MECURE INDUSTRIES PLC

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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1. Name of product
LACLOX CAPSULES

2. Qualitative and Quantitative Composition
Each capsule contains Ampicillin Trihydrate B.P Equivalent to Ampicillin 250mg and Cloxacillin Sodium B.P Equivalent to Cloxacillin 250mg.

Description: Black coloured cap and purple coloured body hard gelatin capsules having printed with "LACLOX" and '500' on the cap and body alternatively, containing almost white powder.

3. Pharmaceutical Form
Capsules
Hard Gelatin Capsules filled with almost white granular powder

4. Clinical Particulars
4.1 Therapeutic Indications
LACLOX is indicated for the treatment of the following infections including mixed Grampositive (except methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant coagulase-negative staphylococcus (MRCoNS)) and Gram-negative infections: Surgery: post-operative wound infections, post-operative pulmonary infections. Respiratory infections: bronchopneumonia, acute exacerbations of chronic bronchitis. Obstetrics: puerperal fever. Other infections such as septicaemia, bone infections e.g., osteomyelitis, ear, nose and throat infections. Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing infection and to determine their susceptibility to LACLOX. Where treatment is initiated before results are available expert advice should be sought when the local prevalence of resistance is such that the utility of LACLOX is questionable (see Pharmacological properties, Pharmacodynamics).

4.2 Posology and method of administration
Adult: One capsule (500mg) every 6 hours
OR
As directed by the Physician.

4.3 Contra-Indications
LACLOX should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (e.g., penicillin, cephalosporin) or excipients (See List of Excipients).

LACLOX is contraindicated for ocular administration.

4.4 Special warnings and precautions for use
Before initiating therapy with LACLOX, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactams.
Cross-sensitivity between penicillin and cephalosporin 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 penicillin. These reactions are more likely to occur in individuals with a history of beta-lactam hypersensitivity.
If an allergic reaction occurs, LACLOX should be discontinued and the appropriate alternative therapy instituted. All adverse reactions should be treated symptomatically.
LACLOX 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 diarrhea during or after antibiotic use. If prolonged or significant diarrhea 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 (See Dosage and Administration, Renal impairment).
Cloxacillin can displace bilirubin from protein-binding sites. Normal caution should therefore be exercised in the treatment of jaundiced neonates.
LACLOX suspension contains sodium benzoate which is a mild irritant to the skin, eyes, and mucous membrane. It may increase the risk of jaundice in newborn babies.
The sodium content of the formulation must be included in the daily allowance of patients on sodium restricted diets.
Each LACLOX 500mg capsule contains 13.17mg of sodium.

4.5 Interaction with other medicinal products for use

Probenecid decreases the renal tubular excretion of LACLOX. Concurrent use with LACLOX may result in increased and prolonged blood levels of LACLOX. As common with other antibiotics, LACLOX may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral contraceptives.
Sulphonamides and acetylsalicylic acid inhibit serum protein binding of cloxacillin in vitro. This may result in increased levels of free cloxacillin in serum in vivo.
Bacteriostatic drugs may interfere with the bactericidal action of LACLOX.
Concurrent administration of allopurinol during treatment with LACLOX can increase the likelihood of allergic skin reactions.

4.6 Pregnancy and Lactation

Adequate human data on use during pregnancy are not available. However, animal studies have not identified any risk to pregnancy or embryo-fetal development.
Adequate human and animal data on use during lactation are not available

4.7 Effects on the ability to drive and use machines

No adverse effects on the ability to drive or operate machinery have been observed.

4.8 Undesirable effects

The following statements reflect the information available on the adverse reaction profile of the individual constituents (ampicillin and cloxacillin) and/or the combination in LACLOX. The majority of the adverse reactions listed below are not unique to ampicillin - cloxacillin and may occur when using other penicillins.
reactions are listed below by system organ class and frequency. Frequencies are defined as: very common (>1/10), common (>1/100, <1/1,000), rare (>1/10, 000, <1/1,000), very rare (<1/10,000), including isolated reports. Common and uncommon adverse reactions were generally determined from pooled safety data from a clinical trial population of 1210 treated patients. Rare and very rare adverse reactions were generally determined from more than 32 years of post-marketing experience data and refer to reporting rate rather than true frequency.

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics

LACLOX is a combination of ampicillin and cloxacillin. Cloxacillin is a narrow-spectrum antibiotic of the isoxazolyl penicillin group; it is not inactivated by staphylococcal betalactamases. 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. LACLOX 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 LACLOX. MRSA and MRCoNS are resistant to LACLOX. For all other indicated bacterial species, the susceptibility of LACLOX is similar to ampicillin including limited activity against Gram-negative organisms.

5.2 Pharmacokinetics

5.2.1 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 LACLOX should therefore be taken 0.5 to 1 hour before meals.

5.2.2 Distribution

LACLOX 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: LACLOX diffuses in only small proportion into the cerebrospinal fluid of subjects whose meninges are not inflamed.
Crossing into breast milk: LACLOX 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.

5.2.3 Metabolism

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

5.2.4 Excretion

LACLOX is eliminated mainly through the kidney. Approximately 30% of the dose administered orally and over 60% of the ampicillin dose administered parenterally 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

Not available

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

LACLOX 250mg/5ml Suspension:

Magnesium Stearate
Empty hard gelatin capsule

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a cool dry place at temperature below 30°C. Store in the original packaging.

6.5 Nature and contents of container

Available in blister pack of 10 x 10s and ALU/ALU tropical pack of 2 x 10s.

6.6 Special precautions for disposal and other handling

None

7. Marketing authorization holder

Me Cure Industries PLC
Plot 6 Block H, Debo Industries Compound,
Oshodi Industrial Scheme,
Oshodi,
Lagos,
Nigeria.

8.0 NAFDAC REGISTRATION NUMBER: A4-4210