1. NAME OF THE MEDICINAL PRODUCT

EMBAMEDICLOX 500 (Ampicillin and Cloxacillin Capsules 500mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard gelatin capsule contains:

Ampicillin Trihydrate	BP	
Eq. to Ampicillin		250 mg
Cloxacillin Sodium	BP	
Eq. to Cloxacillin		250 mg
Excipients		q.s.

Approved colour used in empty capsule shells

3. PHARMACEUTICAL FORM

Hard Gelatin Capsule

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ampicillin and Cloxacillin Capsules 500mg is indicated for the treatment of the following infections including mixed Gram-positive and Gram-negative infections.

Typical infections include Bronchopneumonia, acute exacerbations of chronic bronchitis, Puerperal fever, post-operative wound infections, post-operative pulmonary infections, bone infections e.g., osteomyelitis, ear, nose and throat infections.

4.2 Posology and Method of Administration

Posology

Adult

500mg to 1.0gm every 6 hours or more often depending on the severity of infection or as directed by the Physician.

Children

1 month -2 yrs: ¼ the adult dose.

2 yrs-10 yrs: ½ the adult dose.

Administer the dose

½ to 1 hr. before meals.

Elderly

No dose adjustment is considered necessary.

Renal impairment

In cases of renal failure, the dosage should be adapted in accordance with the following:

Creatinine clearance greater than 50mL/minute:

Normal dose according to indication.

Creatinine clearance between 50 and 10mL/minute:

Dosage (Oral) initial dose: normal dose (according to indication).

Creatinine clearance below 10mL/minute: -

Dosage (oral or parenteral administration) initial dose: normal dose (according to indication).

Dosage (oral or parenteral administration) maintenance dose:

The normal unit dose twice or once daily.

Hepatic impairment

Reduce frequency of administration depending on the severity of the condition.

Method of Administration

For Oral Use.

4.3 Contraindications

Ampicillin and Cloxacillin Capsule should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (e.g., penicillins, cephalosporins) or excipients.

Ampicillin and Cloxacillin is contraindicated for ocular administration.

4.4 Special Warning and Precautions for Use

Hypersensitivity reactions

Before initiating therapy with Ampicillin and Cloxacillin, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactams.

Cross-sensitivity between penicillins and cephalosporins is well documented. Serious and occasionally fatal hypersensitivity reactions (anaphylaxis) have been reported in patients receiving beta-lactam antibiotics. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in individuals with a history of beta-lactam hypersensitivity. If an allergic reaction occurs, Ampicillin and Cloxacillin should be discontinued and the appropriate alternative therapy instituted. All adverse reactions should be treated symptomatically.

Ampicillin and Cloxacillin should be avoided if infectious mononucleosis and/or acute or chronic leukemia of lymphoid origin are suspected. The occurrence of a skin rash has been associated with these conditions following the administration of ampicillin.

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Dosage should be adjusted in patients with renal impairment

Cloxacillin can displace bilirubin from protein-binding sites. Normal caution should therefore be exercised in the treatment of jaundiced neonates.

The sodium content of the formulation must be included in the daily allowance of patients on sodium restricted diets.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Probenecid decreases the renal tubular excretion of Ampicillin and Cloxacillin. Concurrent use with Ampicillin and Cloxacillin may result in increased and prolonged blood levels of Ampicillin and Cloxacillin.

In common with other antibiotics, Ampicillin and Cloxacillin may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral contraceptives.

Bacteriostatic drugs may interfere with the bactericidal action of Ampicillin and Cloxacillin.

Concurrent administration of allopurinol during treatment with Ampicillin and Cloxacillin can increase the likelihood of allergic skin reactions.

4.6 Pregnancy and lactation

Cloxacillin should be used cautiously in pregnant women.

Interruption of nursing has to be considered since Cloxacillin passes through maternal milk.

4.7 Effects on Ability to Drive and Use Machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines.

4.8 Undesirable Effects

The majority of the adverse reactions are diarrhoea, nausea, skin rash, urticaria, and pruritus.

Adverse reactions are listed below by system organ class.

Blood and lymphatic system disorders

Very rare: Hemolytic anemia, leucopenia, thrombocytopenia, and agranulocytosis.

Immune system disorders

Very rare: Anaphylaxis and other hypersensitivity reactions

Skin disorders and interstitial nephritis have been reported as hypersensitivity reactions.

If any hypersensitivity reaction occurs, the treatment should be discontinued.

Nervous system disorders

Very rare: Myoclonus and convulsions

Gastrointestinal disorders

Common: Diarrhoea and nausea

Uncommon: Vomiting

Very rare: Pseudomembranous colitis (See Warnings and Precautions) and hemorrhagic colitis

Hepatobiliary disorders

Very rare: Hepatitis and cholestatic jaundice. A moderate and transient increase in transaminases

Skin and subcutaneous tissue disorders

Common: Skin rash, urticaria, and pruritus.

The incidence of skin rash, pruritus, and urticaria is higher in patients suffering from infectious mononucleosis and acute or chronic leukemia of lymphoid origin.

Very rare: Bullous reactions (including erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis), exfoliative dermatitis and purpura

Skin disorders have also been reported as hypersensitivity reactions (See Immune system disorders).

Renal and urinary disorders

Very rare: Interstitial nephritis

Interstitial nephritis has also been reported as a hypersensitivity reaction.

4.9 Overdose

Over dosage with oral ampicillin and cloxacillin is unlikely to cause serious reactions if renal function is normal. Gastrointestinal effects such as nausea, vomiting, and diarrhoea may be evident. These symptoms should be treated symptomatically

5.0 PHARMACOLOGICAL PROPERTIES

ATC CODE: Ampicillin: J01CA51

Cloxacillin: J01CF02

5.1 Pharmacodynamic properties

Cloxacillin is a narrow-spectrum antibiotic of the isoxazolyl penicillin group; it is not inactivated by staphylococcal beta lactamases. Ampicillin is a broad-spectrum antibiotic of the aminopenicillin group it is not resistant to beta-lactamases. Both ampicillin and Cloxacillin are bactericidal antibiotics and act by interfering with the formation of new bacterial cell wall by dividing organisms. The prevalence of acquired resistance is geographically variable and for select species may be very high. Local information on resistance is desirable, particularly when treating severe infections.

Ampicillin and Cloxacillin susceptibility rates are higher than ampicillin rates due to the Cloxacillin activity against β-lactamase producing staphylococci. Methicillin-susceptible Staphylococcus aureus (MSSA) and methicillin-susceptible coagulase-negative staphylococcus (MSCoNS) are commonly susceptible to Ampicillin and Cloxacillin. MRSA and MRCoNS are resistant to Ampicillin and Cloxacillin. For all other indicated bacterial species, the susceptibility of Ampicillin and Cloxacillin is similar to ampicillin including limited activity against Gram-negative organisms.

5.2 Pharmacokinetic properties

Absorption

Both ampicillin and Cloxacillin are stable in the gastric environment resulting in good absorption. Neither component of the combination of ampicillin and Cloxacillin interferes with the absorption or excretion of the other. The total quantity absorbed by the oral route represents 50% (Cloxacillin) and 40% (ampicillin) of the quantity administered. The presence of food in the stomach may depress oral absorption and Ampicillin and Cloxacillin should therefore be taken 0.5 to 1 hour before meals.

Distribution

Ampicillin and Cloxacillin diffuses well into most tissues and body fluids including, among others, bronchial secretions, sinuses, saliva, cerebrospinal fluid (variable percentage depending on the degree of meningeal inflammation), bile, serous membranes and middle ear. Crossing the meningeal barrier: ampicillin and Cloxacillin diffuses in only small proportion into the cerebrospinal fluid of subjects whose meninges are not inflamed. Crossing into breast milk: Ampicillin and Cloxacillin is excreted in small quantities in breast milk. Plasma half-life for Cloxacillin is 0.5 to 1 hour and 1 to 1.5 hour for ampicillin. Protein binding: the serum protein binding proportion is approximately 94% for Cloxacillin and 18% for ampicillin.

Metabolism

In normal subjects approximately 20% (Cloxacillin) and 40% (ampicillin) of the dose administered is metabolized.

Excretion

Ampicillin and Cloxacillin is eliminated mainly through the kidney. Approximately 30% of the dose administered orally and over 60% of the ampicillin dose administered is eliminated in active form in the urine within 24 hours. The equivalent percentages for Cloxacillin are approximately 20% and 30% respectively. A small proportion (10%) of the dose administered is excreted in bile.

5.3 Preclinical Safety Data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

- Colloidal Anhydrous Silica BP
- Purified Talc BP
- Magnesium Stearate BP
- Sodium Lauryl Sulphate BP
- Isopropyl Alcohol BP
- Dichloromethane BP
- Instacoat (ICMS-2398) IH

- E.H.G. Capsule, Size ‘0’ IH

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Store at a temperature not exceeding 30°C. Protect from light & moisture.

Keep the medicines out of reach of children.

6.5 Nature and Contents of Container

10 Capsules packed in ALU-PVC blisters and such 10 blisters packed in a carton along with pack insert.

6.6 Special Precautions for Disposal and Other Handling

No special requirements.

7. APPLICANT/SOLE AGENT

EMBASSY PHARMACEUTICAL & CHEMICAL LTD.

41, Ademola Street, South West Ikoyi,

Lagos, Nigeria. Tel.: 01-2900791

Manufacturer

LABORATE PHARMACEUTICALS INDIA LIMITED

51, Industrial Area, Gondpur, Paonta Sahib,

District Sirmour, Himachal Pradesh-173025 (India)

HO: E-11, Industrial Area, Panipat – 132103

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