SmPC FOR MIRACLOX CAPSULE

1. Name of the medicinal product

KADLOX Capsules 500MG-Ampicillin-cloxacillin

QUALITATIVE AND QUANTITATIVE COMPOSITION

AMPICLOX 500mg Capsules*:*

Each capsule contains 250mg of Ampicillin trihydrate and 250mg of Cloxacillin Sodium

PHARMACEUTICAL FORM

AMPICLOX 500mg capsule:

Hard Gelatin Capsules filled with almost white granular powder.

CLINICAL PARTICULARS

Indications

AMPICLOX is indicated for the treatment of the following infections including mixed Gram-positive (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 AMPICLOX. 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 AMPICLOX is questionable (see Pharmacological properties, Pharmacodynamics).

AMPICLOX neonatal oral drops are indicated for the prophylaxis or treatment of bacterial infections in premature babies or neonates , caused by known susceptibile strains of bacteria.

Dosage and Administration Route	**Dosage**
Adults and Elderly	
Oral	1 to 2g every 6 hours
Intramuscular (i.m.) injection	250mg to1g every 4 to 6 hours

The dose of AMPICLOX may be increased for the treatment of severe infections.

Children	**Dosage**
2 to 12 years	
Oral	Half adult dose: 5 to 10mL suspension every 6 hours
Injectable	Half adult dose: 250mg every 8 hours
Neonates to 2 years	
Neonatal oral drops	0.6mL (90mg) of reconstituted suspension every 4 hours. Administer 0.5 to 1 hour prior to feeding impairment

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

3 Creatinineclearance greater than 50mL/minute: normal dose according to indication.
Creatinine clearance between 50 and 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 (AMPICLOX 250mg orally, up to 1g i.m. or i.v) three times daily.
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.
In cases of dialysis, an additional normal unit dose (AMPICLOX 250mg orally, up to 1g i.m. or i.v) is to be administered after the procedure.

***Hepatic* impairment**

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

Mode of Administration

***Oral route*:**

AMPICLOX should be administered 0.5 to 1 hour before meals.

Contraindications

- AMPICLOX should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (e.g., penicillins, cephalosporins) or excipients (See List of Excipients).

- AMPICLOXis contraindicated for ocular administration.

Warnings and Precautions

Caution should be observed when administering AMPICLOX neonatal oral drops to babies whose mothers are hypersensitive to penicillin.
Before initiating therapy withAMPICLOX, 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, AMPICLOX should be discontinued and the appropriate alternative therapy instituted. All adverse reactions should be treated symptomatically.
AMPLICLOX 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.

Interactions

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

5.0 In common with other antibiotics, AMPICLOX may affect the gut flora, leading to lower oestrogenreabsorption 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 AMPICLOX.
Concurrent administration of allopurinol during treatment with AMPICLOX can increase the likelihood of allergic skin reactions.

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.
Adequate human and animal data on use during lactation are not available.

Ability to perform tasks that require judgment, motor or cognitive skills

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

Adverse Reactions

The following statements reflect the information available on the adverse reaction profile of the individual constituents (ampicillin and cloxacillin) and/or the combination in *AMPICLOX*. 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 and frequency. Frequencies are defined as: very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000), 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.

Blood and lymphatic system disorders

Very rare: Hemolytic anemia, leucopenia, thrombocytopenia, agranulocytosis

6 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 erythemamultiforme, 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 *(See also Immune system disorders)*.

Immune system disorders

Overdose -

Overdosage with oral AMPICLOX is unlikely to cause serious reactions if renal function is normal. Very 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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

AMPICLOX is a combination of ampicillin and cloxacillin. 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.

AMPICLOX 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 AMPICLOX. MRSA and MRCoNS are resistant to AMPICLOX. For all other indicated bacterial species, the susceptibility of AMPICLOX is similar to ampicillin including limited activity against Gram-negative organisms.

Pharmacokinetics

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.

Metabolism

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

Excretion

AMPICLOX 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.

PHARMACEUTICAL PARTICULARS

List of Excipients

AMPICLOX 500mg Capsules*:*

Magnesium stearate, talc

Colloidal Anhydrous Silica

Incompatibilities

AMPICLOX must not be dissolved in either protein or protein hydrolysate solutions or in lipid solutions, or in blood or plasma.

When AMPICLOX is prescribed together with an aminoglycoside, the two antibiotics should not be mixed in the same container as the one containing the infusion solution because a loss of activity may occur.

6.4 Special Precautions for Storage

AMPICLOX 500mg Capsules

NMT 30^0C.

Shelf-life-3years

6.5**Nature and Contents of Container**

Alu/PVC -AMPICLOX 500mg Capsules-1x10-(10x10)

6.6 Special precautions for disposal and other handling
No special requirements for disposal.

7. Marketing authorisation holder
MIRAFLASH NIGERIA LIMITED (pharmaceuticals)
Ogun State, Nigeria.

8. Marketing authorisation number(s)
E-mail: miraflashnigerialtd@yahoo.com **Tel: 08052006942**