LABCLAV 625MG TABLETS
(AMOXICILLIN TRIHYDRATE BP AND CLAVULANATE POTASSIUM BP)

MODULE 1	:	ADMINISTRATIVE INFORMATION AND PRODUCT INFORMATION

1.6 product information
1.6.1 Prescribing information (Summary of product characteristics)
1. Name of the medicinal product
Labclav 625mg Tablets

2. Qualitative and quantitative composition
Each Film Coated Tablet Contains: Amoxicillin 500mg (As Amoxicillin Trihydrate BP), Clavulanic Acid 125 mg (As Potassium Clavulanate BP) and Excipients q.s

3. Pharmaceutical form
Film Coated Tablet.
White oval shaped film coated tablets embossed '625' on one side 'L' on reverse. Packed in 1 x 10's, 2 x 7's, 2 x 10's & 10 x 10's in a unit box with literature insert.

4. Clinical particulars
4.1 Therapeutic indications.
Labclav is an antibiotic agent with a notably broad spectrum of activity against the commonly occurring bacterial pathogens in hospital& general practice.
The beta-lactamase inhibitory action of clavulanate extends the spectrum of amoxicillin to embrace a wider range of organisms, including many resistant to other beta lactam antibiotics.
Labclav is indicated for short-term treatment of bacterial infections at the following sites:
1 Upper respiratory tract Infections {including ENT) e.g. Tonsillitis, sinusitis, otitis media.
2. Lower respiratory tract infections e.g acute and chronic bronchitis, lobar and bronchopneumonia.
3 Genito-urinary tract infections e.g cystitis, urethritis, pyelonephritis.
4 Skin and soft tissue infections e.g boils, abscesses, cellulitis, wound infections.
5. Bone and joints Infections e.g asteomyelitis
6. Dental infections e.g. dentoalveolar abscess.
7. Other infections e.g septic abortion, puerperal sepsis, intra-abdominal sepsis**.**
Labclav® is bactericidal to a wide range of organisms including beta lactamase producing strains resistant to ampicillin and amoxicillin.
Gram-positive
Aerobes: *Enterococcus faecalis, streptococcus pneumonia, Streptococcus pyogenes, streptococcus viridans. Staphylococcus aureus,* Coalgulase negative Streptococci (including *Streptococcus epidermidis*) Corynebacterium species, *Bacillus anthracis, Usteria monocytogenes.*
Anaerobes: clostridium species, Peptococcus species, Peptostreptococcus.
Gram-negative
Aerobes: *Haemophilus influenza, Escherichia coli, proteus mirabilis, proteus vulgaris,* Klebsiella species, *Moraxella catarrhalis,* salmonella species, shigella species, *Bordetella pertussis,* Brucella species, *Neisseria gonorrhoeae, Neisseria meningitidis, vibrio cholera, pasteurella multocida.*
Aerobes: Bacteroides spp including *B. fragilis.*

4.2 Posology and method of administration
Three times a day dosing regimen.
Usual dosage for the treatment of infection.
Adults and children over 12 years:
Mild-moderate infections: One Labclav 375mg tablet three times a day.
Severe infections: Two Labclav 375mg tablets or one Labclav 625mg tablet three times a day.
Labclav 375mg tablets are not recommended in children of 12 years and under, in such cases Labclav suspension is recommended.
Dosage in dental infection (e.g. dentoalveolar abscess): Adults and children over 12 years: One Labclav 375mg tablet three times a day for five days.
Dosage in renal impairment:

In patients with mild impairment (creatinine clearance>30ml/min) no change in dosage is recommended. IN patients with moderate impairment (creatinine clearance 10-30ml/min) one 375mg tablet 12 hourly is recommended. In patients with severe impairment (creatinine clearance <10ml/min) not more than one 375mg tablet 12 hourly is recommended.
Twice a day regimen
Usual dosages for the treatment of infection.
Adults and children over 12years.
Mild-moderate infections: One Labclav 625mg tablet twice a day.
Severe infections: One Labclav 1g tablet twice a day.
Dosage in dental infections (e.g. dentoalveolar abscess): Adults and children over 12 years. One Labclav 625mg tablets two times a day for five days.
Labclav 625mg and 1g tablets are not recommended in children of 12 years and under, in such cases Labclav suspension is recommended.
Dosage in renal impairment
The Labclav 1g tablet should only be used in patients with a glomerular filtration rate of >30ml/min.
In patients with mild impairment (creatinine clearance >30ml/min) no change in dosage (I.e. either one 625mg tablets bid or one 1g tablet) is recommended.
In patients with moderate impairment (creatinine clearance 10-30ml/min) one 625mg tablet is recommended. The 1g tablet should not be administered. In patients with severe impairment (creatinine clearance 10ml/min) not more than one 625mg tablet every 24 hours is recommended.
Dosage in hepatic impairment.
Dose with caution; monitor hepatic function at regular intervals.
Oral administration
Tablets should be swallowed whole without chewing, if required, tablets may be broken in half and swallowed without chewing. To minimize potential gastrointestinal intolerance, administer at the start of a meal. The absorption of co-amoxiclav is optimized when taken at the start of a meal.
Treatment should not be extended beyond 14 days without review.

4.3 Contraindications
Penicillin hypersensitivity; attention should be paid to possible cross- sensitivity with other beta-lactam antibiotics e.g. Cephalosporins. A previous history of co-amoxiclav or penicillin-associated jaundice/ hepatic dysfunction.

4.4 Special warnings and precautions for use.
Change in liver function tests have been observed in some patients receiving co-amoxiclav. The clinical significance of these changes is uncertain but co-amoxiclav should be used with caution in patients with evidence of hepatic dysfunction. Cholestatic jaundice, which may be severe, but is usually reversible, has been reported rarely. Signs and symptoms may not become apparent for up to six weeks after treatment has ceased. In patients with moderate or severe renal impairment co-amoxiclav dosage should be adjusted as recommended in the dosage and administration section. Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity. Erythematorus rashes have been associated with glandular fever in patients receiving amoxicillin. Co-amoxiclav should be avoided if glandular fever is suspected. Prolonged use may also occasionally result in overgrowth of non-susceptible organisms.

4.5 Interaction with other medicinal products and other forms of interaction
Prolongation of bleeding time and prothrombin time have been reported in some patients receiving co-amoxiclav. Co-amoxiclav should be used with care in patients on anti-coagulation therapy. In common with other broad spectrum antibiotics. Co-amoxiclav may reduce the efficacy or oral contraceptives and patients should be warned accordingly. Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use with co-amoxiclav may result in increased and

prolonged blood levels of amoxicillin but not clavulanic acid. Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions. There are no data on the concomitant use of co-amoxiclav and allopurinol.

4.6 Pregnancy and lactation

There is limited experience of the use of co-amoxiclav in human pregnancy. As with all medicines, use should be avoided in pregnancy, especially during the first trimester, unless considered essential by the physician. Co-amoxiclav may be administered during the period of lactation. With the exception of the risk of sensitization associated with the excretion of trace quantities on breast milk, there are no detrimental effects for the infant.

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

Side effects with amoxicillin, are uncommon and mainly of a mild and transitory nature.

Gastrointestinal reactions.

Effects include diarrhoea, indigestion, nausea and vomiting, candidiasis, antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis) have been reported rarely, nausea, although uncommon, is more often associated with higher oral dosages. If gastrointestinal side effects occur with oral therapy, they may be reduced by taking Labclav at the start of meals.

Hepatic effects

A moderate rise in AST and/or ALT has been noted in patients with semi-synthetic penicillins but the significance of these findings is unknown. Hepatitis and cholestatic jaundice have been reported rarely with co-amoxiclav. They may however be severe and continue for several months. They are reported as occurring predominantly in adult or elderly patients and slightly more frequently in males. Signs and symptoms may occur during treatment but are more frequently reported after cessation of therapy with a delay of up to six weeks. The hepatic events are usually reversible. However, in extremely rare circumstances, deaths have been reported. Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment.

Hypersensitivity reactions

Urticarial and erythematous rashes sometimes occur rarely erythema multiforme. Stevens-Johnson syndrome, toxic epidermal necrolysis and exfoliative dermatitis have been reported. Treatment should be discontinued if one of these types of rash appears. In common with other beta-lactam antibiotics ngioedema, oedema, anaphylaxis, serum sickness-like syndrome and hypersensitivity vasculitis have been reported. Interstitial nephritis can occur rarely.

Hematological effects.

As with other beta-lactams, reversible leucopenia (including neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia have been reported rarely.

CNS Effects.

CNS effects have been seen very rarely. These include reversible hyperactivity, dizziness, headache and convulsions. Convulsions may occur with impaired renal function or in those receiving high doses.

4.9 Overdose

Cases of overdosage with Labclav are unlikely to occur if encountered gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. They may be treated symptomatically with attention to the water electrolyte balance. Co-amoxiclav may be removed from the circulation by haemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Combinations of penicillins, incl. beta-lactamase inhibitors
ATC code: J01CR02
Amoxicillin is a semisynthetic penicillin (bet-lactam antibiotic) that inhibit 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 bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of cell wall which is 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. Clavulanic Acid is a beta-lactam structurally related penicillins. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin. Clavulanic acid alone does not exert a clinically useful antibacterial effect.

5.2 Pharmacokinetic properties

Amoxicillin and clavulanic acid, are fully dissociated in aqueous solution at physiological pH. Both components are rapidly and well absorbed by the oral route of administration. Absorption of amoxicillin/clavulanic acid is optimised when taken at the start of a meal. Following oral administration, amoxicillin and clavulanic acid are approximately 70% bioavailable. The plasma profiles of both components are similar and the time to peak plasma concentration (Tmax) in each case is approximately one hour. About 25% of total plasma clavulanic acid and 18% of total plasma amoxicillin and around 0.2 l/kg for clavulanic acid. Both amoxicillin and clavulanic acid have been shown to cross the placenta barrier. The major route of elimination for amoxicillin is via kidney, whereas for clavulanic acid it is by renal and non-renal mechanisms

5.3 Preclinical data safety

Nonclinical data reveal no special hazard for humans based on studies of safety pharmacology, genotoxicity and toxicity to reproduction. Repeat dose toxicity studies performed in dogs with amoxicillin/clavulanic acid demonstrate gastric irritancy and vomiting, and discolored tongue.
Carcinogenicity studies have not been conducted with Amoxicillin & Clavulanate Potassium tablets USP or its components.

6. Pharmaceutical particulars

6.1 List of excipients

Microcrystalline Cellulose pH 112 (Dried)
Aerosil 200 Pharma
Magnesium Stearate
Croscarmellose Sodium (Dried)
Tab-coat White (MB4S)
Isopropyl Alcohol 99%
Methylene Dichloride

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

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

6.5 Nature and contents of container
White oval shaped film coated tablets embossed '625' on one side 'L' on reverse. Packed in 1 x 10's, 2 x 7's, 2 x 10's & 10 x 10's in a unit box with literature insert.

6.6 Special precautions for disposal and other handling
No special 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.

Manufacturing Site Address:
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

8. Marketing Authorization Number:
Kenya: H2016/CTD4224/688

9. Date of first Registration/ Renewal of the Registration:
Registration -19/12/2016

10. Date of revision of the text:
January 2021