

ABClo_x-CV 625 Tablet/ ABClo_x-CV Dry Syrup

Amoxycillin & Potassium Clavulanate

COMPOSITION

ABClo_x-CV 625 Tablet

Each film-coated tablet contains:	
Amoxycillin Trihydrate IP equivalent to Amoxycillin	500mg
Potassium Clavulanate IP equivalent to Clavulanic Acid	125mg
Colour: Titanium dioxide	

ABClo_x-CV Dry Syrup

Each 5ml of reconstituted suspension contains:	
Amoxycillin Trihydrate IP equivalent to Amoxycillin	200mg
Potassium Clavulanate IP equivalent to Clavulanic Acid	28.5mg
Colour: Titanium dioxide	

CLINICAL PHARMACOLOGY

Pharmacodynamics

ABClo_x-CV is an oral antibacterial combination consisting of the semisynthetic antibiotic Amoxycillin and the β -lactamase inhibitor, clavulanate potassium (the potassium salt of clavulanic acid). Amoxycillin has a broad spectrum of bactericidal activity against many gram-positive and gram-negative microorganisms. Amoxycillin is, however, susceptible to degradation by β -lactamases, and therefore, the spectrum of activity does not include organisms which produce these enzymes.

Clavulanic acid is a β -lactam, structurally related to the penicillins. It possesses the ability to inactivate a wide range of β -lactamase enzymes commonly found in microorganisms resistant to penicillins and cephalosporins. In particular, it has good activity against the clinically important plasmid-mediated β -lactamases frequently responsible for transferred drug resistance.

The formulation of Amoxycillin and clavulanic acid in **ABClo_x-CV** protects Amoxycillin from degradation by β -lactamase enzymes and effectively extends the antibiotic spectrum of Amoxycillin to include many bacteria normally resistant to Amoxycillin and other β -lactam antibiotics. Thus, **ABClo_x-CV** possesses the properties of a broad-spectrum antibiotic and a β -lactamase inhibitor.

Microbiology

Amoxycillin/clavulanic acid has been shown to be active against most strains of the following microorganisms, both *in vitro* and in clinical infections:

Gram-Positive Aerobes:

- *Staphylococcus aureus* (β -lactamase & non- β -lactamase-producing)

Note: Staphylococci which are resistant to methicillin/oxacillin must be considered resistant to Amoxycillin/clavulanic acid.

Gram-Negative Aerobes:

- *Enterobacter species* (Although most strains of *Enterobacter species* are resistant *in vitro*, clinical efficacy has been demonstrated with **ABClo_x-CV** in urinary tract infections caused by these organisms.)

- *Escherichia coli* (β -lactamase & non- β -lactamase-producing)
- *Haemophilus influenzae* (β -lactamase & non- β -lactamase-producing)
- *Klebsiella species* (All known strains are β -lactamase-producing.)
- *Moraxella catarrhalis* (β -lactamase & non- β -lactamase-producing)

The following *in vitro* data are available, but their clinical significance is unknown. Amoxicillin/clavulanic acid exhibits *in vitro* minimal inhibitory concentrations (MICs) of 2 mcg/mL or less against most strains of *Streptococcus pneumoniae*; MICs of 0.06 mcg/mL or less against most strains of *Neisseria gonorrhoeae*; MICs of 4 mcg/mL or less against most strains of staphylococci and anaerobic bacteria; and MICs of 8 mcg/mL or less against most strains of other listed organisms. However, with the exception of organisms shown to respond to Amoxicillin alone, the safety and effectiveness of Amoxicillin/clavulanic acid in treating clinical infections due to these microorganisms have not been established in well-controlled clinical trials. Note: Amoxicillin has greater *in vitro* activity against *S. pneumoniae* than ampicillin or penicillin. Therefore the majority of *S. pneumoniae* strains with intermediate susceptibility to ampicillin/penicillin are susceptible to Amoxicillin.

Gram-Positive Aerobes:

- *Enterococcus faecalis*
- *Staphylococcus epidermidis* (β -lactamase & non- β -lactamase-producing)
- *Staphylococcus saprophyticus* (β -lactamase & non- β -lactamase-producing)
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- Viridans group *Streptococcus*

Gram-Negative Aerobes:

- *Eikenella corrodens* (β -lactamase & non- β -lactamase-producing)
- *Neisseria gonorrhoeae* (β -lactamase & non- β -lactamase-producing)
- *Proteus mirabilis* (β -lactamase & non- β -lactamase-producing)

Anaerobic Bacteria:

- Bacteroides species, including *Bacteroides fragilis* (β -lactamase & non- β -lactamase producing)
- *Fusobacterium species* (β -lactamase & non- β -lactamase-producing)
- *Peptostreptococcus species*

Pharmaokinetics

Amoxicillin and clavulanate potassium are well absorbed from the gastrointestinal tract after oral administration. Dosing in the fasted or fed state has minimal effect on the pharmacokinetics of Amoxicillin. While Amoxicillin and clavulanate potassium can be given without regard to meals, absorption of clavulanate potassium when taken with food is greater relative to the fasted state.

Mean Amoxicillin and clavulanate potassium pharmacokinetic parameters are shown in the table below:

Dose & regimen	AUC ₀₋₂₄ (mcg•hr/mL)		C _{max} (mcg/mL)	
	Amoxicillin (± S.D.)	clavulanate potassium (± S.D.)	Amoxicillin (± S.D.)	clavulanate potassium (± S.D.)
500/125 mg q12h	33.4 ± 6.76	8.6 ± 1.95	6.5 ± 1.41	1.8 ± 0.61
500/125 mg q8h	53.4 ± 8.87	15.7 ± 3.86	7.2 ± 2.26	2.4 ± 0.83

Amoxicillin serum concentrations achieved with **ABCloxCV** are similar to those produced by the oral administration of equivalent doses of Amoxicillin alone. The half-life of Amoxicillin after the oral administration of **ABCloxCV** is 1.3 hours and that of clavulanic acid is 1.0 hour.

Approximately 50% to 70% of the Amoxicillin and approximately 25% to 40% of the clavulanic acid are excreted unchanged in urine during the first 6 hours after administration.

Neither component in **ABCloxCV** is highly protein-bound; clavulanic acid has been found to be approximately 25% bound to serum proteins and Amoxicillin approximately 18% bound.

Amoxicillin diffuses readily into most body tissues and fluids with the exception of the brain and spinal fluid. The results of experiments involving the administration of clavulanic acid to animals suggest that this compound, like Amoxicillin, is well distributed in body tissues.

INDICATIONS

ABCloxCV tablets/Syrup is indicated in the treatment of infections caused by susceptible strains of the designated organisms in the conditions listed below:

Lower Respiratory Infections

Caused by β -lactamase-producing strains of *H. influenzae* and *M. catarrhalis*.

Otitis Media

Caused by β -lactamase-producing strains of *H. influenzae* and *M. catarrhalis*.

Sinusitis

Caused by β -lactamase-producing strains of *H. influenzae* and *M. catarrhalis*.

Skin and Skin Structure Infections

Caused by β -lactamase-producing strains of *S. aureus*, *E. coli*, and *Klebsiella* spp.

Urinary Tract Infections

Caused by β -lactamase-producing strains of *E. coli*, *Klebsiella* spp., and *Enterobacter* spp.

Note: Because Amoxicillin has greater *in vitro* activity against *S. pneumoniae* than does ampicillin or penicillin, the majority of *S. pneumoniae* strains with intermediate susceptibility to ampicillin or penicillin are fully susceptible to Amoxicillin and **ABCloxCV**.

DOSAGE & ADMINISTRATION

ABCloxCV 625 tablet

Adults & Children >12 years

The usual dose is one **ABCloxCV 625 tablet**, every 12 hours. For more severe infections and infections of the lower respiratory tract, the dose should be one **ABCloxCV 625 tablet**, every 8 hours. Treatment should not be extended beyond 14 days without review.

Renal Impairment

Adults

Patients with impaired renal function do not generally require a reduction in dose unless the impairment is severe.

Mild impairment (Creatinine clearance >30 mL/min)	No change in dosage
Moderate impairment (Creatinine clearance 10-30 mL/min)	One ABCloxCV 625 tablet every 12 hours
Severe impairment (Creatinine clearance <10 mL/min)	Not more than one ABCloxCV 625 tablet every 24 hours

Hemodialysis patients should receive **ABCloxx-CV 625 tablet** every 24 hours, depending on severity of the infection. They should receive an additional dose both during and at the end of dialysis.

Hepatic Impairment

Dose with caution; monitor hepatic function at regular intervals.

ABCloxx-CV 625 tablets are not recommended for children of 12 years and under.

ABCloxx-CV Dry Syrup

Children ≤12 years

Children weighing 40 kg or more should be dosed according to adult recommendations.

Children over 6 years upto 12 years

One teaspoonful [tsf] of **ABCloxx-CV** reconstituted suspension 228 mg/5 mL three times a day.

Children aged 12 weeks (3 months) to 6 years

Mild to Moderate infections	25/3.6 mg/kg/day	b.i.d
Severe Infections & Otitis media, Sinusitis, Lower Respiratory Infections	45/6.4 mg/kg/day	b.i.d

Infants with immature kidney function

For infants with immature renal function **ABCloxx-CV** reconstituted suspension 228 mg/5 mL is not recommended.

Renal Impairment

For children with GFR >30 mL/min no adjustment in dosage is required. For children with GFR <30 mL/min **ABCloxx-CV** reconstituted suspension 228/5 mL is not recommended.

Hepatic impairment

Dose with caution; monitor hepatic function at regular intervals. There are, as yet, insufficient data on which to base a dosage recommendation.

Administration

ABCloxx-CV 625 tablets should be swallowed whole without chewing. **ABCloxx-CV tablets/Suspension** may be taken without regard to meals; however, absorption of clavulanate potassium is enhanced when Amoxicillin and clavulanate potassium are administered at the start of a meal. To minimize the potential for gastrointestinal intolerance, **ABCloxx-CV** should be taken at the start of a meal.

CONTRAINDICATIONS

ABCloxx-CV is contraindicated in patients with a history of allergic reactions to any penicillin. It is also contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with Amoxicillin-clavulanate.

WARNINGS

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.

Before initiating therapy with **ABCloxx-CV**, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, **ABCloxx-CV** should be discontinued and the appropriate therapy instituted.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including Amoxicillin and clavulanate potassium, and has ranged in severity from mild to life-threatening. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

ABCloxx-CV should be used with caution in patients with evidence of hepatic dysfunction. Hepatic toxicity associated with the use of **ABCloxx-CV** is usually reversible.

PRECAUTIONS

- While Amoxicillin and clavulanate potassium 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 during prolonged therapy.
- A high percentage of patients with mononucleosis who receive ampicillin develop an erythematous skin rash. Thus, ampicillin-class antibiotics should not be administered to patients with mononucleosis.
- 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 **ABCloxx-CV** 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.

DRUG INTERACTIONS

Probenecid: Probenecid decreases the renal tubular secretion of Amoxicillin. Concurrent use with **ABCloxx-CV** may result in increased and prolonged blood levels of Amoxicillin.

Allopurinol: The concurrent administration of allopurinol and ampicillin increases substantially the incidence of rashes in patients receiving both drugs as compared to patients receiving ampicillin alone. There are no data with Amoxicillin and clavulanate potassium and allopurinol administered concurrently.

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

Anticoagulants: Prolongation of bleeding time and prothrombin time have been reported in some patients receiving amoxicillin/clavulanic acid. **ABCloxx-CV** should be used with care in patients on anti-coagulation therapy.

Drug/Laboratory Test Interactions

Oral administration of **ABCloxx-CV** will result in high urine concentrations of Amoxicillin. High urine concentrations of ampicillin may result in false-positive reactions when testing for the presence of glucose in urine using Clinitest, Benedict's Solution, or Fehling's Solution. Since this effect may also occur with Amoxicillin and therefore **ABCloxx-CV**, it is recommended that glucose tests based on enzymatic glucose oxidase reaction be used.

Following administration of ampicillin to pregnant women, a transient decrease in plasma concentration of total conjugated estriol, estriol-glucuronide, conjugated

estrone, and estradiol has been noted. This effect may also occur with Amoxycillin and therefore **ABClo_x-CV**.

Pregnancy (Category B)

There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Lactation

Ampicillin-class antibiotics are excreted in the milk; therefore, caution should be exercised when **ABClo_x-CV** is administered to a nursing woman.

Pediatrics Use

As per directions given in **DOSAGE & ADMINISTRATION**.

Geriatric Use

ABClo_x-CV is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. 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.

ADVERSE REACTIONS

ABClo_x-CV is generally well tolerated. The majority of side effects observed in clinical trials were of a mild and transient nature and less than 3% of patients discontinued therapy because of drug-related side effects. The most frequently reported adverse effects were diarrhea/loose stools, nausea, skin rashes and urticaria, vomiting, and vaginitis. Other less frequently reported reactions include: Abdominal discomfort, flatulence, and headache

PRESENTATION

ABClo_x-CV 625 Tablet is available in aluminium foil pack of 6's

ABClo_x-CV Dry Syrup is available in 30 ml bottles

STORAGE

Store at 20° to 25°C (68° to 77°F)