Clavicin

CO-AMOXICLAV(Amoxicillin & Potassium Clavulanate) FOR INJECTION BP
1.2 g

WARNINGS

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, the amoxicillin and clavulanic acid combination should be discontinued and the appropriate therapy instituted.

Each vial contains sterile mixture of: Amoxicillin Sodium equivalent to Amoxicillin BP 1 g
Potassium Clavulanate equivalent to Clavulanic Acid BP 200 mg

Description:

Amoxicillin and Potassium clavulanate for Injection (beta-lactam antibacterial penicillin co-formulated with a beta-lactamase inhibitor) is an antibiotic agent with a notably broad spectrum of activity against the commonly occurring bacterial pathogens in general practice and hospital. The beta-lactamase inhibitory action of clavulanate extends the spectrum of amoxicillin to embrace a wider range of organisms, including many resistant to other beta-lactam antibiotics.

The activity of clavulanic acid is dependent upon the drug achieving concentrations at the site of action above the minimum inhibitory concentration (MIC)

Mechanism of Action: Resistance to many antibiotics is caused by bacterial enzymes which destroy the antibiotic before it can act on the pathogen. The clavulanate in Amoxicillin and Clavulanic acid anticipates this defence mechanism by blocking the organisms sensitive to amoxicillin's rapid bactericidal effect at concentrations rapidly attainable in the body.

Clavulanate by itself has little antibacterial activity; however in association with amoxicillin as Amoxicillin and Clavulanic acid, it produces an antibiotic agent of broad spectrum with wide application in hospital and general practice.

Pharmacokinetics: The pharmacokinetics of the 2 components of Amoxicillin and Clavulanic acid are closely matched. Both clavulanate and amoxicillin have low levels of serum binding; about 70% remains free in the serum. Doubling the dosage of the Amoxicillin and Clavulanic acid approximately doubles the serum levels achieved.

Absorption: When taken together with amoxicillin (500mg), absorption of clavulanic acid (250mg) is approximately the same, with a serum peak of around 6mg.l-1 and a peak amoxicillin level of 10mg.l-1, both after1h.The urinary recovery is about 27-32% after a 250mg dose of clavulanic acid in combination with amoxicillin. The plasma half - life is 0.8-1h and plasma protein binding is 22-30%.

Amoxicillin and clavulanate are both well absorbed after oral administration and are stable in the presence of gastric acid. Food does not affect the absorption and this combination product may be given without regard to meals. The oral bioavailability of amoxicillin and potassium clavulanate is approximately 90% and 75% respectively.

Clavulanic acid has about the same plasma elimination half-life (1h) as that of amoxicillin (1.3 hours). Amoxicillin and clavulanic acid are widely distributed to most tissues and body fluids including peritoneal, blister, urine, pleural and middle ear fluid, intestinal tissues and bile. The penetration into CSF through non-inflamed meninges and into purulent bronchial secretions is low. Amoxicillin and clavulanic acid readily cross the placenta and are distributed into breast milk in low concentrations.

Amoxicillin is bound to serum proteins to an extent of 17-20% while clavulanic acid is 20-30% bound to serum proteins. Approximately 10% of the dose of amoxicillin and, 50% of dose of clavulanate are metabolized.

Metabolism and Excretion: Amoxicillin and clavulanic acid is eliminated primarily unchanged through the renal route (glomerular filtration and tubular secretion). Approximately 50-78% of amoxicillin and 15-40% of clavulanic acid are excreted unchanged in urine within the first 6 hours after administration.

Up to 48% of an intravenous dose and up to 38% of an oral dose is excreted unchanged in urine. In animal studies, respiratory and urinary excretion of radiolabeled metabolites was the other major routes although the metabolic pathways are unknown.

Indications

Short term treatment of bacterial infections at the following sites :

Upper respiratory tract infections

1. Recurrent tonsillitis
2. Sinusitis and otitis media

Lower respiratory tract infections

1. Acute and chronic bronchitis
2. Lobar and bronchopneumonia

Genitourinary tract infections

1. Cystitis, urethritis and pyelonephritis

Skin and soft tissue infections

1. Boils, abscesses and cellulitis
2. Wound infections

Bone and joint infections

Contraindications: Penicillin hypersensitivity. Attention should be paid to possible sensitivity with other Beta-lactam antibiotics, e.g. Cephalosporin. A previous history of Amoxicillin and Clavulanic acid or penicillin associated jaundice/hepatic dysfunction.

Warnings and Precautions: Changes in liver function tests have been observed in some patients receiving Amoxicillin and Clavulanic acid. The clinical significance of these changes is uncertain but Amoxicillin and Clavulanic acid should be used with care in patients with evidence of severe hepatic dysfunction. Prolonged use may occasionally result in overgrowth of nonsusceptible organisms.

Pregnancy: Reproduction studies in animals (mice and rats) with orally and parenterally administered Amoxicillin and Clavulanic acid have shown no teratogenic effects. There is limited information on the use in human pregnancy. As with all medicines, use should be avoided in pregnancy, especially during the 1st trimester, unless considered essential by the physician.

Nursing Mothers: Amoxicillin and Clavulanic acid may be administered during the period of lactation. With the exception of the risk of sensitisation, associated with the excretion of trace quantities in breast milk, there are no detrimental effects on the infant.

Geriatric Use: No special precautions have to be taken when prescribing for the elderly.

Interaction with other medicinal products and other forms of interaction

Prolongation of bleeding time and prothrombin time has been reported in some patients receiving Amoxicillin and Clavulanic acid. It should be used with care in patients on anticoagulation therapy. In common with other broad - spectrum antibiotics, Amoxicillin and Clavulanic acid may reduce the efficacy of oral contraceptives and patients should be warned accordingly. Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use with Amoxicillin and Clavulanic acid may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.

Toxicology: The administration of amoxicillin and clavulanic acid to rats and mice at 10 times the usual human dose had no adverse fetal effects.

Adverse effects: Side effects include diarrhea, indigestion, nausea and vomiting. Candidiasis and antibiotic -associated colitis have been reported rarely. Nausea, although uncommon, is more often associated with higher oral dosages.

Hypersensitivity reactions:

Urticarial and erythematous rashes sometimes occur. Rarely erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and exfoliative dermatitis have been reported. Treatment should be discontinued if one of these types of rash appears. Intestinal nephritis can occur rarely.

Overdosage:

Symptoms: Cases of Overdosage with Amoxicillin and Clavulanic acid are usually asymptomatic. If encountered gastrointestinal symptoms and disturbances of the fluid and electrolyte balances may be evident

Treatment: They may be treated symptomatically with attention to the water electrolyte balance. Amoxicillin and Clavulanic acid can be removed from the circulation by haemodialysis. During the administration of high doses of Amoxicillin and Clavulanic acid adequate fluid intake and urinary output should be maintained to minimize the possibility of amoxicillin crystalluria.

Dosage and Administration:

Adults and Children: Usually 1.2 g - 8 hourly. In more serious infections increase frequency to 6 -hourly intervals.

Infants upto 3 months: 30 mg / kg Amoxicillin and Clavulanic acid every 12 hours in premature infants and in full-term infants during the perinatal period, increasing to 8 hrs thereafter.

The solution should be injected immediately after preparation. The solution should be used within 20 minutes after reconstitution.

Directions for use: Dissolve the contents in 20 ml of Sterile Water for Injection for IV use.
The reconstituted solution should be used immediately after preparation.

Storage: Store below 25°C. Protect from light. Keep out of reach of children.

Presentation: 1 vial packed in a carton.

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