Bosch

For Medical Professional only

CALAMOX® DROPS

(Co-amoxiclav)

کیلاموکس ڈراپس

(کو۔اموکسی کلیو)

DESCRIPTION:
CALAMOX is an oral antibacterial combination consisting of amoxicillin and the beta-lactamase inhibitor, clavulanate potassium (the potassium salt of clavulanic acid).

Amoxicillin is an analog of ampicillin, derived from the basic penicillin nucleus, 6-aminopenicillanic acid. The amoxicillin molecular formula is $C_{16}H_{19}N_3O_5S \cdot 3H_2O$, and the molecular weight is 419.46. Chemically, amoxicillin 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.

Clavulanic acid is produced by the fermentation of Streptomyces clavuligerus. It is a beta-lactam structurally related to the penicillins and possesses the ability to inactivate some beta-lactamases by blocking the active sites of these enzymes. The clavulanate potassium molecular formula is $C_8H_8KNO_5$, and the molecular weight is 237.25. Chemically, clavulanate potassium is potassium (Z)(2R,5R)-3-(2-hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]-heptane-2-carboxylate.

COMPOSITION:
When reconstituted as directed each ml contains :
Amoxicillin Trihydrate U.S.P. eq. to 50mg Amoxicillin
Clavulanate Potassium U.S.P. eq. to 12.5mg Clavulanic acid
(Product Specs.: U.S.P.)

CLINICAL PHARMACOLOGY:
Pharmacodynamic Properties:
Pharmacotherapeutic group: Combinations of penicillins, incl. beta-lactamase inhibitors; ATC code: J01CR02

Mechanism 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 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:
Gram-Positive Bacteria:
- Staphylococcus aureus
- Enterococcus faecalis
- Staphylococcus epidermidis
- Staphylococcus saprophyticus
- Streptococcus pneumoniae
- Streptococcus pyogenes
- Viridans group Streptococcus

Gram-Negative Bacteria:
- Enterobacter species
- Escherichia coli
- Haemophilus influenzae
- Klebsiella species
- Moraxella catarrhalis
- Eikenella corrodens
- Proteus mirabilis

Anaerobic Bacteria:
- Bacteroides species
- Bacteroides fragilis
- Fusobacterium species
- Peptostreptococcus species

Pharmacokinetic Properties
Absorption:
Dosing in the fasted or fed state has minimal effect on the pharmacokinetics of amoxicillin. While CALAMOX can be given without regard to meals, absorption of clavulanate potassium when taken with food is greater relative to the fasted state. In one study, the relative bioavailability of clavulanate was reduced when CALAMOX was dosed at 30 and 150 minutes after the start of a high-fat breakfast.

Distribution:
Neither component in CALAMOX is highly protein-bound; clavulanic acid is approximately 25% bound to human serum and amoxicillin approximately 18% bound. Amoxicillin diffuses readily into most body tissues and fluids with the exception of the brain and spinal fluid. Two hours after oral administration of a single 35 mg/kg dose of suspension of CALAMOX to fasting children, average concentrations of 3 mcg/mL of amoxicillin and 0.5 mcg/mL of clavulanic acid were detected in middle ear effusions.

Metabolism and Excretion:
The half-life of amoxicillin after the oral administration of CALAMOX is 1.3 hours and that of clavulanic acid is 1 hour. Approximately 50% to 70% of the amoxicillin and approximately 25% to 40% of the clavulanic acid are excreted unchanged in urine during the first 6 hours after administration of a single 250-mg or 500-mg tablet of CALAMOX.

SPECIFIC POPULATIONS
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. Doses in renal impairment must therefore prevent undue accumulation of amoxicillin while maintaining adequate levels of clavulanic acid.

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

Pediatrics:
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.

Elderly:
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.

THERAPEUTIC INDICATIONS:
CALAMOX infant drops are indicated for short-term treatment of bacterial infections at the following sites: Upper respiratory tract Infections (including ENT) e.g. recurrent tonsillitis, sinusitis, otitis media. Lower respiratory tract infections e.g. acute exacerbation of chronic bronchitis, lobar and bronchopneumonia. Genitourinary tract infections e.g. cystitis, urethritis, pyelonephritis. Skin and soft tissue infections, e.g. boils, abscesses, cellulitis, wound infections. Bone and joint infections e.g. osteomyelitis. Other infections e.g. intra abdominal sepsis. Infections caused by amoxicillin-susceptible organisms are amenable to CALAMOX treatment due to its amoxicillin content. Mixed infections caused by amoxicillin-susceptible organisms in conjunction with CALAMOX-susceptible β-lactamase producing organisms may therefore be treated with CALAMOX.

DOSAGE AND ADMINISTRATION:
The usual recommended daily dosage is 25 mg/kg/day in divided doses every eight hours. In more serious infections the dosage may be increased up to 50 mg/kg/day in divided doses every eight hours. Each 25 mg CALAMOX provides 20mg amoxicillin and 5 mg clavulanate. Calamox Drops should be administered by using the supplied dropper. The Dropper has marking according to the volume per drop providing convenience of dosing. For example at a marking of 1ml (equivalent to approx. 25 drops) should then be orally administered to the child. A similar dose should be administered after 8 hours interval according to the weight of the child. The dosage chart of Calamox Drops which corresponds to the weight (Kg) and Age (months) are shown below:

Weight of child (kg)	Volume (ml) of Co-amoxiclav (Calamox) infant drops*
1	0.13
1.5	0.20
2	0.27
2.5	0.33
3	0.40
3.5	0.47
4	0.53
4.5	0.60
5	0.67
5.5	0.73
6	0.80
6.5	0.87
7	0.93
7.5	1.00
8	1.07
8.5	1.14
9	1.20
9.5	1.27
10	1.34

* These doses may be doubled in cases of severe infection.

Dosage in renal impairment

Mild impairment (Creatinine clearance >30 ml/min)	Moderate impairment (Creatinine clearance 10-30 ml/min)	Severe impairment (Creatinine clearance <10ml/min)
No change in dosage, i.e., the recommended dose given three times daily*	The recommended dose given twice daily instead of three times per day*	The recommended dose given once daily instead of three times per day*

* In more serious cases this dose may be doubled.

Dosage in hepatic impairment
Dose with caution; monitor hepatic function at regular intervals.

Administration:
To minimise potential gastrointestinal intolerance, administer at the start of a meal. The absorption of CALAMOX is optimised when taken at the start of a meal. Duration of therapy should be appropriate to the indication and should not be extended beyond 14 days without review.

CONTRAINDICATIONS:
Hypersensitivity to the active substances, 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). History of jaundice/hepatic impairment due to amoxicillin/clavulanic acid.

WARNINGS AND PRECAUTIONS:
Before initiating therapy with co-amoxiclav, careful enquiry should be made concerning previous hypersensitivity reactions to penicillin, cephalosporin or other allergens. 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. Co-amoxiclav 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. Prolonged use may also occasionally result in overgrowth of non-susceptible organisms. Prolongation of prothrombin time has been reported rarely in patients receiving Co-amoxiclav. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Changes 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 renal impairment Co-amoxiclav dosage should be adjusted as recommended in the Dosage and Administration section. In patients with reduced urine output, crystalluria has been observed very rarely predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria.

DRUG INTERACTIONS:
Use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use with CALAMOX may result in increased and prolonged blood levels of amoxicillin but not of clavulanate. 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. In common with other antibiotics, Co-amoxiclav may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral contraceptives.

ADVERSE EFFECTS:
Common:
Mucocutaneous candidiasis, Blood and lymphatic system disorders, Diarrhoea, nausea, vomiting.

Uncommon:
Dizziness, headache, Indigestion, A moderate rise in AST and/or ALT, Skin rash, pruritus, urticaria.

Rare:
Reversible leucopenia (including neutropenia) and thrombocytopenia, Erythema multiforme.

Very Rare:
Reversible agranulocytosis and haemolytic anaemia. Prolongation of bleeding time and prothrombin time, Angioneurotic oedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis, Reversible hyperactivity and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses, Antibiotic-associated

colitis (including pseudomembranous colitis and haemorrhagic colitis). Superficial tooth discolouration has been reported very rarely in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing, Hepatitis and cholestatic jaundice. These events have been noted with other penicillins and cephalosporins, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthemous pustulosis (AGEP), Interstitial nephritis, crystalluria.

USE IN PREGNANCY AND LACTATION:

Pregnancy:

Teratogenic Effects: Pregnancy Category B

There are, however, no adequate and well controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Lactation:

Both substances are excreted into breast milk. 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/clavulanic acid should only be used during breast-feeding after benefit/risk assessment by the physician in charge.

OVERDOSE:

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance. Amoxicillin/clavulanic acid can be removed from the circulation by haemodialysis.

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING:

Add a small quantity of pre boiled cool water in the bottle and shake well, then add more water upto the mark given on the label and shake well to make suspension. Once reconstituted, the plastic dropper dosing device should then be used in place of the screw cap. The device is used to dose patients upto 6 months according to the schedule in the Dosage and Administration section.

INSTRUCTIONS:

Do not take if seal is Broken.

Before reconstitution protect from heat, sunlight & moisture, store below 25°C.

Reconstituted suspension should be stored in a refrigerator (2°C-8°C) and used within seven days. Do not freeze.

The Expiration date refer to the product correctly stored at required condition.

Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.

Keep out of the reach of children.

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

PRESENTATION:

Calamox Drops 62.5mg/ml: 20ml (after reconstitution) in 30ml Amber Glass Bottle.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:- صرف سیل بند بوتل خریدیں۔

غیر تیار شدہ دوا کو دھوپ، گرمی اور نمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

بچوں کی پہنچ سے دور رکھیں۔

احتیاط: دوا تیار کرنے کے بعد ریفریجریٹر میں رکھیں اور سات دن کے اندر استعمال کرلیں۔

استعمال کے بعد ڈھکن کو اچھی طرح بند رکھیں۔ صرف معتمد ڈاکٹر کے نسخے پر فروخت کے لئے۔

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ISO 9001:2015 Certified Company