Bosch

For Medical Professional only

Supramox

Injection 0.25G/0.5G/1G

(Amoxycillin B.P.)

Broad Spectrum Antibiotic

(Product Specs.: B.P.)

سپراموکس

انجکشن

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Supramox(amoxicillin) and other antibacterial drugs, Supramox should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION:
Formulations of Supramox contain amoxicillin, a semisynthetic antibiotic, an analog of ampicillin, with a broad spectrum of bactericidal activity against many gram-positive and gram-negative microorganisms. Chemically, it is(2S,5R,6R)-6-[(R)-(-)-2-amino-2-(phydroxyphenyl)acetamido]-3,3-dimethyl-7-oxo-4-thia-1 azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate. The amoxicillin molecular formula is $C_{16}H_{19}N_3O_5S \cdot 3H_2O$, and the molecular weight is 419.45.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES
Pharmacotherapeutic group: penicillins with extended spectrum; ATC code: J01CA04

Mechansim of action:
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.

MICROBIOLOGY:
Amoxicillin is similar to ampicillin in its bactericidal action against susceptible organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptide. Amoxicillin has been shown to be active against most strains of the following microorganisms

Aerobic Gram-positive micro-organism: Enterococcus faecalis Staphylococcus, Streptococcus pneumonia Streptococcus , Staphylococci which are susceptible to amoxicillin but resistant to methicillin/oxacillin should be considered as resistant to amoxicillin.

Aerobic Gram-negative micro-organisms: Escherichia coli, Haemophilus influenza , Neisseria gonorrhea ,Proteus mirabilis

Gram-positive Aerobes : Enterococcus, Staphylococcus, Streptococcus (except S. pneumoniae)

Gram- negative Aerobes: Enterobacteriaceae, H. influenza

PHARMACOKINETIC PROPERTIES:
Absorption
Amoxicillin fully dissociates in aqueous solution at physiological pH. Amoxicillin is stable in the acid gastric secretion and is rapidly absorbed from the gastrointestinal tract after oral administration. Following oral administration, amoxicillin is approximately 70% bioavailable. The time to peak plasma concentration (Tmax) is approximately one hour.The absorption is not influenced by simultaneous food intake. Haemodialysis can be used for elimination of amoxicillin.

Distribution
About 18% of total plasma amoxicillin is bound to protein and the apparent volume of distribution is around 0.3 to 0.41/kg. Following intravenous administration, amoxicillin has been found in gall bladder, abdominal tissue, skin, fat, muscle tissue, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid. Amoxicillin has been shown to cross the placental barrier.

Biotransformation
Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25% of the initial dose.

Excretion:
The major route of elimination for amoxicillin is via the kidney.
Amoxicillin has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/hour in healthy subjects. Approximately 60 to 70% of an orally administered dose is excreted unchanged in the urine during the first 6 hours after administration of a single 250mg or 500mg dose of amoxicillin. Various studies have found the urinary excretion to be 50-85% for amoxicillin over a 24 hour period.Concomitant use of probenecid delays amoxicillin excretion

Age
The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Renal impairment
The total serum clearance of amoxicillin decreases proportionately with decreasing renal function

Hepatic impairment
Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

CLINICAL PARTICULARS:
Therapeutic indications
Amoxicillin is indicated for the treatment of the following infections in adults and children.
- Severe infections of the ear, nose and throat (such as mastoiditis, peritonsillar infections, epiglottitis, and sinusitis when accompanied by severe systemic signs and symptoms)
- Acute exacerbations of chronic bronchitis
- Community acquired pneumonia
- Acute cystitis
- Acute pyelonephritis
- Severe dental abscess with spreading cellulitis
- Prosthetic joint infections
- Lyme disease
- Bacterial meningitis

Amoxicillin is also indicated for the treatment and prophylaxis of endocarditis.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

DOSAGE AND ADMINISTRATION
Adults and children ≥ 40 kg

INDICATION	DOSE
Severe infections of the ear, nose and throat (such as mastoiditis peritonsillar infections, epiglottis and sinusitis when accompanied by severe systemic signs and symptoms	750 mg to 2 g every 8 hours, or 2 g every 12 hours, maximum of 12 g/day
Acute exacerbations of chronic bronchitis	
Community acquired pneumonia	
Acute cystitis	
Acute pyelonephritis	
Severe dental abscess with spreading cellulitis	
Prosthetic joint infections	750 mg to 2g every 8 hours, or 2g every 12 hours, maximum of 12 g/day
Prophylaxis of endocarditis	2 g single dose 30 to 60 minutes before procedure.
Treatment of endocarditis	1 g to 2 g every 4 to 6 hours, maximum of 12 g/day
Bacterial meningitis	1 g to 2g every 4 to 6 hours, maximum of 12 g/day
Lyme disease	Late stage (systemic involvement):2g every 8 hours
Bacteraemia that occurs in association with, or is suspected to be associated with, any of the infection	1 g to 2 g every 4, 6 or 8 hours, maximum of 12 g/day

Intramuscular:
Maximum daily dosage: 4 g/day.
Maximum single dose: 1 g.
Children < 40 kg

Infants and toddlers >3 months and children < 40 kg Indication	DOSE
Severe infections of the ear, nose and throat (such as mastoiditis peritonsillar infections, epiglottis and sinusitis when accompanied by severe systemic signs and symptoms	20 to 200 mg/kg/day given in 2 to 4 equally divided doses of up to 25 mg/kg or infusions of up to 50 mg/kg
Community acquired pneumonia	
Acute cystitis	
Acute pyelonephritis	
Severe dental abscess with spreading cellulitis	
Prophylaxis of endocarditis	50 mg/kg single dose 30 to 60 minutes before procedure
Treatment of endocarditis	200 mg/kg/day in 3 to 4 equally divided does of up to 25 mg/kg or infusions of up to 50 mg/kg
Bacterial meningitis	100 to 200 mg/kg/day in 3 to 4 equally divided doses of up to 25 mg/kg or infusions of up to 50 mg/kg
Lyme disease	Early stage: 25 to 50 mg/kg/day in three divided doses for 10 days (range 10 to 21 days) Late stage (systemic involvement): 50 mg/kg/day in three divided doses
Bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections	50 to 150 mg/kg/day given in 3 equally divided doses of up to 25 mg/kg or infusions of up to 50 mg/kg

Neonates ≥ 4kg and infants up to 3 months	DOSE
Most infections	Usual daily dose of 20 to 150 mg/kg/day given in 3 equally divided doses of up to 25 mg/kg or infusions of up to 50 mg/kg
Treatment of endocarditis	150 mg/kg/day given in 3 equally divided doses of up to 25 mg/kg or infusions of up to 50 mg/kg
Bacterial meningitis	150 mg/kg/day given in three divided doses
Lyme disease	Early stage: 25 to 50 mg/kg/day in three divided doses for 10 days (range 10 to 21 days) Late stage (systemic involvement): 50 mg/kg/day in three divided doses
Bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections.	Usual daily dose of 50 to 150 mg/kg/day given in 3 equally divided doses of up to 25 mg/kg or infusions of up to 50 mg/kg
Premature Neonates < 4kg Indication	**DOSE**
Most infections	Usual daily dose of 20 to 100 mg/kg/day given in 2 equally divided doses of up to 25 mg/kg or infusions of up to 50 mg/kg
Treatment of endocarditis	100 mg/kg/day given in two divided doses
Bacterial meningitis	100 mg/kg/day given in two divided doses
Lyme disease	Early stage: 25 to 50 mg/kg/day in two divided doses for 10 days (range 10 to 21 days)
Bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections.	Late stage (systemic involvement): 50 mg/kg/day in two divided doses Usual daily dose of 50 to 100 mg/kg/day given in 2 equally divided doses of up to 25 mg/kg or infusions of up to 50 mg/kg

Intramuscular:
Maximum daily dosage 120 mg/kg/day as 2 to 6 equally divided doses.

Elderly
No adjustment needed for adults.
Renal impairment

	Adults and children ≥ 40 kg	
GFR (ml/min)	Intravenous	Intramuscular
greater than 30	No adjustment	No adjustment
10 to 30	1g stat, then 500 mg to 1 g twice day	500 mg every 12 hours
less than 10	1 g stat, then 500 mg/day	500 mg/day given as a single dose
	Children < 40 kg	
GFR (ml/min)	Intravenous	Intramuscular
greater than 30	No adjustment	No adjustment
10 to 30	25 mg/kg twice daily	15 mg/kg every 12 hours
less than 10	25 mg/kg/day given as a single dose	15 mg/kg/day given as a single dose

In patients receiving haemodialysis and peritoneal dialysis
Amoxicillin may be removed from the circulation by haemodialysis.

	Haemodialysis	
GFR (ml/min)	Intravenous	Intramuscular
Adults and children ≥ 40 kg	1 g at the end of dialysis, then 500 mg every 24 hours	500 mg during dialysis, 500 mg at the end, then 500 mg every 24 hours
Children < 40 kg	25 mg/kg stat and 12.5 mg/kg at the end of the dialysis, then 25 mg/kg/day	15 mg/kg during and at the end of dialysis, then 15 mg/kg every 24 hours
	Peritoneal dialysis	
GFR (ml/min)	Intravenous	Intramuscular
Adults and children ≥ 40 kg	1 g stat, then 500 mg/day	500 mg/day given as a single dose
Children < 40 kg	25 mg/kg/day given as a single dose	15 mg/kg/day given as a single dose

Method of administration
The standard recommended route of administration is by intravenous injection or intravenous infusion. Intramuscular administration should only be considered when the intravenous route is not possible or less appropriate for the patient.

Intravenous Injection:
Dissolve 250mg in 5mL Water for Injections
Dissolve 500mg in 10mL Water for Injections
Dissolve 1g in 20mL Water for Injections
Amoxicillin Sodium for Injection BP, when diluted may be injected slowly into a vein or infusion line over a period of three to four minutes.

Intravenous Infusion:
Prepare as above and add to an iv solution in a minibag or in-line burette. Administer over 30 to 60 minutes. Alternatively the appropriate volume of iv fluid may be transferred from the infusion bag into the vial, using a suitable reconstitution device, and drawn back into the bag after dissolution.

Intramuscular Injection:
Add 1.5mL Water for Injections Ph Eur to 250mg and shake vigorously
Add 2.5mL Water for Injections Ph Eur to 500mg and shake vigorously
The maximum single dose is 1 g in adults and children ≥ 40 kg.
Do not inject more than 60 mg/kg at one time in children < 40 kg.

CONTRAINDICATION:
Hypersensitivity to the active substance, to any of the penicillins or to any of the excipients.

History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam).

WARNINGS AND PRECAUTIONS:
Hypersensitivity reactions
Before initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents.

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis . 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.

These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals. If an allergic reaction occurs, amoxicillin therapy must be discontinued and appropriate alternative therapy instituted.Amoxicillin should preferably not be given to patients with undiagnosed pharyngitis or patients with lymphatic leukaemia or possibly HIV infection who may also be at increased risk of developing skin rashes with amoxicillin.

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.

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. 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.

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 diarrhea 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 contra-indicated in this situation.

Anticoagulants
Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

DRUG INTERACTIONS:
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.

Tetracyclines
Tetracyclines and other bacteriostatic drugs may interfere with the bactericidal effects of amoxicillin.

Oral anticoagulants
Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin.

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

USE IN PREGNANCY AND LACTATION:
Pregnancy:
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 sensitisation. 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 breast-feeding after benefit/risk assessment by the physician in charge.

ADVERSE EFFECTS:
The most commonly reported adverse drug reactions (ADRs) are diarrhea, nausea and skin rash.

Common: Diarrhea, nausea and skin rash
Uncommon: Vomiting, Urticaria and pruritus
Not known: Bronchospasm, Acute severe dyspnoea and allergic pneumonitis; generally associated with large intravenous doses of amoxicillin or impaired renal function, Sore mouth or tongue, commonly occur after oral administration but may also occur following parenteral administration, Encephalopathy has been reported following intrathecal administration and can be fatal, Electrolyte disturbances such as hypokalaemia, Jarisch-Herxheimer reaction.

Very Rare: Mucocutaneous candidiasis, Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible

thrombocytopenia and haemolytic anaemia ,prolongation of bleeding time and prothrombin time, Severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis, Hyperkinesia, dizziness and convulsions, Antibiotic associated colitis, Hepatitis and cholestatic jaundice. A moderate rise in ASTor ALT, Skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis, acute generalised exanthematous pustulosis, Interstitial nephritis, Crystalluria .

OVERDOSAGE:

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

Amoxicillin has been reported to precipitate in bladder catheters, predominantly after intravenous administration of large doses. A regular check of patency should be maintained

Treatment of intoxication

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

Amoxicillin can be removed from the circulation by haemodialysis

PHARMACEUTICAL PARTICULARS

INCOMPATIBILITIES

Amoxicillin should not be mixed with blood products, other proteinaceous fluids such us protein hydrolysates or with intravenous lipid emulsions. If prescribed concomitantly with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because of loss of activity of the aminoglycoside under these conditions.

Amoxicillin and aminoglycoside injections should be administered at separate sites.

Amoxicillin should not be mixed with ciprofloxacin.

Amoxicillin solutions should not be mixed with infusions containing dextran or bicarbonate.

DIRECTIONS:

- Protect from light and moisture, store in a cool and dry place below 25°C.
- Use immediately after reconstitution.
- For single use only.
- Discard any unused solution.
- Keep out of the reach of children.
- For suspected adverse drug reaction for BOSCH products, report at ade@bosch-pharma.com

WARNING:

To be sold on the prescription of registered medical practitioner only.

ہدایات :۔

روشنی اور نمی سے محفوظ خشک ٹھنڈی جگہ پر ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

بچوں کی پہنچ سے دُور رکھیں۔

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

انتباہ : صرف رجسٹرڈ میڈیکل پریکٹیشنر کے نسخے پر فروخت کے لئے۔

Manufactured by:

Bosch Pharmaceuticals (Pvt) Ltd.

209, Sector 23, Korangi Industrial Area,
Karachi - Pakistan

ISO 9001:2015 Certified Company

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(Amoxycillin B.P.)

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PHARMACEUTICAL COMPANY