# Clamox Film-Coated Tablets 1g

## Co-amoxiclav Tablets 875 mg/125 mg

**PRODUCT NAME**
Clamox Film-Coated Tablets 1g

**NAME AND STRENGTH OF ACTIVE SUBSTANCE(S):**
Amoxicillin 875mg and Clavulanic Acid 125mg

**PRODUCT DESCRIPTION:**
White to off white capsule shaped, biconvex tablets de bossed with "I 07" on one side and plain on the other side

**LIST OF EXCIPIENTS:**
Microcrystalline Cellulose,
Colloidal Silicon Dioxide,
Magnesium Stearate,
Sodium Starch Glycolate,
Colloidal Silicon Dioxide,
Opadry 21H580002 White (Hypromellose, Titanium Dioxide, Propylene Glycol, Talc, Ethyl cellulose).

**PHARMACODYNAMICS/PHARMACOKINETICS:**
***Pharmacodynamics:***
Resistance to many antibiotics is caused by bacterial enzymes which destroy the antibiotic before it can act on the pathogen. The clavulanate in amoxicillin/clavulanic acid anticipates this defence mechanism by blocking the beta-lactamase enzymes, thus rendering the organisms susceptible 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 amoxicillin/clavulanic acid it produces an antibiotic agent of broad spectrum with wide application in hospital and general practice.
In the list below, organisms are categorised according to their *in vitro* susceptibility to amoxicillin/clavulanic acid.
*In vitro* susceptibility of micro-organisms to amoxicillin/clavulanic acid
Where clinical efficacy of amoxicillin/clavulanic acid has been demonstrated in clinical trials this is indicated with an asterisk (*).
Organisms that do not produce beta-lactamase are identified (with †). If an isolate is susceptible to amoxicillin, it can be considered susceptible to amoxicillin/clavulanic acid.
**Commonly susceptible species**
**Gram-positive aerobes:**
*Bacillius anthracis*
*Enterococcus faecalis*
*Gardnerella vaginalis*
*Listeria monocytogenes*
*Streptococcus pneumoniae*†*
*Streptococcus pyogenes*†*
*Streptococcus agalactiae*†*
*Viridans group streptococcus*†
*Streptococcus spp. (other beta-hemolytic)*†*
*Staphylococcus aureus (methicillin susceptible)**
*Staphylococcus saprophyticus (methicillin susceptible)*
*Coagulase negative staphylococcus (methicillin susceptible)*
**Gram-negative aerobes:**
*Bordetella pertussis*
*Haemophilus influenzae**
*Helicobacter pylori*
*Moraxella catarrhalis**
*Neisseria gonorrhoeae*
*Pasteurella multocida*
*Vibrio cholerae*
**Gram-positive anaerobes:**
*Clostridium spp.*
*Peptococcus niger*
*Peptostreptococcus magnus*
*Peptostreptococcus micros*
*Peptostreptococcus spp.*
**Gram-negative anaerobes:**
*Bacteroides fragilis*
*Bacteroides spp.*
*Fusobacterium nucleatum*
*Fusobacterium spp.*
**Species for which acquired resistance may be a problem**
**Gram-negative aerobes:**
*Escherichia coli**
*Klebsiella oxytoca*
*Klebsiella pneumoniae**
*Klebsiella spp.*
*Proteus mirabilis*
*Proteus vulgaris*
*Proteus spp.*
*Salmonella spp.*
*Shigella spp.*
**Gram-positive aerobes:**
*Corynebacterium spp.*
*Enterococcus faeciium*
**Inherently resistant organisms**
**Gram-negative aerobes:**
*Acinetobacter spp.*
*Citrobacter freundii*
*Enterobacter spp.*
*Hafnia alvei*
*Legionella pneumophila*
*Morganella morganii*
*Providencia spp.*
*Pseudomonas spp.*
*Serratia spp.*
*Stenotrophomas maltophilia*
*Yersinia enterolitica*
**Others:**
*Chlamydia pneumoniae*
*Chlamydia psittaci*
*Chlamydia spp.*
*Coxiella burnetti*
*Mycoplasma spp.*

***Pharmacokinetics:***
The pharmacokinetics of the two components of amoxicillin/clavulanic acid are closely matched. Peak serum levels of both occur about 1 hour after oral administration. Absorption of amoxicillin/clavulanic acid is optimized at the start of a meal.
Doubling the dosage of amoxicillin/clavulanic acid approximately doubles the serum levels achieved.
Both clavulanate and amoxicillin have low levels of serum binding; about 70% remains free in the serum.

**INDICATIONS:**
Amoxicillin/clavulanic acid 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.
Amoxicillin/clavulanic acid should be used in accordance with local official antibiotic-prescribing guidelines and local susceptibility data.
Amoxicillin/clavulanic acid oral presentations for twice daily dosing, are indicated for short-term treatment of bacterial infections at the following sites:
*Upper respiratory tract infections (including ENT)* e.g. tonsillitis, sinusitis, otitis media.
*Lower respiratory tract infections* e.g. acute exacerbation of chronic bronchitis, lobar and bronchopneumonia.
*Genito-urinary tract infections* e.g. cystitis, urethritis, pyelonephritis.
*Skin and soft tissue infections* e.g. boils, abscesses, cellulitis, wound infections.
*Bone and joint infections* e.g. osteomyelitis.
*Dental infections* e.g. dentoalveolar abscess, pericoronitis, acute periodontitis.
*Other infections* e.g. septic abortion, puerperal sepsis, intra-abdominal sepsis.
Susceptibility to amoxicillin/clavulanic acid will vary with geography and time (see *Pharmacological Properties, Pharmacodynamics* for further information). Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

**RECOMMENDED DOSAGE:**
Dosage depends on the age and renal function of the patient and the severity of the infection.
To minimise potential gastrointestinal intolerance, administer at the start of a meal. The absorption of amoxicillin/clavulanic acid is optimised when taken at the start of a meal.
Treatment should not be extended beyond 14 days without review.
Therapy can be started parenterally and continued with an oral preparation.
Amoxicillin/clavulanic acid tablets are not recommended in children of 12 years and under.

***Adults and Children over 12 years***
The usual recommended daily dosage is:

| | |
|---|---|
| Severe infections | One amoxicillin/clavulanic acid 1 g tablet every 12 hours. |

**Renal Impairment**
No adjustment in dose is required in patients with creatinine clearance (CrCl) greater than 30 mL/min. The amoxicillin/clavulanic acid 1g tablet should only be used in patients with a creatinine clearance (CrCl) rate of more than 30 mL/min.

**Hepatic Impairment**
Dose with caution; monitor hepatic function at regular intervals.

**MODE/ROUTE OF ADMINISTRATION:**
Amoxicillin/clavulanic acid is for oral use.

**CONTRAINDICATIONS:**
Amoxicillin/clavulanic acid is contraindicated in patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.
Amoxicillin/clavulanic acid is contraindicated in patients with a previous history of amoxicillin/clavulanic acid -associated jaundice/hepatic dysfunction.

**WARNING AND PRECAUTIONS:**
Before initiating therapy with amoxicillin/clavulanic acid, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens.
Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity (see *Contraindications*).
Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction. Presenting symptoms of such reactions can include chest pain occurring in association with an allergic reaction to Amoxicillin/clavulanic (see Adverse Reactions).
If an allergic reaction occurs, amoxicillin/clavulanic acid therapy must be discontinued and appropriate alternative therapy instituted.
Serious anaphylactic reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous (i.v.) steroids and airway management (including intubation) may also be required.
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.
Prolonged use may also occasionally result in overgrowth of non-susceptible organisms.
Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant

diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.
Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin/clavulanic acid and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.
Changes in liver function tests have been observed in some patients receiving amoxicillin/clavulanic acid. The clinical significance of these changes is uncertain. Amoxicillin/clavulanic acid should be used with caution in patients with evidence of hepatic dysfunction.
Cholestatic jaundice, which may be severe, but is usually reversible, has been reported rarely. Signs and symptoms may not become apparent for up to six weeks after treatment has ceased.
In patients with renal impairment, amoxicillin/clavulanic acid dosage should be adjusted as recommended in the *Dosage and Administration* section.
In patients with reduced urine output, crystalluria has been observed very rarely, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria (see *Overdose*).

**INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION:**
Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use with amoxicillin/clavulanic acid may result in increased and prolonged blood levels of amoxicillin but not of clavulanate.
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 amoxicillin/clavulanic acid and allopurinol.
In common with other antibiotics, amoxicillin/clavulanic acid may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.
In the literature there are rare 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/clavulanic acid.
In patients receiving Mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid 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.

**PREGNANCY AND LACTATION:**
Reproduction studies in animals (mice and rats) with orally and parenterally administered amoxicillin/clavulanic acid have shown no teratogenic effects. In a single study in women with preterm, premature rupture of the foetal membrane (pPROM), it was reported that prophylactic treatment with amoxicillin/clavulanic acid 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.
Amoxicillin/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 for the infant.
**Effects on Ability to Drive and Use Machines**
Adverse effects on the ability to drive or operate machinery have not been observed.

**ADVERSE EFFECTS/UNDESIRABLE EFFECTS:**
Data from large clinical trials were used to determine the frequency of very common to rare undesirable effects. The frequencies assigned to all other undesirable effects (i.e., those occurring at <1/10,000) were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.
The following convention has been used for the classification of frequency:
very common ≥1/10
common ≥1/100 to <1/10
uncommon ≥1/1000 to <1/100
rare ≥1/10,000 to <1/1000
very rare <1/10,000.
**Infections and infestations**
Common Mucocutaneous candidiasis

**Blood and lymphatic system disorders**
Rare: Reversible leucopenia (including neutropenia) and thrombocytopenia
Very; rare Reversible agranulocytosis and haemolytic anaemia. Prolongation of bleeding time and prothrombin time.
**Immune system disorders**
Very rare : Angioneurotic oedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis.
**Nervous system disorders**
Uncommon Dizziness, headache
Very rare: Reversible hyperactivity, aseptic meningitis, convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.
**Cardiac disorders**
Very rare Kounis syndrome (see Warnings and Precautions).
**Gastrointestinal disorders**
***Adults***
Very common: Diarrhoea
Common: Nausea, vomiting
***Children***
Common Diarrhoea, nausea, vomiting
***All populations***
Nausea is more often associated with higher oral dosages. If gastrointestinal reactions are evident, they may be reduced by taking amoxicillin/clavulanic acid at the start of a meal.
Uncommon: Indigestion
Very rare: Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis – see *Warnings and Precautions*).
Black hairy tongue
**Hepatobiliary disorders**
Uncommon: A moderate rise in AST and/or ALT has been noted in patients treated with beta-lactam class antibiotics, but the significance of these findings is unknown.
Very rare: Hepatitis and cholestatic jaundice. These events have been noted with other penicillins and cephalosporins.
Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been very rarely reported in children.
Signs and symptoms usually occur during or shortly after treatment but in some cases may not become apparent until several weeks after treatment has ceased. These are usually reversible. Hepatic events may be severe and in extremely rare circumstances, deaths have been reported. These have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects.
**Skin and subcutaneous tissue disorders**
Uncommon: Skin rash, pruritus, urticaria
Rare: Erythema multiforme
Very rare: Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthematous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS)
If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued.
**Renal and urinary disorders**
Very rare: Interstitial nephritis, crystalluria (see *Overdose*)

**OVERDOSE AND TREATMENT:**
Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. Gastrointestinal symptoms may be treated symptomatically with attention to the water-electrolyte balance.
Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see Warnings and Precautions).
Amoxicillin/clavulanic acid can be removed from the circulation by haemodialysis.

**STORAGE:**
Store below 30ºC, protect from moisture. Keep out from the reach of children.

**SHELF LIFE:**
12 months

**DOSAGE FORMS OR PRESENTATION:**
Film coated tablets
Alu-Alu blisters (10's)

**NAME AND ADDRESS OF MANUFACTURER:**
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