Super CV 375/ 625/1000

Amoxicillin and Potassium Clavulanate Tablets USP

COMPOSITION:

Super CV 375: Each film coated tablet contains Amoxicillin USP as Trihydrate equivalent to anhydrous Amoxicillin 250 mg and Diluted Potassium Clavulanate BP equivalent to Clavulanic Acid 125 mg

Super CV 625: Each film coated tablet contains Amoxicillin USP as Trihydrate equivalent to anhydrous. Amoxicillin 500 mg and Diluted Potassium Clavulanate BP equivalent to Clavulanic Acid 125 mg

Super CV 1000: Each film coated tablet contains Amoxicillin USP as Trihydrate equivalent to anhydrous Amoxicillin 875 mg and Diluted Potassium Clavulanate BP equivalent to Clavulanic Acid 125 mg

DESCRIPTION:

Amoxicillin is a semisynthetic antibiotic with a broad spectrum of bactericidal activity, covering both gram-negative and gram-positive microorganisms. Addition of clavulanate inhibits beta- lactamase-producing bacteria, allowing amoxicillin extended spectrum of action. Combination of Amoxicillin and Potassium clavulanate is also called **Co-amoxiclav.**

THERAPEUTIC CLASS: Combinations of penicillins and beta-lactamase inhibitor

CLINICAL PARTICULARS:

Therapeutic indications:

- Acute bacterial sinusitis (adequately diagnosed)
- Acute otitis media
- Acute exacerbations of chronic bronchitis (adequately diagnosed)
- Community acquired pneumonia
- Pyelonephritis
- Cystitis
- Skin and soft tissue infections in particular cellulitis, animal bites, severe dental abscess with spreading cellulitis.
- Bone and joint infections, in particular osteomyelitis.

POSOLOGY AND METHOD OF ADMINISTRATION:

Posology:

The dosage of Co-amoxiclav depends on:

- The expected pathogens and their likely susceptibility to antibacterial agents
- The severity and the site of the infection
- The age, weight and renal function of the patient

The use of alternative presentations of Co-amoxiclav (e.g. those that provide higher doses of amoxicillin and/or different ratios of amoxicillin to clavulanic acid) should be considered as necessary.

Treatment should not be extended beyond 14 days without review.

SUPER CV 375

Adults and children ≥ 40 kg: One 250 mg/125 mg tablet taken three times a day.

Children < 40 kg: Co-amoxiclav 250 mg/125 mg tablets are not recommended in children < 40 kg.

Renal impairment: Dose adjustments are based on the maximum recommended level of amoxicillin. No adjustment in dose is required in patients with creatinine clearance (CrCl) greater than 30 ml/min.

Adults and children ≥ 40 kg

CrCl: 10-30 ml/min	250 mg/125 mg twice daily
CrCl< 10 ml min	250 mg/125 mg once daily
Haemodialysis	Two doses of 250 mg/125 mg every 24 hours, plus two doses of 250 mg/125 mg during dialysis, to be repeated at the end of dialysis (as serum concentrations of both amoxicillin and clavulanic acid are decreased)

Children < 40 kg:

In children < 40 kg with creatinine clearance less than 30 ml/min, the use of Co-amoxiclav presentations with an amoxicillin to clavulanic acid ratio of 2:1 is not recommended, as no dose adjustments are available. In such patients, Co-amoxiclav formulations with an amoxicillin to clavulanic acid ratio of 4:1 are recommended.

SUPER CV 625

Adults and children ≥ 40 kg: One 500 mg/125 mg dose taken three times a day.

Children < 40 kg: 20 mg/ 5 mg/kg/day to 60 mg/ 15 mg/kg/day given in three divided doses.

Children aged 6 years and below or weighing less than 25 kg should preferably be treated withCo-amoxiclav suspension.

No clinical data are available on doses of Co-amoxiclav 4:1 formulations higher than 40 mg/10 mg/kg per day in children under 2 years

Renal impairment: Dose adjustments are based on the maximum recommended level of amoxicillin. No adjustment in dose is required in patients with creatinine clearance (CrCl) greater than 30 ml/min.
Adults and children ≥ 40 kg

CrCl: 10-30 mlmin	500 mg/125 mg twice daily

CrCl < 110 ml/min	500 mg/125 mg once daily
Haemodialysis	500 mg/125 mg every 24 hours, plus 500 mg/125 mg during dialysis, to be repeated at the end of dialysis (as serum concentrations of both amoxicillin and clavulanic acid are decreased)
Children < 40 kg	
CrCl: 10-30 ml/min	15 mg/3.75 mg/kg twice daily (maximum 500 mg/125 mg twice daily)
CrCl < 10 ml/min	15 mg/3.75 mg/kg as a single daily dose (maximum 500 mg/125 mg)
Haemodialysis	15 mg/3.75 mg/kg per day once daily, Prior to haemodialysis 15 mg/3.75 mg/kg. In order to restore circulating drug levels, 15 mg/3.75 mg per kg should be administered after haemodialysis.

SUPER CV 1000

Adults and children ≥ 40 kg

- Usual dose-1 tablet two times a day
- Higher dose- 1 tablet three times a day

Children < 40 kg: Amoxicillin 875 mg/ Clavulanic acid 125 mg tablets are not recommended for children weighing less than 40 kg.

Renal impairment: Severely impaired patients with a glomerular filtration rate of <30 mL/min. should not receive the 875/ 125 mg Co-amoxiclav tablet.

Elderly: No dose adjustment is considered necessary.

Hepatic impairment: Dose with caution and monitor hepatic function at regular intervals

Method of administration:

Co-amoxiclav is for oral use.

Co-amoxiclav should be administered with a meal to minimize potential gastrointestinal intolerance.

Space the doses as evenly as possible throughout the day. If you are taking the tablets twice a day, take a dose about every 12 hours.

Take this medicine at the same time each day. Taking it at the same time each day will have the best effect and will also help you remember when to take it.

If you forget to take it: If it is almost time to take your next dose, skip the missed dose and take your next dose at the usual time. Otherwise, take it as soon as you remember and then go back to taking your medicine as you would normally. Do not take a double dose to make up for missed dose.

CONTRAINDICATIONS:

Hypersensitivity to the active substances, to any of the penicillins

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

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

- Before initiating therapy with amoxicillin/clavulanic acid, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam antibiotics.
- Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy.
  Note: If an allergic reaction occurs, amoxicillin/clavulanic acid therapy must be discontinued and appropriate alternative therapy instituted.
- Do not use this combination when there is a high risk that the presumptive pathogens have reduced susceptibility or resistance to beta-lactam agents that is not mediated by beta-lactamases susceptible to inhibition by clavulanic acid (e.g. penicillin- insusceptible *S. pneumonia*).
- 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. The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP). This reaction requires Co-amoxiclav discontinuation and contra-indicates any subsequent administration of amoxicillin.
- Amoxicillin/clavulanic acid should be used with caution in patients with evidence of hepatic impairment.
- Antibiotic-associated colitis has been reported with nearly all antibacterial agents including amoxicillin and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of any antibiotics.
- If antibiotic-associated colitis occur, amoxicillin/ clavulanic acid should immediately be discontinued, a physician be consulted and an appropriate therapy initiated.
- Anti-peristaltic medicinal products are contraindicated in this situation. Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.
- 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.

UNDESIREABLE EFFECTS:

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and vomiting.

Very common: Diarrhoea

Common: Mucocutaneous candidosis, nausea, vomiting,

Uncommon dizziness, headache, indigestion, rise in AST or ALT, skin rash, praries, articaria Rare; erythema multiforme, thrombocytopenia, reversible leucopenia

PREGNANCY AND BREAST-FEEDING:

Pregnancy: Use should be avoided during pregnancy, unless considered essential by the physician.

Breast-feeding: Amoxicillin/Clavulanic acid should only be used during breast-feeding after benefit/risk assessment by the physician in charge.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g., allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machine.

INTERACTION WITH OTHER MEDICINAL PRODUCTS 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.

Pregnancy

Use should be avoided during pregnancy, unless considered essential by the physician.

Breast-feeding

Both substances are excreted into breast milk (nothing is known of the effects of clavulanic acid on the breast-fed infant). Amoxicillin/clavulanic acid should only be used during breast-feeding after benefit/risk assessment by the physician in charge.

OVERDOSE:

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 water/electrolyte balance.

Amoxicillin/clavulanic acid can be removed from the circulation by haemodialysis

PHARMACOLOGICAL PROPERTIES:

Pharmacodynamic Properties:

Amoxicillin binds to penicillin-binding proteins, thus inhibiting final transpeptidation step of peptidoglycan synthesis in bacterial cell walls. This leads to weakening of the cell wall, which is usually followed by cell lysis and death. Clavulanic acid is a beta-lactam structurally related to penicillins. It inactivates some beta-lactamase enzymes thereby preventing inactivation of amoxicillin.

Amoxicillin kills the bacteria and inhibits the growth of bacteria and Clavulanic acid enhances the action of Amoxicillin against bacteria.

Commonly susceptible species

Aerobic Gram-positive micro-organisms

Enterococcus faecalis, Staphylococcus aureus (methicillin-susceptible), Coagulase-negative staphylococci (methicillin-susceptible), Streptococcus agalactiae. Streptococcus pneumoniae. Streptococcus pyogenes and other beta-haemolytic streptococci, Streptococcus viridans group

Aerobic Gram-negative micro-organisms

Capnocytophaga spp., Eikenella corrodens, Haemophilus influenza, Moraxella catarrhalis, Pasteurella multocida

Anaerobic micro-organisms

Bacteroides fragilis, Fusobacterium nucleatum, Prevotella spp.

Species for which acquired resistance may be a problem

Aerobic Gram-positive micro-organisms

Enterococcus faecium

Aerobic Gram-negative micro-organisms

Escherichia coli, Klebsiella oxytoca, Klebsiella pneumonia, Proteus mirabilis, Proteus vulgo

Inherently resistant organisms

Aerobic Gram-negative micro-organisms

Acinetobacter sp., Citrobacter freundi, Enterobacter sp.. Morganella morganit, Providencias Pseudomonas sp.. Serratia sp., Stenotrophomonas multophilia

Natural intermediate susceptibility in the absence of acquired mechanism of resistance.

All methicillin-resistant staphylococci are resistant to amoxicillin/clavulanic acid *Streptococcus pneumoniae* that is fully susceptible to penicillin may be treated with thi presentation of amoxicillin/clavulanic acid. Organisms that show any degree of reduced susceptibility to penicillin should not be treated with this presentation.

Strains with decreased susceptibility have been reported in some countries in the EU with frequency higher than 10%.

Pharmacokinetic properties:

Absorption: Amoxicillin and clavulanic acid, are fully dissociated in 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.

Distribution: About 25% of total plasma clavulanic acid and 18% of total plasma amoxicillin is bound to protein. Amoxicillin does not adequately distribute into the cerebrospinal fluid.

Metabolism: 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 faeces, and as carbon dioxide in expired air.

Elimination: The major route of elimination for amoxicillin is via the kidney, whereas for clavulanic acid it is by both renal and non-renal mechanisms.

STORAGE:

Store below 25°C. Keep away from children. Store away from sunlight and moisture.

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National Healthcare