug. Risk of respiratory depression.

- OnabotulinumtoxinA

  Lincomycin increases effects of onabotulinumtoxinA by pharmacodynamic synergism. Avoid or Use Alternate Drug. Risk of respiratory depression.

- Pancuronium

  Lincomycin increases effects of pancuronium by pharmacodynamic synergism. Avoid or Use Alternate Drug. Risk of respiratory depression.

- Rapacuronium

  Lincomycin increases effects of rapacuronium by pharmacodynamic synergism. Avoid or Use Alternate Drug. Risk of respiratory depression.

- Rocuronium

  Lincomycin increases effects of rocuronium by pharmacodynamic synergism. Avoid or Use Alternate Drug. Risk of respiratory depression.

- Succinylcholine

  Lincomycin increases effects of succinylcholine by pharmacodynamic synergism. Avoid or Use Alternate Drug. Risk of respiratory depression.

- Vecuronium

  Lincomycin increases effects of vecuronium by pharmacodynamic synergism. Avoid or Use Alternate Drug. Risk of respiratory depression.

- RimabotulinumtoxinB

  Lincomycin, rimabotulinumtoxinB. Either increases effects of the other by pharmacodynamic synergism. Use Caution/Monitor. Aminoglycosides may enhance botulinum toxin effects. Closely monitor for increased neuromuscular blockade.

- Sodium picosulfate/magnesium oxide/anhydrous citric acid

  Lincomycin decreases effects of sodium picosulfate/magnesium oxide/anhydrous citric acid by altering metabolism. Use Caution/Monitor. Coadministration with antibiotics decreases efficacy by altering colonic bacterial flora needed to convert sodium picosulfate to active drug.

  Take on an empty stomach. Food decreases absorption.

4.5 Pregnancy and Lactation

Pregnancy

There are no adequate studies done on lincomycin to determine safe and effective use in pregnant women.

Clinical Considerations

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 revealed no ill effects related to pregnancy.

Animal Data

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).

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

Lactation

Risk Summary

- Lincomycin may be excreted in small amounts in breast milk. Therefore, caution should be exercised before using it in nursing mothers.

Clinical Considerations

- To avoid the potential harm to nursing infants, a decision should be made whether to discontinue drug or discontinue nursing before using in nursing mothers.

4.6 Effects on ability to drive and usemachines

Lincomycin has no or negligible influence on the ability to drive and use machines.

4.7 Undesirable effects

Get emergency medical help if you have signs of an allergic reaction (hives, difficult breathing, swelling in your face or throat) or a severe skin reaction (fever, sore throat, burning eyes, skin pain, red or purple skin rash with blistering and peeling).

Antibiotic medicine can cause overgrowth of normally harmless bacteria in the intestines. This can lead to an infection that causes mild to severe diarrhea, even months after your last antibiotic dose. If left untreated this condition can lead to life-threatening intestinal problems.

Call your doctor at once if you have:

- severe stomach pain, diarrhea that is watery or bloody (even if it occurs months after your last dose);
- little or no urination;
- blisters or ulcers in your mouth, red or swollen gums, trouble swallowing;
- jaundice (yellowing of the skin or eyes); or
- low blood cell counts--fever, chills, tiredness, skin sores, easy bruising, unusual bleeding, pale skin, cold hands and feet, feeling light-headed or short of breath.

Older adults and those who are ill or debilitated may be more sensitive to the effects of diarrhea caused by this medication.

Common side effects include:

- diarrhea, stomach pain;
- nausea, vomiting, swollen or painful tongue;
- vaginal itching or discharge;
- mild itching or rash;
- ringing in your ears; or
- dizziness.

- ***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, dermatitisbullous, dermatitis exfoliative, erythema multiforme, rash, urticaria, pruritus

- ***Infections And Infestations***
- Vaginal infection, pseudomembranous colitis, Clostridium difficilecolitis

- ***Blood And lymphatic System Disorders***
- Pancytopenia, agranulocytosis, aplastic anemia, leukopenia, neutropenia, thrombocytopenic purpura

- ***Immune System***
- disorders Anaphylactic reaction, angioedema, serum sickness

- ***Hepatobiliary Disorders***
- Jaundice, liver function test abnormal, transaminases increased

- ***Renal And Urinary Disorders***
- Renal impairment, oliguria, proteinuria, azotemia

- ***Cardiac Disorders***
- Cardio-respiratory arrest

- ***Vascular Disorders***
- Hypotension, thrombophlebitis†

- ***Ear And Labyrinth Disorders***
- Vertigo, tinnitus

- ***Neurologic Disorders***
- Headache, dizziness, somnolence

4.8 Overdose

Clinical Presentation

Someone that has overdosed has serious symptoms such as passing out or trouble breathing

Treatment of Overdose

If there has been an overdose, call your poison control center or get medical care right away. Be ready to tell or show what was taken, how much, and when it happened.

5. PHARMACOLOGICALPROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Benzomorphan derivatives}, ATC code: NO2ADO1

Mechanism of Action

Lincomycin inhibits protein synthesis in susceptible bacteria by binding to the 50 S subunits of bacterial ribosomes and preventing peptide bond formation upon transcription. It is usually considered bacteriostatic, but may be bactericidal in high concentrations or when used against highly susceptible organisms.

Pharmacodynamics

Lincomycin is a lincosamide antibiotic that produced by Streptomyces lincolnensis. Lincomycin has been shown to be active in vitro against the following microorganisms: Aerobic gram-positive cocci: Streptococcus pyogenes and Viridans group streptococci; Aerobic gram-positive bacilli: Corynebacterium diphtheriae; Anaerobic gram-positive non-sporeforming bacilli: Propionibacterium acnes; Anaerobic gram-positive sporeforming bacilli: Clostridium tetani and Clostridium perfringens.

5.2 Pharmacokinetic properties

Absorption

Rapidly absorbed from the gastrointestinal tract following oral administration. Approximately 20 to 30% absorbed orally in fasting state; absorption decreased when taken with food.

Volume of distribution

Not Available

Protein binding

Protein binding decreases with increased plasma concentrations. Range, 28 to 86% (average, 70 to 75%). Albumin is not thought to be the primary binding component.

Metabolism

Presumed hepatic, however metabolites have not been fully characterized.

Route of elimination

Urinary excretion after this dose ranges from 1.8 to 24.8 percent (mean: 3 percent). Biliary excretion is also an important route of excretion.

Half-life

The biological half-life after intramuscular or intravenous administration is 5.4 ± 1.0 hours. The serum half-life may be prolonged in patients with severe impairment of renal function. Half life may be extended up to 2-fold in patients with hepatic impairment.

Clearance

Not Available

Toxicity

Not Available

Affected organisms

- Enteric bacteria and other eubacteria

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on studies of repeat dose toxicity, reproductive toxicity or genotoxicity. Carcinogenicity studies have not been conducted.

In dogs, repeated high oral doses produced ulceration of the mucosa of the stomach and gall bladder.

6. PHARMACEUTICALPARTICULARS

6.1 List of excipients

Sodium Lauryl Sulphate
Lactose 200
Aerosil 200
Magnesium Stearate

6.2 Incompatibilities

None have been reported or are known

6.3 Shelflife

36 Months

6.4 Special precautions forstorage

Store below 30^{o}C in tight container protected from light and moisture.

6.5 Nature and contents of container and special equipment for use, administration orimplantation

Biocine Capsule is presented in blister of 10 capsules, and 2 of such blisters in a pack.

6.6 Special precautions for disposal and otherhandling

No special requirements.

7. APPLICANT/MANUFACTURER

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