IDAMAN PHARMA MANUFACTURING

SYNAMOX CAPSULES 250MG

DESCRIPTION

Synamox Capsules 250mg
Clean, uniform, dry, telescope type hard gelatin. Capsules are shiny and not smudged or sticky. Printed "SYNAMOX 250mg" and "Idaman" on the capsules.
Colour: Cap: Opaque Purple
Body: Opaque Grey
Odour: Characteristics of penicillin
Size: No.2
Powder: A white to slightly yellow coarse powder
Each capsule contains AMOXICILLIN TRIHYDRATE equivalent to 250 mg of AMOXICILLIN.

PHARMACODYNAMICS

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 bactericidal 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.

PHARMACOKINETICS

Absorption: Amoxicillin is stable in the presence of gastric acid and is rapidly and well absorbed after oral administration, even in the presence of food. Orally administered doses of 250 mg and 500 mg amoxicillin result in average peak serum levels 1 to 2 hours after administration of 5.0 mcg/mL - 10.8 mcg/L respectively.

Distribution: Amoxicillin diffuses rapidly into most body tissues and fluids, with the exception of brain fluid except when meninges are inflamed. Amoxicillin has been shown to diffuse into sputum and saliva. It is not highly protein-bound which only 17% protein-bound in serum.

Excretion: Amoxicillin is excreted mainly via urine where it exist in a high concentration and is excreted in the urine both unchanged and as penicilloic acid. About 75% of a 1g 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 3g dose is excreted via urine as 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 leveling off a higher dose of oral amoxicillin. Excretion can be delayed by the concurrent administration of probenecid thus prolonging its therapeutics effects.

Half-life: The half-life is 61.3 minutes with normal renal function and in the absence of renal function 16 - 20 hours.

INDICATIONS

Amoxicillin is indicated in the treatment of:

i. Ear, nose and throat infections caused by *Streptococci*, *Pneumococci*, nonpenicillinase-producing *Staphylococci* and Haemophilus influenza.
ii. Genitourinary tract infections caused by *Escherichia coli*, *Proteus mirabilis* and *Streptococcus faecalis*.
iii. Acute uncomplicated anogenital and urethral gonorrhaea in males and females caused by strains of *Neisseria gonorrhoea* sensitive to amoxicillin.
iv. Skin and soft tissues infections caused by *Streptococci*, non penicillinase-producing *Staphylococci*, *E. coli* and *Proteus mirabilis*.

CONTRAINDICATIONS

In patients hypersensitive to active substance or to other beta-lactam antibiotics (e.g., penicillins and cephalosporins) or to any of the excipients.

ADVERSE EFFECTS

Infections and Infestations
Very rare: Mucocutaneous candidiasis.

Blood and Lymphatic system disorders
Very rare: Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia, prolongation of bleeding time and prothrombin time.

Immune system disorders
Very rare: Severe allergic reactions including angioneurotic oedema, anaphylaxis, serum sickness, and hypersensitivity vasculitis.
Not known: Jarisch-Herxheimer reaction.

Nervous system disorders
Very rare: Hyperkinesia, dizziness and convulsions.

Gastrointestinal disorders
Common: Diarrhoea and nausea.
Uncommon: Vomiting.
Very rare: Antibiotic associated colitis including pseudomembranous colitis and haemorrhagic colitis and black hairy tongue.

Hepatobiliary disorders
Very rare: Hepatitis and cholestatic jaundice. Moderate rise in AST and/or ALT.

Skin and subcutaneous tissue disorders
Common: Skin rash.
Uncommon: Urticaria and pruritus.
Very rare: Skin reactions such as erythema multiforme, Steven-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP) and drug reaction with eosinophilia and systemic symptoms (DRESS).

Renal and urinary tract disorders
Very rare: Interstitial nephritis, crystalluria.

WARNINGS AND PRECAUTIONS

Hypersensitivity reactions
Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving therapy with beta-lactams. Before initiating therapy with Synamox Capsules 250mg, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems or other beta-lactam agents. If an allergic reaction occurs, this product must be discontinued immediately and appropriate alternative therapy instituted.

Non-susceptible microorganisms
Amoxicillin is not suitable for the treatment of some types of infection unless the pathogen is already documented and known to be susceptible or there is a very high likelihood that the pathogen would be suitable for treatment with amoxicillin. This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat.

Convulsions
Convulsions may occur in patients with impaired renal function or in those receiving high doses or in patients with predisposing factors (e.g. history of seizures, treated epilepsy or meningeal disorders).

Renal impairment
In patients with renal impairment, the dose should be adjusted according to the degree of impairment.

Skin reactions
The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP). This reaction requires amoxicillin discontinuation and contraindicates any subsequent administration.

Amoxicillin should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Patients with lymphatic leukaemia and possibly with HIV infection are particularly prone to developing erythematous rashes with amoxicillin. Amoxicillin should be discontinued if a skin rash occurs.

Jarisch-Herxheimer reaction
The Jarisch-Herxheimer reaction has been seen following amoxicillin treatment of Lyme disease. It results directly from the bactericidal activity of amoxicillin on the causative bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Overgrowth of non-susceptible microorganisms
Prolonged use may occasionally result in overgrowth of non-susceptible organisms (superinfection).

Antibiotic-associated colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during, or subsequent to, the administration of any antibiotics. Should antibiotic-associated colitis occur, amoxicillin should immediately be discontinued, a physician consulted and an appropriate therapy initiated. Anti-peristaltic medicinal products are contraindicated in this situation.

Prolonged therapy
Periodic assessment of organ system functions; including renal, hepatic and haematopoietic function is advisable during prolonged therapy. Elevated liver enzymes and changes in blood counts have been reported.

Crystalluria
In patients with reduced urine output, crystalluria has been observed very rarely, predominantly with parenteral therapy.

Interference with diagnostic tests
Elevated serum and urinary levels of amoxicillin are likely to affect certain laboratory tests. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods. It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used. The presence of amoxicillin may distort assay results for oestriol in pregnant women.

PREGNANCY AND LACTATION
Pregnancy
Pregnancy Category B.
Limited data on the use of amoxicillin during pregnancy in humans do not indicate an increased risk of congenital malformations. Amoxicillin may be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Lactation
Amoxicillin is excreted into breast milk in small quantities with the possible risk of sensitization. Consequently, diarrhoea and fungus infection of the mucous membranes are possible in the breast-fed infant, so that breast-feeding might have to be discontinued. Amoxicillin should only be used during breastfeeding after benefit/risk assessment by the physician in charge.

EFFECTS ON THE 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 reaction, dizziness, convulsions), which may influence the ability to drive and use machine.

INTERACTION WITH OTHER MEDICAMENT
Be alert for the possible drug interaction and their related problems when amoxicillin is used with the following:
Other antibacterials – Chloramphenicol, sulfonamides, and tetracyclines may interfere with the bactericidal effects of penicillin, including amoxicillin.

Probenecid – Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin.

Allopurinol – Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Oral anticoagulants – Abnormal prolongation of prothrombin time (increased international normalized ratio [INR]) has been reported in patients receiving amoxicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Methotrexate – Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Oral typhoid vaccine – The oral typhoid vaccine is inactivated by antibacterial.

DOSAGE AND ADMINISTRATION
Usual Adult Dose:
Oral, the equivalent of anhydrous amoxicillin - 250 mg to 500 mg every 8 hours.

Note: Gonorrhoea; Oral, the equivalent to anhydrous amoxicillin - 3 grams and 1 gram of Probenecid simultaneously as a single dose.

Usual Adult Prescribing Limits:
The equivalent of anhydrous amoxicillin - up to 4.5 grams daily.

Route of administration: For oral administration only.

OVERDOSE AND TREATMENT
Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and should be treated symptomatically with attention to the water/electrolyte balance. Crystalluria, in some cases leading to renal failure, has also been reported after amoxicillin overdosage in adult and pediatric patients.In case of overdosage, adequate fluid intake and diuresis should be maintained to reduce the risk of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained.

Renal impairment appears to be reversible with cessation of drug administration. High blood levels may occur more readily in patients with impaired renal function because of decreased renal clearance of amoxicillin. Amoxicillin maybe removed from circulation by haemodialysis.

Convulsions may occur in patients with impaired renal function or in those receiving high doses.

PRESENTATION
Synamox Capsules 250 mg
(Malaysia Reg. No.: MAL19890331AZ)
Pack in Blister of 10 Capsules in carton box (50 x 10's)

STORAGE CONDITIONS
Keep container tightly closed in a dry place, below 30°C; Protect from light.

USER INSTRUCTIONS
i. Take this medicine at regular intervals (on hourly basis) and the prescribed course should be completed even when you feel better.
ii. Do not miss the doses prescribed.
iii. This medicine may be taken on full or empty stomach.
iv. Keep this medicine out of reach of children.
v. Check with your doctor if no improvement within a few days.

SHELF LIFE
3 years from the date of manufacture.
For further information, please consult your doctor or your pharmacist.

Date of Revision: 13th August 2020

PRODUCT REGISTRATION HOLDER / MANUFACTURER:
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