KEMOXYL 500 CAPSULES
(AMOXICILLIN CAPSULES.)

MODULE 1	ADMINISTRATIVE INFORMATION AND PRESCRIBING INFORMATION

1.4 product information
1.4.1 Prescribing information (Summary of product characteristics)
1. Name of the medicinal product
Kemoxyl 500 capsules

2. Qualitative and quantitative composition
Each capsule contains Amoxicillin Trihydrate equivalent to Amoxicillin 500mg for full list of Excipients, see section 6.1.

3.Pharmaceutical form
Maroon/Yellow Hard Gelatin Capsule size '0' imprinted company logo and Kemoxyl 500mg, containing white granular powder.

4. Clinical particulars
4.1 Therapeutic indications.
Kemoxyl preparations are indicated for the treatment of infections caused by or associated with pathogens sensitive to amoxicillin. It is used in the treatment of respiratory tract infections such as bronchitis, pneumonia and tracheobronchitis. It is also used in the treatment of bone and joint infections including Lyme`s disease, biliary tract infections, actinomycosis, endocarditis, mouth infections, otitis media, spleen disorders, typhoid and paratyphoid fever, urinary tract infections including gonorrhea and gastro-enteritis (including Escherichia coli and Salmonella enteritis).

4.2 Posology and method of administration
Method of Administration: Oral route.
Kemoxyl preparations are administered by the oral route. Kemoxyl powder are reconstituted to make 100ml or 60ml.
Kemoxyl DT tablets are recommended to be dispersed in 5 - 10mI of water in order to form dispersion which is administered by the oral route.
DOSE:
The usual dose of Amoxicillin is as follows:
Adult: 250 to 500mg every 8 hours, doubled in severe infections.
Children up to 10 years of age: 125mg to 250mg every 8 hours or 1 to 2 teaspoonfuls every 8hours; doubled in severe infections. Shake the bottle well before taking each dose.
The dose of Amoxicillin may vary depending on the disease, duration and severity of the infection.

Diagnosis	Dose	
Severe or recurrent purulent respiratory infections	Adults 3g every 12 hours	2-5 years: 750mg every 12hours. 5-10 years: 1.5g every 12 hours.
Otitis Media	-	750mg twice daily for 2 days.
Urinary tract infections (UTI)	3g repeated after 10 - 12 hours	Single dose of 50mg/kg body wt. with 25mg/kg probenecid.
Gonorrhoea	Single dose of 2 – 3g with probenecid.	1g Single dose of 50mg/kg with probenecid.
Dental abscesses	1g repeated after 8 hours	-

4.3 Contraindications
Amoxicillin is contra-indicated in patients with hypersensitivity to penicillins.
Attention should also be paid to possible cross-reactivity with other beta-lactam antibiotics e.g., cephalosporins. It should not be given to patients with infectious mononucleosis (glandular fever) since they are especially susceptible to amoxicillin-induced skin rashes.

4.4 Special warnings and precautions for use.

1. Kemoxyl is contra-indicated in patients with known hypersensitivity to Amoxicillin or other penicillins.
2. Prolonged use of the preparation may result in overgrowth of non-susceptible pathogens including fungi and, in such cases, appropriate medication should be instituted immediately.
3. The side-effects occasionally associated with the preparations include; vomiting, nausea. Diarrhoea, rashes, pruritus, fever, urticaria and pseudomembranous colitis.
4. The treatment regimen which involves Amoxicillin and probenecid should be avoided in children under 2 years of age since probenecid is contraindicated in such children.

4.5 Interaction with other medicinal products and other forms of interaction

Allopurinol

Concomitant administration of allopurinol may promote the occurrence of allergic cutaneous reactions and is therefore not advised.

Digoxin

An increase in the absorption of digoxin is possible on concurrent administration with amoxicillin. A dose adjustment of digoxin may be necessary.

Disulfiram

Simultaneous administration of disulfiram is contraindicated.

Anticoagulants

Concomitant administration of amoxicillin and anticoagulants, from the coumarin class, may prolong the bleeding time. A dose adjustment of anticoagulants may be necessary.

Probenecid

By inhibiting the renal elimination of amoxicillin, the concomitant administration of probenecid leads to an increase in the concentrations of amoxicillin in serum and bile.

Other antibiotics

In general amoxicillin should not be combined with bacteriostatic chemotherapeutics/antibiotics (like tetracyclines, macrolids, sulfonamids or chloramphenicol), because in vitro antagonism is observed. When used simultaneously with aminoglycosides a synergistic effect may occur.

Methotrexate

Interaction between amoxicillin and methotrexate leading to methotrexate toxicity has been reported. Serum methotrexate levels should be closely monitored in patients who receive amoxicillin and methotrexate simultaneously. Amoxicillin decreases the renal clearance of methotrexate, probably by competition at the common tubular secretion system.

Caution is recommended when amoxicillin is given concomitantly with:

Oral hormonal contraceptives

Administration of amoxicillin can transiently decrease the plasma level of estrogens and progesterone, and may reduce the efficacy of oral contraceptives. It is therefore recommended to take supplemental non-hormonal contraceptive measures.

Other forms of interactions:

- Forced diuresis leads to a reduction in blood concentrations by increased elimination of amoxicillin.
- The occurrence of diarrhoea may impair the absorption of other medicaments and consequently adversely affect the efficacy.
- It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.
- Amoxicillin may decrease the amount of urinary estriol in pregnant women.
- At high-risk concentrations, amoxicillin may diminish the results of serum glycemia levels
- Amoxicillin may interfere with protein testing when colormetric methods are used

4.6 Fertility, Pregnancy and lactation

Use in pregnancy:
Animal studies with Amoxicillin have shown no teratogenic effects. The product has been in extensive clinical use since 1972 and its suitability in human pregnancy has been well documented in clinical studies.
When antibiotic therapy is required during pregnancy, Amoxicillin may be considered appropriate when the potential benefits outweigh the potential risks associated with treatment.
Use in lactation:
Amoxicillin may be given during lactation. With the exception of the risk of sensitisation associated with the excretion of trace quantities of amoxicillin in breast milk, there are no known detrimental effects for the breast-fed infant.
Fertility
There are no data on the effects of amoxicillin on fertility in humans. Reproductive studies in animals have shown no effects on fertility.
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 effect
The following convention has been utilised for the classification of undesirable effects:
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).
The majority of side effects listed below are not unique to amoxicillin and may occur when using other penicillins.
Unless otherwise stated, the frequency of adverse events has been derived from more than 30 years of post-marketing reports.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Infections and infestations
Very Rare:
Muco-cutaneous candidiasis
Blood and lymphatic system disorders
Very rare:
Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia.
Prolonged prothrombin and bleeding times
Immune system disorders
Very rare:
As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and vasculitis
If any hypersensitivity reaction occurs the treatment should be discontinued (See also Skin and subcutaneous tissue disorders).
Nervous system disorders
Very rare:
Hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.
Unknown:
Paraesthesia
Gastrointestinal disorders
Clinical Trial Data
***Common:**
Diarrhoea and nausea.
***Uncommon:**

Vomiting.

Post-marketing Data

Very rare:

Antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitis).

Black hairy tongue

Superficial tooth discolouration has been reported in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.

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Hepato-biliary disorders

Very rare:

Hepatitis and cholestatic jaundice. A moderate rise in AST and/or ALT.

The significance of a rise in AST and/or ALT is unclear.

Skin and subcutaneous tissue disorders

Clinical Trial Data

***Common:**

Skin rash

***Uncommon:**

Urticaria and pruritus

Post-marketing Data

Very rare:

Skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP)

(See also Immune system disorders).

Renal and urinary tract disorders

Very rare:

Interstitial nephritis.

Very rare:

Crystalluria

*The incidence of these AEs was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose and treatment

Symptoms and signs of overdose:

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance of the fluid and electrolyte balances may be evident. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed. Convulsions may occur in patients with impaired renal function or in those receiving high doses

Treatment of intoxication:

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance.

Amoxicillin may be removed from the circulation by haemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: penicillins with extended spectrum

ATC Code: J01CA04

Mechanism of action

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Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.
Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.
Pharmacokinetic/pharmacodynamic relationship.
The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for amoxicillin.
Mechanisms of resistance
The main mechanisms of resistance to amoxicillin are:
• Inactivation by bacterial beta-lactamases.
• Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.
Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.
Breakpoints
MIC breakpoints for amoxicillin are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) version 5.0.

Organism	**MIC breakpoint (mg/L)**	
	Susceptible ≤	**Resistant >**
Enterobacteriaceae	8[1]	8
Staphylococcus spp.	Note[2]	Note[2]
Enterococcus spp.[3]	4	8
Streptococcus groups A, B, C and G	Note[4]	Note[4]
Streptococcus pneumoniae	Note[5]	Note[5]
Viridans group steprococci	0.5	2
Haemophilus influenzae	2[6]	2[6]
Moraxella catarrhalis	Note[7]	Note[7]
Neisseria meningitidis	0.125	1
Gram positive anaerobes except *Clostridium difficile*[8]	4	8
Gram negative anaerobes[8]	0.5	2
Helicobacter pylori	0.125[9]	0.125[9]
Pasteurella multocida	1	1
Non- species related breakpoints[10]	2	8

[1]Wild type Enterobacteriaceae are categorised as susceptible to aminopenicillins. Some countries prefer to categorise wild type isolates of *E. coli* and *P. mirabilis* as intermediate. When this is the case, use the MIC breakpoint S ≤ 0.5 mg/L
[2]Most staphylococci are penicillinase producers, which are resistant to amoxicillin. Methicillin resistant isolates are, with few exceptions, resistant to all beta-lactam agents.
[3]Susceptibility to amoxicillin can be inferred from ampicillin
[4]The susceptibility of streptococcus groups A, B, C and G to penicillins is inferred from the benzylpenicillin susceptibility.
[5]Breakpoints relate only to non-meningitis isolates. For isolates categorised as intermediate to ampicillin avoid oral treatment with amoxicillin. Susceptibility inferred from the MIC of ampicillin.
[6]Breakpoints are based on intravenous administration. Beta-lactamase positive isolates should be reported resistant.
[7]Beta lactamase producers should be reported resistant
[8]Susceptibility to amoxicillin can be inferred from benzylpenicillin.
[9]The breakpoints are based on epidemiological cut-off values (ECOFFs), which distinguish wild-type isolates from those with reduced susceptibility.
[10]The non-species related breakpoints are based on doses of at least 0.5 g x 3or 4 doses daily (1.5 to 2 g/day).

The prevalence of resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable

***In vitro* susceptibility of micro-organisms to Amoxicillin**
Commonly Susceptible Species
Gram-positive aerobes: *Enterococcus faecalis* Beta-hemolytic streptococci (Groups A, B, C and G) *Listeria monocytogenes*
Species for which acquired resistance may be a problem
Gram-negative aerobes: *Escherichia coli* *Haemophilus influenzae* *Helicobacter pylori* *Proteus mirabilis* *Salmonella* typhi *Salmonella* paratyphi *Pasteurella multicides*
Gram-positive aerobes: Coagulase negative staphylococcus *Staphylococcus aureus*[£] *Streptococcus pneumoniae* Viridans group streptococcus
Gram-positive anaerobes: *Clostridium* spp.
Gram-negative anaerobes: *Fusobacterium* spp.

Other: *Borealis burgdorferi*
Inherently resistant organisms[7]
Gram-positive aerobes: *Enterococcus faecium*†
Gram-negative aerobes: *Acinetobacter* spp. *Enterobacter* spp. *Klebsiella* spp. *Pseudomonas* spp.
Gram-negative anaerobes: *Bacteroides* spp. (many strains of *Bacteroides fragilis* are resistant).
Others: *Chlamydia* spp. *Mycoplasma* spp. *Legionella* spp.
† Natural intermediate susceptibility in the absence of acquired mechanism of resistance. £ Almost all *S. aureus* are resistant to amoxicillin due to production of penicillinase. In addition, all methicillin-resistant strains are resistant to amoxicillin.

5.2 Pharmacokinetic properties

Absorption:

The absolute bioavailability of amoxicillin depends on the dose and ranges between 75 and 90%. In the dose range between 500 mg and 750 mg the bioavailability (parameters: AUC and/or recovery in urine) is linearly proportional to the dose. At higher doses the extent of absorption decreases. The absorption is not affected by concomitant food intake. Oral administration of a single dose of 500 mg amoxicillin results in plasma concentrations of 6 - 11 mg/l. After administration of a single dose of 3 g amoxicillin, the plasma concentrations reach 27 mg/l. Peak plasma concentrations are present about 1-2 hours after administration.

Distribution:

Protein binding for amoxicillin is approximately 17%. Therapeutic drug levels are rapidly achieved in serum, lung tissue, bronchial secretions, middle ear fluid, bile and urine. In healthy meninges amoxicillin diffuses badly in the liquor cerebrospinalis. In inflamed meninges the concentration can reach approximately 20 % of the concentration in blood. Amoxicillin crosses the placenta and a small percentage is excreted into the breast milk.

Biotransformation and elimination:

The main route of excretion of amoxicillin is the kidney. About 60-80% of an oral dose of amoxicillin are excreted in unchanged active form in the urine within 6 hours of administration, and a small fraction is excreted in the bile. Approximately 7 - 25% of the administered dose is metabolised to inactive penicilloic acid. The serum half-life in patients with normal renal function is approximately 1 – 1.5 hour. In patients with end-stage renal failure the half-life ranges between 5 to 20 hours. The substance is haemodialysable.

5.3 Preclinical data safety

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6. Pharmaceutical particulars

6.1 List of excipients

- Sodium Lauryl Sulphate
- Croscarmellose Sodium
- Aerosil 200 Pharma
- Purified Talc
- Magnesium Stearate
- Empty Gelatin Capsules size ‘0’ maroon/ Yellow

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store in a dry place below 30°C.
Protect form light.
Keep all medicines out of reach of children.

6.5 Nature and contents of container

Maroon/ Yellow Hard Gelatin Capsule size ‘0’ imprinted company logo and Kemoxyl 500mg, containing White granular powder, packed in blisters of 10 x 10’s in a unit box and 500’s in HDPE container with literature insert.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder and Manufacturing Site Addresses Marketing Authorization Holder:

Company Name: LABORATORY & ALLIED LTD
Address: Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road,
P.O. Box 42875 GPO 00100, Nairobi,
Country : Kenya
Telephone : +254 20 8040306
Telefax : +254 20 8040309
E-Mail : info@laballied.com.

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Telefax: +254 20 8040309
E-Mail: info@laballied.com

9. Date of first Registration/ Renewal of the Registration:
Marketing Authorization Number: H2008/18298/528.
First registration date: 7th/04/2009.
Renewal: Retained annually.
10. Date of revision of the text:
February 2024.