1. NAME OF THE MEDICINAL PRODUCT

Brand Name: Dailiclox 500 mg Capsule
Generic Name: Ampicillin and Cloxacillin Capsule 500 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

- Ampicillin Trihydrate BP equivalent to 250 mg of Ampicillin base.
- Cloxacillin Sodium BP equivalent to 250 mg of Cloxacillin base

Excipients with known effect:

EXCIPIENTS	FUCTION
Magnesium Sterate	Lubricant
AEROSIL	Glidant
Empty hard gelatin capsules of size "0" IH	Capsule shell

- Aerosil USP
- Magnesium Stearate USP
- Empty hard gelatin capsules of size "0" IH Capsule Shell

3. PHARMACEUTICAL FORM

Amethyst and Black colored Hard Gelatin size '0' STRENGTH 500 MG Capsules printed DAILICLOX on the Cap and 500MG on the body containing white to off-white powder**.**

4. Clinical particulars

4.1 Therapeutic indications

Dailiclox is indicated for the treatment of the following infections.

- In Surgery: Post-operative wound infections, post-operative pulmonary infections.
- Respiratory infections: Bronchopneumonia, acute exacerbations of chronic bronchitis.
- Obstetrics: Puerperal fever.
- Other infections such as septicemia, bone infections e.g. osteomyelitis, ear, nose and throat infections upon appropriate culture and susceptibility tests performed before treatment to isolate and identify organisms causing infection and determine their susceptibility to ampicillin and Cloxacillin capsule. 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 ampicillin and Cloxacillin capsule is questionable (see Pharmacological properties, Pharmacodynamics)
- Mixed Gram-positive (other than methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant coagulase-negative staphylococcus (MRCoNS)) and Gram-negative infections:

4.2 Posology and method of administration

Dosage:

Adult: 500 mg 1 capsule every 6 hrs. or more as directed by the Physician.

Children: Aged between1 month -2 yrs.: ¼ the adult dose 125mg. Age 2 yrs-10 yrs. ½ the adult dose 250mg. Administer the dose ½ to 1 hr. before meals

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.
- For Hepatic impairment: Reduce frequency of administration depending on the severity of the condition.

Method of administration
Dailiclox 500mg capsule may be swallowed with a drink of water for Adults and children (over two years)

4.3 Contraindications

Ampicillin and Cloxacillin capsule should not be administered to patients with a history of hypersensitivity to beta-lactam antibiotics (e.g., penicillins, cephalosporins) or excipients (See List of Excipients). – Ampicillin and Cloxacillin is contraindicated for ocular administration.

4.4 Special warnings 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 leukaemia 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 (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. 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 oestrogen 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

Adequate human data on use during pregnancy are not available. However, animal studies have not identified any risk to pregnancy or embryo-foetal development. Cloxacillin should therefore 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.

4.8 Undesirable effects

The majority of the adverse reactions listed below are not unique to ampicillin - cloxacillin and may occur when using other penicillins. 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 (See Warnings and Precautions) and other hypersensitivity reactions Skin disorders and interstitial nephritis have been reported as hypersensitivity reactions. (See also Skin and subcutaneous tissue disorders and Renal and urinary disorders). 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 haemorrhagic 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 leukaemia of lymphoid origin.
Very rare: Bullous reactions (including erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis), exfoliative dermatitis and purpura

- **Renal and urinary disorders**

Very rare: Interstitial nephritis

Overdose
Over dosage with oral ampicillin and cloxacillin is unlikely to cause serious reactions if renal function is normal. High dosage of i.v. administered ampicillin and/or high dosage of cloxacillin in renal failure may provoke neurotoxic reactions similar to those seen with benzylpenicillin in excess.
Gastrointestinal effects such as nausea, vomiting, and diarrhoea may be evident. These symptoms should be treated symptomatically.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Mechanism of action
Ampicillin is a broad-spectrum antibiotic of the aminopenicillin group; it is not resistant to beta-lactamases.
Cloxacillin is a narrow-spectrum antibiotic of the isoxazolyl penicillin group; it is not inactivated by staphylococcal betalactamases.
Both ampicillin and cloxacillin are bacterial agents and act by interfering with the synthesis of the peptidoglycan layer of the cell wall, which normally protects the bacterium from its environment. Defective wall synthesis renders the cell incapable of withstanding the osmotic gradient between the cell and its environment so that it swells and explodes.
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 **½** 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.

- **Elimination**

Ampicillin and cloxacillin is eliminated mainly through the kidney. Approximately 30% of the dose is 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

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

EXCIPIENTS	FUCTION
Magnesium Sterate	Lubricant
AEROSIL	Glidant
Empty hard gelatin capsules of size "0" IH	Capsule shell

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 30°C in cool and dry place.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Alu/PVC blisters of 10 Capsules

6.6 Special precautions for disposal

No special requirements.

7. APPLICANT/MANUFACTURER

Daily Need Industries Limited

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Off Ladipo Street,

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