CO-AMOXICLAV

625 mg Film-Coated Tablet
ANTIBACTERIAL (PENICILLIN)

℞

Formulation:
Each film-coated tablet contains:
Amoxicillin (as Trihydrate) USP ..... 500 mg
Clavulanate Potassium
(as Clavulanic acid) USP .....125 mg
Excipients..... q.s.

Product Description:
White to off white oval shaped film-coated tablets having scoring on one side.

Pharmacodynamic Properties:
Pharmacotherapeutic group: Combinations of penicillins, incl. beta-lactamase inhibitors.

Mechanism of Actions:
Amoxicillin + Clavulanic Acid is a novel concept in antibiotic therapy. Resistance to many antibiotics is caused by bacterial enzymes which destroy the antibiotic before it can act on the pathogen. The Clavulanate anticipates this defense mechanism by blocking the ß-lactamase enzymes, thus rendering the organisms sensitive to Amoxicillin's rapid bactericidal effect at concentrations readily attainable in the body. Clavulanate by itself has little antibacterial activity; however, in association with Amoxicillin, it produces a novel antibiotic agent of the broad spectrum with wide application in hospital and general practice.

Pharmacokinetic Properties:
Absorption
Amoxicillin and clavulanic acid, are fully dissociated in an aqueous solution at physiological pH. Both components are rapidly and well-absorbed by the oral route of administration. Following oral administration, amoxicillin and clavulanic acid are approximately 70% bioavailable. The plasma profiles of both components are similar and the time to peak plasma concentration (Tmax) in each case is approximately one hour.
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 the gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.
From animal studies, there is no evidence for significant tissue retention of drug-derived material for either component. Amoxicillin, like most penicillins, can be detected in breast milk. Trace quantities of clavulanic acid can also be detected in breast milk.
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 the initial dose. Clavulanic acid is extensively metabolized in man and eliminated in urine and feces, and as carbon dioxide in expired air.
Elimination
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 6h after administration of single Co-Amoxiclav 250 mg/125 mg or 500 mg/125 mg tablets. 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.
Concomitant use of probenecid delays amoxicillin excretion but does not delay renal excretion of clavulanic acid.
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.
Gender
Following oral administration of amoxicillin/clavulanic acid to healthy males and female subjects, gender has no significant impact on the pharmacokinetics of either amoxicillin or clavulanic acid.
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.

Indications:
Used for the treatment of urinary tract infections due to susceptible organisms; for otitis media or sinusitis due to resistant microorganism (e.g., *H. influenzae, S. pneumoniae, M. catarrhalis*); for lower respiratory tract and skin infections due to susceptible organism; and for polymicrobial infections with mixed aerobic and anaerobic such as diabetic foot, gynecologic infections and intra-abdominal infections.

Dosage and Administration:
The usual adult dose is one Amoxicillin and Clavulanate potassium tablet, 500 mg/125 mg every 12 hours or one Amoxicillin and Clavulanate potassium tablet, 250 mg/125 mg every 8 hours. For more severe infections and infections of the respiratory tract, the dose should be one Amoxicillin and Clavulanate potassium tablet, 875 mg/125 mg every 12 hours or one Amoxicillin and Clavulanate potassium tablet, 500 mg/125 mg every 8 hours.
Or as prescribed by the physician.

Contraindications:
A history of allergic reaction to ß-lactams (e.g., penicillins or cephalosporins) is a contraindication. Amoxicillin + Clavulanic Acid is contraindicated in patients with previous history of Amoxicillin + Clavulanic Acid associated jaundice/hepatic dysfunction.

Warnings:
Drugs that delay peristalsis, (e.g., opiates and diphenoxylate with atropine) may prolong and/or worsen the condition and should not be used. Fluids, electrolytes and protein replacement therapy should be provided when indicated.

Precautions:
Amoxicillin + Clavulanic Acid should be used with care in patients with evidence of hepatic dysfunction. Amoxicillin + Clavulanic Acid syrups contain aspartame and should be used with caution in patients with phenylketonuria.

Use in Pregnancy:
There is limited experience of the use of Amoxicillin + Clavulanic Acid in human pregnancy. As with all medicines, use should be avoided in pregnancy, especially during the first trimester, unless considered essential by the physician.

Use in Lactation:
Amoxicillin is excreted in breast milk; there are no data on the excretion of Clavulanic Acid in human milk. Therefore, caution should be exercised when administering to a nursing woman.

Adverse Drug Reactions:
Gastrointestinal Reactions: Gastritis, stomatitis, glossitis, black "hair" tongue, indigestions, nausea, vomiting, diarrhea, enterocolitis, pseudomembranous colitis and candidiasis have been reported.
Hypersensitivity Reactions: Skin rashes and urticaria have been reported. These reactions may be controlled with antihistamines and if necessary, systemic corticosteroids. Rare cases of erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and an occasional case of exfoliative dermatitis have been reported.
Interstitial nephritis can occur rarely. Serious and occasional fatal hypersensitivity (anaphylactic) reactions and angioneurotic edema have been reported in patients on penicillin therapy. Cross-sensitivity with other beta-lactam antibiotics (eg. cephalosporins), may occur.
Hepatic Effects: As with some other antibacterial agents, a few cases of transient hepatitis and cholestatic jaundice have been reported.
Hematologic Effects: Anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia and agranulocytosis have been reported during therapy with penicillins.
Local Reactions: Phlebitis at the site of injection has also been reported.

Drug Interactions:
Following administration of Ampicillin to pregnant women a transient decrease in plasma concentration of total conjugated estriol, estradiol has been noted. This effect may also occur with amoxicillin and therefore with Amoxicillin + Clavulanic Acid. Probenecid decreases the renal tubular secretion of Amoxicillin but does not affect clavulanic acid excretion. Concurrent use with Amoxicillin + Clavulanic Acid may result in increased and prolonged blood levels of Amoxicillin but not for Clavulanic acid. The concurrent administration of allopurinol and ampicillin increases substantially the incidence of rashes in patients receiving both medicines as compared to patients receiving Ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperuricemia present in these patients. No information is available about the concurrent use of Amoxicillin + Clavulanic Acid and Alcohol. However, the ingestion of alcohol whilst being treated with the beta-lactam antibiotics latamoxef, cefoperazone and cefamandole has precipitated a disulfiram (Antabuse) like reaction in some patients. Therefore, the ingestion of alcohol should be avoided during and for several days after treatment with Amoxicillin + Clavulanic Acid.

Overdose and Treatment:
Signs and Symptoms 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.

Caution:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

ADR Reporting Statement:
For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.
Seek medical attention immediately at the first sign of any adverse drug reaction.

Storage Condition:
Store at temperatures not exceeding 30°C.

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.

Availability:
Alu/Alu Blister Pack x 7's (Box of 14's)

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