Bosch

For Medical Professional only

CALAMOX®

Injection

0.3G, 0.6G & 1.2G

(Co-amoxiclav for Injection B.P.)

INTRAVENOUS

(Product Specs.: B.P.)

کیلاموکس انجکشن

(کو۔اموکسی کلیو)

DESCRIPTION:

Calamox is a formulation of amoxicillin , a bactericidal broad spectrum penicillin and clavulanic acid, a progressive and irreversible inhibitor of ß-lactamase enzymes. The presence of clavulanic acid protects amoxicillin from destruction and subsequent loss of antibacterial activity by the ß-lactamase enzymes produced by many Gram-negative and Gram-positive bacteria. The spectrum of amoxicillin thus widened to include organisms normally resistant by virtue of their ability to produce ß-lactamase. Calamox will not only eliminate but also will not be inactivated by non-pathogenic ß-lactamase producing organisms at the site of infection.

FORMULATION:

CALAMOX 0.3g intravenous vial: Each containing 250mg amoxicillin and 50mg clavulanic acid

CALAMOX 0.6g intravenous vial: Each containing 500mg amoxicillin and 100mg clavulanic acid.

CALAMOX 1.2g intravenous vial: Each containing 1g amoxicillin and 200mg clavulanic acid.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Combinations of penicillins, including beta-lactamase inhibitors; ATC code: J01CR02.

Mechansim of action:

Calamox 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.

Clavulanic acid is a beta-lactam structurally related to penicillins. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin. Clavulanic acid alone does not exert a clinically useful antibacterial effect.

MICROBIOLOGY:

Calamox is a semisynthetic antibiotic with in vitro bactericidal activity against Gram-positive and Gram-negative bacteria. Calamox is however, susceptible to degradation by beta-lactamases, and therefore, the spectrum of activity does not include organisms which produce these enzymes. Clavulanic acid is a beta-lactam, structurally related to the penicillins, which possesses the ability to inactivate some beta-lactamase enzymes commonly found in microorganisms resistant to penicillins and cephalosporins. In particular, it has good activity against the clinically important plasmid-mediated beta-lactamases frequently responsible for transferred drug resistance.

Aerobic Gram-positive micro-organism: Staphylococcus aureus Enterococcus faecalis,Gardnerella vaginalis Staphylococcus aureus (methicillin-susceptible), Streptococcus agalactiae, Streptococcus pneumonia, Streptococcus pyogenes and other beta-haemolytic Streptococci, Streptococcus viridans group

Aerobic Gram-negative micro-organisms: Actinobacillus actinomycetemcomitans, Capnocytophaga spp. Eikenella corrodens Haemophilus influenza, Moraxella catarrhalis,Neisseria gonorrhoeae, Pasteurella multocida.

Other micro-organism:

Chlamydia trachomatis,Chlamydophila pneumonia,Chlamydophila psittaci,Coxiella burnetti,Mycoplasma pneumoniae

Pharmacokinetic Properties:

Absorption / Distribution:

About 25% of total plasma clavulanic acid and 18% of total plasma amoxicillin is bound to protein. The apparent volume of distribution is around 0.3-0.4 l/kg for amoxicillin and around 0.2 l/kg for clavulanic acid.

Following intravenous administration, both amoxicillin and clavulanic acid have been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.Both amoxicillin and clavulanic acid have 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 theinitial dose. Clavulanic acid is extensively metabolized in man, and eliminated in urine and faeces and as carbon dioxide in expired air.

Excretion:

The major route of elimination for amoxicillin is via the kidney, whereas for clavulanic acid it is by both renal and non-renal mechanisms. Amoxicillin/clavulanic acid has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/h in healthy subjects. Approximately 60 to 70% of the amoxicillin and approximately 40 to 65% of the clavulanic acid are excreted unchanged in urine during the first 6 h after administration of a single 500/100 mg or a single 1000/200 mg bolus intravenous injection. Various studies have found the urinary excretion to be 50-85% for amoxicillin and between 27-60% for clavulanic acid over a 24 hour period. In the case of clavulanic acid, the largest amount of drug is excreted during the first 2 hours after administration.

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/clavulanic acid decreases proportionately with decreasing renal function. The reduction in drug clearance is more pronounced for amoxicillin than for clavulanic acid, as a higher proportion of amoxicillin is excreted via the renal route.

Hepatic impairment

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

CLINICAL PARTICULARS:

Therapeutic indications

CALAMOX 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
- Cystitis, Pyelonephritis
- Skin and soft tissue infections in particular cellulitis, animal bites, severe dental abscess with spreading cellulitis
- Bone and joint infections, in particular osteomyelitis
- Intra-abdominal infections, Female genital infections.

Prophylaxis against infections associated with major surgical procedures in adults, such as those involving the:

- Gastrointestinal tract
- Pelvic cavity
- Head and neck
- Biliary tract surgery, joint replacement surgery.

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

DOSAGE AND ADMINISTRATION

Administration may be by intravenous injection or intermittent infusion. Calamox is not suitable for intramuscular administration.

Adults and children ≥ 40 kg:

FOR TREATMENT OF INFECTIONS	1000 MG/ 200 MG EVERY 8 HOURS
For surgical prophylaxis	For procedures less than 1 hour in duration, the recommended dose of Calamox is 1000 mg/200 mg to 2000 mg/200 mg given at induction of anaesthesia. For procedures greater than 1 hour in duration, the recommended dose of Calamox is 1000 mg/200 mg to 2000 mg/200 mg given at induction of anaesthesia, with up to 3 doses of 1000 mg/200 mg in 24 hours. Clear clinical signs of infection at operation will require a normal course of intravenous or oral therapy post-operatively.

Children ≤ 40 kg

Recommended doses:

- Children aged 3 months and over: 25 mg/5 mg per kg every 8 hours
- Children aged less than 3 months or weighing less than 4 kg: 25 mg/5 mg per kg every 12 hours.

Renal impairment:
Dosing adjustments are based on the maximum recommended level of amoxicillin.

No dose adjustment is required in patients with creatinine clearance (CrCl) greater than 30 ml/min.

Adults and children ≥ 40 kg

	Creatinine clearance <10 mL/min	Creatinine clearance 10-30 mL/min	Haemodialysis
Intravenous	Initial dose of 1000 mg/200 mg and then 500 mg/100 mg given every 24 hours	Initial dose of 1000 mg/200 mg and then 500 mg/100 mg given twice daily	Initial dose of 1000 mg/200 mg and then followed by 500 mg/100 mg every 24 hours, plus a dose of 500 mg/100 mg at the end of dialysis

Children ≤ 40 kg

	Creatinine clearance <10 mL/min	creatinine clearance 10-30 mL/min	Haemodialysis
Intravenous	25 mg/5 mg per kg given every 24 hours	25 mg/5 mg per kg given every 12 hours	25 mg/5 mg per kg given every 24 hours, plus a dose of 12.5 mg/2.5 mg per kg at the end of dialysis

Hepatic impairment:
Dose with caution; monitor hepatic function at regular intervals for both adults and children.

Method of administration
Calamox is for intravenous use.

Calamox may be administered either by slow intravenous injection over a period of 3 to 4 min directly into a vein or via a drip tube or by infusion over 30 to 40 min. Calamox is not suitable for intramuscular administration.

Children aged less than 3 months should be administered Calamox by infusion only.

Treatment with Calamox may be initiated by the use of an intravenous preparation and completed with an appropriate oral presentation as considered appropriate for the individual patient.

CONTRAINDICATION:
Calamox is contraindicated in patients with hypersensitivity to penicillin antibiotics.

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

History of jaundice/hepatic impairment due to amoxicillin/clavulanic acid

WARNINGS AND PRECAUTIONS:
Before initiating therapy with amoxicillin/clavulanic acid, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents Serious and occasionally fatal hypersensitivity reactions have been reported in patients on penicillin therapy.

This presentation of amoxicillin/clavulanic acid may not be suitable for use when there is a high risk that the presumptive pathogens have resistance to beta-lactam agents that is not mediated by beta-lactamases susceptible to inhibition by clavulanic acid.

Convulsions may occur in patients with impaired renal function or in those receiving high doses Amoxicillin/clavulanic acid 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.

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Amoxicillin/clavulanic acid should be used with caution in patients with evidence of hepatic impairment Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been very rarely reported in children. In all populations, signs and symptoms usually occurduring or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased.

In patients with renal impairment, the dose should be adjusted according to the degree of impairment During treatment with amoxicillin, enzymatic glucose oxidase methods should be used whenever testing for the presence of glucose in urine because false positive results may occur with non-enzymatic methods.

The presence of clavulanic acid in Calamox may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION:
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. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary.

Methotrexate

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

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 but not of clavulanic acid.

Mycophenolate mofetil

In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid (MPA) of approximately 50% has been reported following commencement of oral amoxicillin plus clavulanic acid. The change in pre-dose level may not accurately represent changes in overall MPA exposure. Therefore, a change in the dose of mycophenolate mofetil should not normally be necessary in the absence of clinical evidence of graft dysfunction. However, close clinical monitoring should be performed during the combination and shortly after antibiotic treatment.

USE IN PREGNANCY AND LACTATION:

Pregnancy: The product has been used in human pregnancy in a limited number of cases, with no untoward effect; however use in pregnancy is not recommended unless considered essential by the physician.

Lactation: During lactation, trace quantities of penicillins can be detected in breast milk. Amoxicillin/clavulanic acid 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 diarrhoea, nausea and vomiting.

The following adverse effects have been observed with the amoxicillin/clavulanic acid therapy.

Common: Mucocutaneous candidiasis, Diarrhea,

Uncommon: Dizziness, Headache, Rises in AST/ALT, Skin rash, Pruritus, Urticaria, Nausea, Vomiting, Indigestion.

Not known: Overgrowth of non-susceptible organisms, Reversible agranulocytosis, Haemolytic anaemia, Prolongation of bleeding time and prothrombin time, Anaphylaxis, Serum sickness-like syndrome, Hypersensitivity vasculitis, Convulsion, Aseptic meningitis, Antibiotic-associated colitis, Hepatitis,Cholestatic jaundice, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Bullous exfoliative-dermatitis, Interstitial nephritis, Crystalluria

Rare: Reversible leucopenia, Thrombocytopenia, Erythema multiforme

OVERDOSAGE:

Symptoms and signs of overdose

Gastrointestinal symptoms 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/clavulanic acid can be removed from the circulation by haemodialysis

PHARMACEUTICAL PARTICULARS

Stability and Compatibility:

Intravenous infusions of CALAMOX may be given in a range of different intravenous fluids. Satisfactory antibiotic concentrations are retained at 5°C and at room temperature (25°C) in the recommended volume of the following infusion fluids.

If reconstituted and maintained at room temperature, infusions should be completed within the times stated.

Intravenous Infusion Fluid	Stability at 5°C	Stability at 25°C
Water for Injection	8 hours	4 hours
Normal Sailne (0.9%)	8 hours	4 hours
Sodium Lactate		4 hours
Compound Sodium Lactate (Ringer Lactate: Hartmann's Solution)	-	3 hours
Compound Sodium Chloride (Ringer's Solution)	-	3 hours

The stability of Calamox intravenous solutions is concentration dependent. In the event that the use of more concentrated solutions is required, the stability period should be adjusted accordingly.

For storage at 5°C, the reconstituted solution should be added to pre-refrigerated infusion bag which can be stored for upto 8 hrs. Thereafter, the infusion should be administered immediately after reaching room temperature.

Calamox is less stable in infusions containing glucose, dextran or

bicarbonate. Reconstituted solutions of Calamox may be injected into the drip tubing over a period of 3-4 minutes. Any residual antibiotic solution should be discarded.

Calamox vials are not suitable for multi-dose use.
Calamox should be administered within 20 minutes of reconstitution.

INCOMPATIBILITIES
CALAMOX Intravenous should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates or with intravenous lipid emulsions.

If CALAMOX is prescribed concurrently with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because loss of activity of the aminoglycoside can occur under these conditions.

Shelf Life:
The expiry is indicated on the packaging.

PRESENTATION:
CALAMOX I.V 0.3g vial:
Each containing 250mg amoxycillin and 50mg clavulanic acid

CALAMOX I.V 0.6g vial:
Each containing 500mg amoxycillin and 100mg clavulanic acid.

CALAMOX I.V 1.2g vial:
Each containing 1g amoxycillin and 200mg clavulanic acid.

DIRECTIONS:
- Protect from light and moisture store at 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 :-

صرف انٹراوینس استعمال کے لئے۔
روشنی اور نمی سے محفوظ 25°C سے کم درجہ حرارت پر رکھیں۔
انجکشن کو پٹھے میں مت لگوائیں۔
محلول تیار کرنے کے بعد فوراً استعمال کریں اور جمنے نہ دیں۔
بچّوں کی پہنچ سے دُور رکھیں۔ ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

Manufactured by:
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ISO 9001:2015 Certified Company