Natrapharm

Co-Amoxiclav

Natravox®

625 mg Film-Coated Tablet
1 g Film-Coated Tablet
Antibacterial
(Penicillin + Beta-Lactamase Inhibitor Combination)

℞

Each film-coated tablet contains:
Amoxicillin Trihydrate BP
Equivalent to Amoxicillin 500 mg
Diluted Potassium Clavulanate BP
Equivalent to Clavulanic Acid 125 mg

Each film-coated tablet contains:
Amoxicillin Trihydrate BP
Equivalent to Amoxicillin 875 mg
Diluted Potassium Clavulanate BP
Equivalent to Clavulanic Acid 125 mg

INDICATIONS
Co-amoxiclav is used for the treatment of urinary tract infections due to susceptible organisms; for otitis media or sinusitis due to resistant microorganisms (e.g., H. influenzae, S. pneumoniae, M. catarrhalis); for lower respiratory tract and skin infections due to susceptible organisms; and for polymicrobial infections with mixed aerobic and anaerobic such as diabetic foot, gynecologic infections, intraabdominal infections.

DOSAGE AND ADMINISTRATION

PRODUCT	UPPER RESPIRATORY TRACT INFECTION (otitis media) *H. influenza H. parainfluenzae*	LOWER RESPIRATORY TRACT INFECTION (bronchitis) *H. influenza H. parainfluenzae*	URINARY TRACT INFECTION *E. coli Klebsiella pneumoniae*	SKIN AND SOFT TISSUE INFECTION *Staphylococcus aureus*
Co-amoxiclav 625 mg	1 tablet every 8 hours	1 tablet every 8 hours	1 tablet every 8 hours	1 tablet every 8 hours
Co-amoxiclav 1000 mg	1 tablet every 12 hours	1 tablet every 12 hours	1 tablet every 12 hours	1 tablet every 12 hours

Route of Administration: Oral

CONTRAINDICATIONS
Hypersensitivity to beta-lactams, e.g. penicilllins and cephalosporins and clavulanic acid.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE
The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving Pseudomonas or Candida), the drug should be discontinued and/or appropriate therapy instituted.
Prescribing Co-amoxiclav in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity that have experienced severe reactions when treated with cephalosporins. Before initiating therapy with Co-amoxiclav, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, Co-amoxiclav should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should also be administered as indicated.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including Co-amoxiclav, and has ranged in severity from mild to life-threatening; therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents. Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of Clostridia.

DRUG INTERACTION
Prolongations of bleeding time and prothrombin time have been reported in some patients receiving Co-amoxiclav. Co-amoxiclav should be used with care in patients on anticoagulation therapy. In common with other broad-spectrum antibiotics, it may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

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.

USE DURING PREGNANCY & LACTATION
Use in pregnancy
Reproduction studies in animals (mice and rats) with orally and parenterally administered Co-amoxiclav have shown no teratogenic effects. In a single study in women with preterm, premature rupture of the fetal membrane (pPROM), it was reported that prophylactic treatment with Co-amoxiclav may be associated with an increased risk of necrotising enterocolitis in neonates. As with all medicines, use should be avoided in pregnancy, especially during the first trimester, unless considered essential by the physician.

Use in lactation
Co-Amoxiclav may be administered during the period of lactation with the exception of the risk of sensitization, associated with the excretion of trace quantities in breast milk, there are no known detrimental effects for the breast-fed infant.

EFFECTS ON ABILITY TO DRIVE AND TO USE MACHINES
Adverse effects on the ability to drive or operate machinery have not been observed.

OVERDOSE
Following overdosage, patients have experienced primarily gastrointestinal symptoms including stomach and abdominal pain, vomiting, and diarrhea. Rash, hyperactivity, or drowsiness have also been observed in a small number of patients.

In the case of overdosage, discontinue Co-amoxiclav, treat symptomatically, and institute supportive measures as required. If the overdosage is very recent and there is no contraindication, an attempt at emesis or other means of removal of drug from the stomach may be performed.

A prospective study of 51 pediatric patients at a poison control center suggested that overdosages of less than 250 mg/kg of amoxicillin are not associated with significant clinical symptoms and do not require gastric emptying.

Interstitial nephritis resulting in oliguric renal failure has been reported in a small number of patients after overdosage with amoxicillin. Crystalluria, in some cases leading to renal failure, has also been reported after amoxicillin overdosage in adult and pediatric patients. In case of overdosage, adequate fluid intake and diuresis should be maintained to reduce the risk of amoxicillin crystalluria. Renal impairment appears to be reversible with cessation of drug administration. High blood levels may occur more readily in patients with impaired renal function because of decreased renal clearance of both amoxicillin and clavulanate. Both amoxicillin and clavulanate are removed from the circulation by hemodialysis.

PHARMACOLOGY
Co-amoxiclav is an antibiotic agent with a notably broad spectrum of activity against the commonly occurring bacterial pathogens in general practice and hospital setting. The novel action of clavulanate extends the spectrum of amoxicillin to embrace a wider range of organisms, including many resistant to other ß-lactam antibiotics. Co-amoxiclav is bactericidal to a wide range of organisms.

PHARMACOLOGICAL ACTION
Co-amoxiclav 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 in Co-amoxiclav 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 as Co-amoxiclav it produces a novel broad spectrum antibiotic agent (of broad spectrum) with wide application in hospital and general practice.

MECHANISM OF ACTION
In vitro and in vivo evidence suggests that clavulanic acid, a potent inhibitor of many bacterial beta-lactamase enzymes, will increase the spectrum of amoxicillin to include, at achievable serum concentrations, *Haemophilus influenzae, H. ducreyi, Neisseria gonorrhoeae, Staphylococcus aureus and Branhamella catarrhalis* and, at achievable urine levels, many beta-lactamase-producing strains of *E.coli, Klebsiella, Proteus and Citrobacter.*

Clavulanic acid is a beta-lactamase inhibitor sometimes combined with penicillin group antibiotics to overcome certain types of antibiotic resistance. Specifically, it is used to overcome resistance in bacteria that secrete beta-lactamase enzymes, which otherwise inactivate most penicillins. Most commonly, the potassium salt potassium clavulanate is combined with amoxicillin (Co-amoxiclav) or ticarcillin. Clavulanic acid has negligible intrinsic antimicrobial activity, despite sharing the ß-lactam ring that is characteristic of beta-lactam antibiotics. However, the similarity in chemical structure allows the molecule to act as a competitive inhibitor of beta-lactamases secreted by certain bacteria to confer resistance to beta-lactam antibiotics. This inhibition restores the antimicrobial activity of beta-lactam.

PHARMACOKINETIC DATA
The pharmacokinetics of the two components of Co-amoxiclav are closely matched. Peak serum levels of both occur about 1 hour after oral administration. The elimination half-lives of amoxicillin and clavulanic acid both range from 60-80 minutes. Following administration, approximately 70% of the dose of amoxicillin is excreted as amoxicillin and approximately 30-40% of an oral dose of clavulanic acid is excreted in the urine as clavulanic acid, during the first six hours after administration. Smaller amounts of two metabolites of clavulanic acid, 1-amino-4-hydro-xybutan-2-one and 2, 5- dihydro-4-(2-hydroxyethyl)-5-oxo-1H-pyrrole-3-carboxylic acid have also been identified in the urine. Clavulanic acid has been found to be approximately 13% bound to human serum and amoxicillin approximately 20%.

In patients with moderate or severe renal impairment, Co-amoxiclav dosage should be adjusted as recommended in the Dosage and Administration section. Co-amoxiclav may be taken at the start of meals with no effect on its absorption. Co-amoxiclav should be used with care in patients with severe hepatic dysfunction.

Doubling the dosage of Co-amoxiclav approximately doubles the serum levels achieved.

TOXICOLOGY
An Unusual Case of Amoxicillin/Clavulanic Acid-Related Hepatotoxicity
M.G. Nathani, M.D.a, M.G. Mutchnick, M.D., F.A.C.G.a, D.J. Tynes, M.D.a, and M.N. Ehrinpreis, M.D., F.A.C.G.a

Amoxicillin/clavulanic acid is a widely used antibiotic. Hepatic dysfunction is a rare adverse reaction associated with this combination antibiotic. We report the case of a 40-yr-old woman with a somewhat unusual presentation of amoxicillin/clavulanate-related cholestatic hepatotoxicity and multiple duodenal erosions whose diagnosis was delayed until inadvertent re-challenge with the antibiotic combination. The relevant literature is also reviewed and discussed. The diagnosis may be missed because the onset of signs/symptoms may occur several weeks after the cessation of therapy.

The hepatic dysfunction, which may be severe and is more prevalent in elderly patients, is usually reversible, although chronic liver disease and deaths have been reported. Immunological hypersensitivity is considered to be the most likely mechanism resulting in liver injury. Amoxicillin/clavulanate should be used with caution in patients with underlying liver disease and in the elderly.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate carcinogenic potential. The mutagenic potential of Co-amoxiclav was investigated in vitro with an Ames test, a human lymphocyte cytogenetic assay, a yeast test, and a mouse lymphoma forward mutation assay, and in vivo with mouse micronucleus tests and a dominant lethal test. All were negative apart from the in vitro mouse lymphoma assay, where weak activity was found at very high, cytotoxic concentrations.

Co-amoxiclav at oral doses of up to 1,200 mg/kg/day (1.9 times the maximum human dose of amoxicillin and 15 times the maximum human dose of clavulanate based on body surface area) was found to have no effect on fertility and reproductive performance in rats dosed with a 2:1 ratio formulation of amoxicillin-clavulanate.

Preclinical safety data
a) Acute toxicity
Investigations of the acute toxicity (LD50) of amoxicillin and clavulanic acid in adult animals and neonates have confirmed very low toxicity potential. The LD50 of clavulanic acid (potassium salt) is determined by the potassium content. Administration of clavulanic acid

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■ BLACK		**290 mm x 220 mm**

(potassium salt) together with amoxicillin does not result in any unexpected or synergistic toxicity.

b) Chronic toxicity /subchronic toxicity

Not relevant.

c) Mutagenic and tumorigenic potential

In vitro and in vivo studies did not reveal any signs of any mutagenic effects of the combination of amoxicillin and clavulanic acid.

d) Reproductive toxicity

After treatment of various infections in pregnant women (approximately 560 pregnancies) with Amoxicillin and Potassium Clavulanate no increased occurrence of malformations was observed. Amoxicillin and clavulanic acid diffuse through the placenta and are excreted into the breast.

CAUTION

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

STORAGE

Store at temperatures not exceeding 30°C.
Keep out of reach of children.

AVAILABILITY

Co-Amoxiclav
500 mg/125 mg Film-Coated Tablet: Alu/Alu Blister Pack x 6's (Box of 48's)
Co-Amoxiclav
875 mg/125 mg Film-Coated Tablet: Alu/Alu Blister Pack x 6's (Box of 48's)

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.

Co-Amoxiclav (Natravox®) 625 mg (DRP-10090-02)
Date of Authorization: 27 APR 2026
Co-Amoxiclav (Natravox®) 1 g (DRP-7046-03)
Date of Authorization: 22 APR 2026
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DUMMY

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