

COMPOSITION :

NEOCLAV-625 :

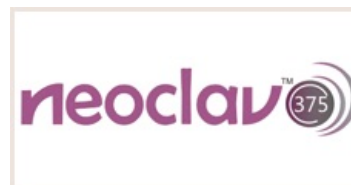
Each film coated tablet contains :



Amoxicillin Trihydrate IP equivalent to Amoxicillin	500 mg.
Potassium clavulanate IP equivalent to Clavulanic acid	125 mg.

NEOCLAV-375 :

Each film coated tablet contains :



Amoxicillin Trihydrate IP equivalent to Amoxicillin	250 mg.
Potassium clavulanate IP equivalent to Clavulanic acid	125 mg.

NEOCLAV SYRUP :

Each 5 ml of reconstituted suspension contains :



Amoxicillin Trihydrate IP equivalent to Amoxicillin	200 mg.
Potassium clavulanate IP equivalent to Clavulanic acid	28.5 mg.

NEOCLAV is an oral antibacterial combination consisting of the semisynthetic antibiotic amoxicillin and the β -lactamase inhibitor clavulanic acid.

MECHANISM OF ACTION :

NEOCLAV is an oral antibacterial combination consisting of the semisynthetic antibiotic amoxicillin and the β -lactamase inhibitor clavulanate potassium (the potassium salt of clavulanic acid).

Amoxicillin : Amoxicillin is an analog of ampicillin, derived from the basic penicillin nucleus 6-aminopenicillanic acid. It inhibits cross-linkage between the linear peptidoglycan polymer chains that make up a major component of the cell walls of both Gram-positive and Gram-negative bacteria. Amoxicillin inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Bacteria eventually lyse due to ongoing activity of cell wall autolytic enzymes (autolysins and murein hydrolases) while cell wall assembly is arrested.

Clavulanic acid is a β -lactam structurally related to the penicillins and possesses the ability to inactivate a wide variety of β -lactamases by blocking the active sites of these enzymes. Clavulanic acid is particularly active against the clinically important plasmid-mediated β -lactamases frequently responsible for transferring drug resistance to penicillins and cephalosporins.

Rationale for combination : Amoxicillin is susceptible to degradation by β -lactamases. The clavulanic acid component of NEOCLAV protects amoxicillin from degradation by β -lactamase enzymes and effectively extends the antibiotic spectrum of amoxicillin to include many bacteria normally resistant to amoxicillin and other β -lactam antibiotics.

INDICATIONS :

NEOCLAV formulations are indicated for the treatment of infections caused by amoxicillin resistant organisms producing beta-lactamases sensitive to clavulanic acid: Upper respiratory tract infections, such as sinusitis, recurrent otitis media, tonsillitis. Lower respiratory tract infections, such as bronchitis (caused by amoxicillin resistant beta-lactamase producing *Escherichia coli*, *Haemophilus influenzae* and *Haemophilus para-influenzae*), bronchopneumonia. Genito-urinary tract infections, such as cystitis, urethritis, pyelonephritis. Skin and soft tissue infections.

NEOCLAV formulations will also be effective in the treatment of infections caused by amoxicillin sensitive organisms at the appropriate amoxicillin dosage since in this situation the clavulanic acid component does not contribute to the therapeutic effect.

DOSAGE AND DIRECTIONS FOR USE :

Tablets should be taken immediately before a meal.

Dosages:

General Information:

For infections caused by amoxicillin-sensitive organisms the dosage is that approved for amoxicillin as the clavulanic acid component does not contribute to the therapeutic effect.

Adult:

The adult dose for **NEOCLAV** is one or two **NEOCLAV 375** tablet(s) every eight hours at the start of a meal. For more severe infections and infection of the respiratory tract, the dose should be one **NEOCLAV 625** tablet every eight hours at the start of a meal.

Since **NEOCLAV 375** and **625** tablets contain the same amount of clavulanic acid (125 mg, as the potassium salt), two **NEOCLAV 375** tablets are not equivalent to one **NEOCLAV 625** tablet. Therefore, two **NEOCLAV 375** tablets should not be substituted for one **NEOCLAV 625** tablet for the treatment of more severe infections.

DOSAGE GUIDE:

AMOXYCILLIN SENSITIVE ORGANISMS

PRODUCT	UPPER RESPIRATORY TRACT INFECTIONS	LOWER RESPIRATORY TRACT INFECTIONS	URINARY TRACT INFECTIONS	SKIN AND SOFT TISSUE INFECTIONS
ADULTS:				
NEOCLAV 375	1 - 2 tablets 8 hourly	1 - 2 tablets 8 hourly	1 - 2 tablets 8 hourly	1 - 2 tablets 8 hourly
NEOCLAV 625	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly

AMOXYCILLIN RESISTANT ORGANISMS

PRODUCT	UPPER RESPIRATORY TRACT INFECTIONS (otitis media) H. influenzae H. para influenzae	LOWER RESPIRATORY TRACT INFECTIONS (bronchitis) H. influenzae H. para influenzae	URINARY TRACT INFECTIONS E. coli Klebsiella pneumoniae	SKIN AND SOFT TISSUE INFECTIONS Staphylococcus aureus
ADULTS:				
NEOCLAV 375	2 tablets 8 hourly	2 tablets 8 hourly	2 tablets 8 hourly	2 tablets 8 hourly
NEOCLAV 625	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly

CONTRA-INDICATIONS :

In patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins. Safety in pregnancy has not been established. There is limited information on the use of **NEOCLAV** in human pregnancy.

Use should be avoided in pregnancy unless considered essential by the physician. **NEOCLAV** is contra-indicated in patients with a previous history of **NEOCLAV**-associated jaundice/hepatic dysfunction.

ADVERSE EFFECTS :

The majority of side effects observed were of a mild and transient nature. The most frequently reported adverse effects which were suspected or probably drug-related were diarrhea (14.5%), vaginal mycosis (3.3%) nausea (2.1%), and loose stools (1.6%).

Other adverse effects that are common for the ampicillin group of antibiotics and may occur during use of amoxicillin are: GI effects like diarrhea, nausea, vomiting, indigestion, gastritis, stomatitis, glossitis, black "hairy" tongue, mucocutaneous candidiasis, enterocolitis, and hemorrhagic/pseudo-membranous colitis; Hypersensitivity reactions like skin rashes, pruritus, urticaria, angioedema, serum sickness-like reactions; A moderate rise in AST (SGOT) and/or ALT (SGPT), interstitial nephritis and hematuria; CNS effects like agitation, anxiety, behavioral changes, confusion, convulsions, dizziness, headache, insomnia.

WARNINGS / PRECAUTIONS :

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.

Prolonged use may result in fungal or bacterial super infection, including *C. difficile*-associated diarrhea (CDAD) and pseudo-membranous colitis; CDAD has been observed >2 months post antibiotic treatment.

While amoxicillin/clavulanate potassium combination possesses the characteristic low toxicity of the penicillin group of antibiotics, periodic assessment

of organ system functions, including renal, hepatic, and hematopoietic function, is advisable if therapy is for longer than the drug is approved for administration.

DRUG INTERACTIONS :

Allopurinol: The concurrent administration of allopurinol may increase the incidence of rashes in patients receiving both drugs as compared to patients receiving amoxicillin alone.

BCG Vaccine: Antibiotics may diminish the therapeutic effect of BCG.

Fusidic Acid: May diminish the therapeutic effect of Penicillins.

Methotrexate: Penicillins may decrease the excretion of Methotrexate.

Mycophenolate: Penicillins may decrease serum concentrations of the active metabolite(s) of Mycophenolate. This effect appears to be the result of impaired enterohepatic recirculation.

Oral Contraceptives: In common with other broad-spectrum antibiotics, amoxicillin may reduce the efficacy of oral contraceptives.

Probenecid: decreases the renal tubular secretion of amoxicillin. Concurrent use with amoxicillin may result in increased and prolonged blood levels of amoxicillin. Co-administration of probenecid cannot be recommended.

Tetracycline Derivatives: May diminish the therapeutic effect of Penicillins.

Typhoid Vaccine: Antibiotics may diminish the therapeutic effect of Typhoid Vaccine. Only the live attenuated Ty21a strain is affected.

PACKAGING INFORMATION :

NEOCLAV-625: Available in a strip of 6 tablets.

NEOCLAV-375: Available in a strip of 6 tablets.

NEOCLAV SYRUP: Available in 30 ml bottle pack.