DESCRIPTION:
BETAMOX CAPSULE 250 MG : A size 2, grey / yellow capsule with marking 'DUO 861'
BETAMOX CAPSULE 500 MG : A size 0, grey / yellow capsule with marking 'DUO 861'

COMPOSITION:
BETAMOX CAPSULE 250 MG : Each capsule contains Amoxycillin Trihydrate equivalent to Amoxycillin 250 mg.
BETAMOX CAPSULE 500 MG : Each capsule contains Amoxycillin Trihydrate equivalent to Amoxycillin 500 mg.
Gelatin for capsule: Halal certified bovine source.

PHARMACODYNAMICS: Amoxycillin differs *in vitro* from benzylpenicillin in the Gram-negative spectrum. Amoxycillin has the same Gram-positive and Gram-negative spectrum as ampicillin.
In vitro most strains of *Haemophilus influenzae, Neisseria gonorrhoea, Neisseria meningitidis, Proteus mirabilis, Salmonellae, alpha- and beta-haemolytic streptococci, Diplococcus pneumoniae,* non-penicillinase producing *Staphylococci and Streptococcus faecalis*, are sensitive to amoxycillin at serum concentrations which may be expected following the recommended doses. However, some of the organisms were sensitive to amoxycillin only at concentrations achieved in the urine (see ***Indications***).
Escherichia coli isolates are becoming increasingly resistant to amoxycillin *in vitro* due to the presence of penicillinase-producing strains.
Strains of gonococci which are relatively resistant to benzylpenicillin may be sensitive to amoxycillin.
Amoxycillin is not effect against penicillinase-producing bacteria, particularly resistant staphylococci, which now have a high prevalence.
All strains of Pseudomonas, Klebsiella, Enterobacter, indole-positive Proteus, *Serratia marcescens*, Citrobacter, penicillinase-producing *N.gonorrhoea* and penicillinase-producing *H.influenzae* are also resistant.
Like benzylpenicillin, amoxycillin is bactericidal against sensitive organisms during the stage of active multiplication. It is believed to act through the inhibition of biosynthesis of cell wall mucopeptide.

PHARMACOKINETICS: Amoxycillin is stable in the presence of gastric acid and is rapidly and well absorbed after oral administration, even in the presence of food. Amoxycillin diffuses rapidly into most body tissues and fluids, with the exception of brain and spinal fluid except when meninges are inflamed.
Amoxycillin has been shown to diffuse into sputum and saliva and is excreted mainly via the urine where it exists in a high concentration.
The amount to be found in the bile is variable depending on normal biliary secretory function.
The half-life of amoxycillin is 61.3 minutes with normal renal function and in the absence of renal function 16-20 hours.
Amoxycillin is excreted in the urine both unchanged and as penicilloic acid. About 75% of a 1 g dose is excreted in the urine in 6 hours in the presence of normal renal function (60% is biologically active and 15% is penicilloic acid). However about 32% of a 3 g dose is excreted via the urine as the biologically active component in 8 hours (by which time most of the urinary excretion is complete). This proportional difference in the amount excreted from the different doses reflects a lack of linearity between doses and extent of absorption with a levelling off at higher doses of oral amoxycillin.
Excretion of amoxycillin can be delayed by concurrent administration of probenecid thus prolonging its therapeutic effect.
Amoxycillin is not highly protein-bound, being only 17% protein-bound in serum as measured by ultrafiltration or equilibrium dialysis.
Orally administered doses of 250 mg and 500 mg amoxycillin result in average peak serum levels one to two hours after administration of 5.0 mcg / mL and 6.6 – 10.8 mcg / mL respectively. Detectable serum levels of amoxycillin are present 8 hours after ingestion of a single dose.

INDICATIONS: Amoxycillin is indicated for the treatment of the following infections due to susceptible strains of sensitive organisms.
Note: Therapy should be guided by bacteriological studies, including sensitivity tests, and by clinical response. However, in emergency cases where the causative organism has not been identified, therapy with amoxycillin may be useful. Clinical judgement will decide whether combination with another antibiotic would provide a sufficiently broad spectrum of activity pending sensitivity test results.
Skin and skin structure: Staphylococcus, non-penicillinase producing; Streptococcus; *E.coli* (see ***Microbiology***).
Respiratory (Acute and Chronic): H. influenzae, Streptococcus; S. pneumoniae; staphylococcus, non-penicillinase-producing; *E. coli* (see **Microbiology**).
Genitourinary Tract (complicated and uncomplicated, Acute and chronic): *E. coli* (see ***Microbiology***), *P. mirabilis and S. faecalis*.
Gonorrhoea: *N. gonorrhoea* (non-penicillinase producing).
Prophylaxis of endocarditis: Amoxycillin may be used for the prophylaxis of bacterial endocarditis in individuals at particular risk, such as those with a prosthetic heart valve or those who have previously had endocarditis.

RECOMMENDED DOSAGE:
Upper respiratory tract infections; Genitourinary tract infections; Skin and soft tissue infections.
Adults – 250 mg 8 hourly.
Children – 20 mg / kg / day in equally divided doses 8 hourly. In severe infection or those caused by less susceptible organisms 500 mg 8 hourly for adults and 40 mg / kg / day in equally divided doses 8 hourly for children may be needed.
Lower respiratory tract infections
Adults – 500 mg 8 hourly.
Children (under 20 kg) – 40 mg / kg / day in equally divided doses 8 hourly.
Urethritis, gonococcal
Adults – 3 g as single dose. Cases of gonorrhoea with a suspected lesion of syphilis should have darkfield examinations before receiving amoxycillin and monthly serological tests for a minimum of four months.
Acute, uncompliated lower urinary tract infections in non-pregnant adult female.
Adults – 3 g as single dose.

Note: Experience in neonates is too limited to make any recommendations regarding dosage or the appropriateness of the oral route.
The children's dosage is intended for individuals whose weight will not cause dosage to be calculated greater than that recommended for adults. Children weighing more than 20 kg should be dosed according to the adult recommendations.
In renal impairment the excretion of the antibiotic will be delayed, and depending on the degree of impairment, it may be necessary to reduce the total daily dosage.

In patients receiving peritoneal dialysis, the maximum recommended dose is 500 mg / day. Amoxycillin may be removed from the circulation by haemodialysis.

It should be recognized that in the treatment of chronic urinary tract infections, frequent bacteriological and clinical appraisals are necessary. Smaller doses than those recommended above should not be used. In stubborn infections, therapy may be required for several weeks. It may be necessary to continue clinical and / or bacteriological follow-up for several months after cessation of therapy. Treatment should be continued for a minimum of 48 to 72 hours beyond the time that the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. It is recommended that there be at least ten days treatment for any infection caused by haemolytic streptococci to prevent the occurrence of acute rheumatic fever or glomerulonephritis.

ROUTE OF ADMINISTRATION: Oral

CONTRAINDICATIONS: Amoxycillin is a penicillin and should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (eg. penicillins, cephalosporins).

WARNINGS AND PRECAUTIONS: 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 therapy. Before commencing therapy with any penicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, appropriate therapy should be instituted and Amoxicillin therapy discontinued.

Serious anaphylactic reactions require immediate treatment with adrenaline. Oxygen, intravenous steroids and an airway management, including intubation, should also be administered as indicated.

Antibiotic associated pseudomembranous colitis has been reported with many antibiotics including amoxycillin. A toxin produced with Clostridium difficile appears to be the primary cause. The severity of the colitis may range from mild to life threatening. It is important to consider this diagnosis in patients who develop diarrhoea or colitis in association with antibiotic use (this may occur up to several weeks after cessation of antibiotic therapy). Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibiotic agent effective against Clostridium difficile should be considered. Fluids, electrolytes and protein replacement should be provided when indicated. Drugs which delay peristalsis, eg. opiates and diphenoxylate with atropine (Lomotil) may prolong and / or worsen the condition and should not be used.

As with any potent drug, periodic assessment of renal, hepatic and haematopoietic function should be made during prolonged therapy. The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving Aerobacter, Pseudomonas or Candida), the drug should be discontinued and / or appropriate therapy instituted.

Amoxycillin, an aminopenicillin, is not the treatment of choice in patients presenting with sore throat or pharyngitis because of the possibility that the underlying cause is infections mononucleosis, in the presence of which there is a high incidence of rash if amoxycillin is used.
Amoxycillin should be given with caution to patients with lymphatic leukaemia since they are especially susceptible to ampicillin-induced skin rashes.
Following single dose therapy of acute lower urinary tract infections, the urine should be cultured. A positive culture may be evidence of a complicated or upper urinary tract infection and call for longer or larger course of therapy.

Adequate fluid intake and urinary output must be maintained in patients receiving high doses of amoxycillin. Dosage should be adjusted in patients with renal impairment (see ***Dosage and Administration***).
Amoxycillin paediatric drops and sugar free syrups contain sodium benzoate.

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reaction) have been reported in patients receiving therapy with beta-lactams. Before initiating therapy with BETAMOX, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems or other beta-lactam agents. If an allergic reaction occurs, BETAMOX must be discontinued immediately and appropriate alternative therapy instituted.

ADVERSE EFFECTS/UNDESIRABLE EFFECTS:
Gastrointestinal: nausea, vomiting, diarrhoea, intestinal candidiasis and antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis) have been reported rarely (see ***Warnings***).

Hypersensitivity reactions: Erythematous maculopapular rash, pruritus and urticaria have been reported occasionally. Rarely, skin reactions such as erythema multiforme and Stevens- Johnson syndrome, toxic epidermal necrolysis and bullous and exfoliative dermatitis have been reported. As with other antibiotics, severe allergic reactions including angioneurotic oedema, anaphylaxis, serum sickness, hypersensitivity vasculitis and interstitial nephritis have been reported rarely.

Whenever such reactions occur, amoxycillin should be discontinued (Note: Urticaria, other skin rashes and serum sickness-like reactions may be controlled with antihistamines, and if necessary, systemic corticosteroids). Anaphylaxis is the most serious reaction experienced (see ***Warnings***).
Liver: A moderate rise in AST and/or ALT has occasionally been noted, but the significance of this finding is unknown. As with other beta-lactam antibiotics, hepatitis and cholestatic jaundice have been reported rarely.

Haemic and Lympathic systems: Reactions such as anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia and leucopenia (including neutropenia or agranulocytosis) have been reported during therapy with other penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. Prolongation of bleeding time and prothrombin time have also been reported rarely.
CNS effects: CNS effects have been seen rarely. They include hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Skin and subcutaneous tissue disorders: Frequency 'very rare': Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

INTERACTION WITH OTHER MEDICAMENTS: Drug / Laboratory Test Interactions: Oral administration of amoxycillin will result in high urine concentrations of amoxycillin. Since high urine concentrations of amoxycillin may result in false positive reactions when testing for the presence of glucose in urine using Clinitest, Benedict's Solution or Fehling's Solution, it is recommended that glucose tests based on enzymatic glucose oxidase reactions (such as Clinistix, or Testape) be used.

PREGNANCY AND LACTATION:
Use in pregnancy: Animal studies with amoxycillin 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.
Amoxicillin may be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.
Use in lactation: Ampicillin class antibiotics are excreted in the milk; therefore, caution should be exercised when amoxycillin is administered to a nursing woman.

SYMPTOMS AND TREATMENT OF OVERDOSE: Cases of overdosage with amoxycillin are usually asymptomatic. If encountered, gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and symptoms of water / electrolyte imbalance should be treatment symptomatically. During the administration of high doses of amoxycillin, adequate fluid intake and urinary output must be maintained to minimize the possibility of amoxycillin crystalluria.
Amoxycillin can be removed from the circulation by haemodialysis.

STORAGE CONDITIONS:
Capsule : Store below 30ºC. Protect from light.
Keep out of reach of children. *Jauhkan daripada kanak-kanak.*

SHELF LIFE: Please refer to outer package.

PACKING / PACK SIZES:
Betamox Capsule : Blister pack of 3x10's, 5x10's, 10x10's, 50x10's and 100x10's capsules in a box.

PRODUCT REGISTRATION & MANUFACTURER:
DUOPHARMA (M) SDN BHD
Lot 2599 Jalan Seruling 59, Kawasan 3
Taman Klang Jaya, 41200 Klang,
Selangor Darul Ehsan, MALAYSIA