100x150 mm **Front**

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

Rx AMOXYCILLIN AND POTASSIUM CLAVULANATE INJECTION IP

WIXICLAV™-1.2

Composition :
Each vial contains :
Amoxycillin Sodium (Sterile) IP
Eq. to Anhydrous Amoxycillin 1000 mg
Potassium Clavulanate (Sterile) IP
Eq. to Clavulanic Acid 200 mg

INDICATIONS:
WIXICLAV® Injection is indicated for the treatment of the following infections when caused by susceptible bacteria in adults and children:
- Severe infections of the ear, nose and throat (such as mastoiditis, peritonsillar infections, epiglottitis, and sinusitis when accompanied by severe systemic signs and symptoms)
- Acute exacerbations of chronic bronchitis
- Community acquired pneumonia
- Cystitis
- Pyelonephritis
- Skin and soft tissue infections such as cellulitis, animal bites, severe dental abscess with spreading cellulitis
- Bone and joint infections such as osteomyelitis
- Intra-abdominal infections
- Female genital infections.
- Prophylaxis against infections associated with major surgical procedures in adults.

DOSAGE AND ADMINISTRATION:
For intravenous use only.
Doses are expressed in terms of amoxycillin/clavulanic acid content.

Adults and children ≥ 40 kg
Usual recommended dose: 1000 mg/ 200 mg (amoxycillin/clavulanic acid) every 8 hours.

For surgical prophylaxis
For procedures less than 1 hour in duration, the recommended dose is 1000 mg/200 mg to 2000 mg/200 mg given at induction of anaesthesia (Doses of 2000 mg/200 mg can be achieved by using an alternative intravenous formulation).
For procedures greater than 1 hour in duration, the recommended dose is 1000 mg/200 mg to 2000 mg/200 mg given at induction of anaesthesia, with up to 3 doses of 1000 mg/200 mg in 24 hours.
WIXICLAV® powder for solution for injection or infusion provides a total daily dose of 3000 mg amoxycillin and 600 mg clavulanic acid when administered in usual recommended dosage.
If higher daily dose of drug is required, an alternative plain amoxycillin should be administered to avoid administration of unnecessarily high daily doses of clavulanic acid.

Children < 40 kg
Recommended doses:
- Children over 3 months: 25 mg/5 mg per kg every 8 hours
- Children aged less than 3 months or weighing less than 4 kg: 25 mg/5 mg per kg every 12 hours.

Elderly
No dose adjustment is considered necessary.

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

Renal impairment
No dose adjustment is required in patients with creatinine clearance (CrCl) greater than 30 ml/min. In patients with renal impairment, the dose should be adjusted according to the degree of impairment as follows:

Adults and children ≥ 40 kg

CrCl: 10-30 ml/min	Initial dose of 1000 mg/200 mg and then 500 mg/100 mg given twice daily
CrCl< 10 ml /min	Initial dose of 1000 mg/200 mg and then 500 mg/100 mg given every 24 hours
Haemodialysis	Initial dose of 1000 mg/200 mg and then followed by 500 mg/100 mg every 24 hours, plus a dose of 500 mg/100 mg at the end of dialysis.

Children < 40 kg

CrCl: 10-30 ml/min	25 mg/5 mg per kg given every 12 hours
CrCl< 10 ml /min	25 mg/5 mg per kg given every 24 hours
Haemodialysis	25 mg/5 mg per kg given every 24 hours, plus a dose of 12.5 mg/2.5 mg per kg at the end of dialysis.

The duration of therapy depends on type/site of infection, severity of infection, and response of the patient to the drug therapy. Treatment should not be extended beyond 14 days without review.

Method of administration
WIXICLAV® Injection may be administered either by slow intravenous injection over a period of 3 to 4 min directly into a vein or by infusion over 30 to 40 min. This injection is not suitable for intramuscular administration.
Children aged less than 3 months should be administered by IV infusion only.

Precautions for disposal and other handling
For single use only. Discard any unused solution.
The reconstitution/dilution is to be made under aseptic conditions. The solution is to be inspected visually for particulate matter and discoloration prior to administration. The solution should only be used if the solution is clear and free from particles.Any unused medicinal product or waste material should be disposed immediately.

Directions for reconstitution
Powder should be dissolved with 20 ml of provided Sterile Water for Injection. Reconstituted solutions are normally colourless or a pale straw colour. The reconstituted solution should be used or diluted immediately, within 20 minutes. Reconstituted solutions of amoxycillin/clavulanic acid may be injected into the drip tubing over a period of 3 to 4 min.

Compatible diluents
For administration as intravenous infusion, reconstituted solution should be added to 100 ml of infusion fluid. If reconstituted and maintained at room temperature (25°C), infusions should be completed within the times stated in the table below.

Intravenous infusion	Stability period at 25°C
Water for Injection	3 hours
0.9% w/v Sodium Chloride intravenous infusion (9 mg/ml)	3 hours
Compound Sodium Chloride Injection 1959 (Ringer's)	2 hours
Compound Sodium Lactate Intravenous Infusion (Ringer-Lactate:Hartmann's)	2 hours
0.3% w/v Potassium Chloride and 0.9% w/v Sodium Chloride Intravenous Infusion (3 mg/ml and 9 mg/ml)	2 hours

Reconstituted solutions may be added to pre-refrigerated infusion bags containing either Water for Injection or sodium chloride infusion (0.9% w/v), which may be stored for up to 8 hours at 5 °C. Thereafter, the infusion should be administered immediately after reaching room temperature.

Incompatibilities:
WIXICLAV® should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates or with intravenous lipid emulsions. If prescribed concomitantly with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because loss of activity of the aminoglycoside can occur under these conditions.
For dilution, reconstituted solutions should not be mixed with infusions containing glucose, dextran or bicarbonate.

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CONTRAINDICATIONS:
- Hypersensitivity to amoxycillin, clavulanic acid, penicillin class of drugs, or any excipient of the formulation.
- 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 Amoxycillin/clavulanic acid.

WARNINGS AND PRECAUTIONS:
Before initiating therapy with amoxycillin/clavulanic acid, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other beta-lactam agents.
Serious and occasionally fatal hypersensitivity (anaphylactoid) 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 in atopic individuals. If an allergic reaction occurs, amoxycillin/clavulanic acid therapy should be discontinued and appropriate alternative therapy instituted.
Convulsions may occur in patients with impaired renal function or in those receiving high doses. Amoxycillin/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 amoxycillin.
Concomitant use of allopurinol during treatment with amoxycillin 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 generalisedexanthemouspustulosis (AGEP). This reaction requires amoxycillin/clavulanic acid discontinuation and contra-indicates any subsequent administration of amoxycillin.
In patients with renal impairment, the dose should be adjusted according to the degree of impairment. In patients with reduced urine output crystalluria has been observed very rarely, predominantly with parenteral therapy. During administration of high doses of amoxycillin it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxycillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained.
Amoxycillin/clavulanic acid should be used with caution in patients with evidence of hepatic impairment. 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. In all populations, 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.
Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.
Antibiotic-associated colitis has been reported with nearly all antibacterial agents including amoxycillin 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. Should antibiotic-associated colitis occur, WIXICLAV® should immediately be discontinued, a physician be consulted and an appropriate therapy initiated. Anti-peristaltic drugs are contra-indicated in this situation.
This medicinal product contains sodium and potassium. To be taken into consideration by patients on a controlled sodium/potassium diet.

DRUG INTERACTIONS:
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 amoxycillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxycillin. 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 amoxycillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxycillin but not of clavulanic acid.
Mycophenolatemofetil: In patients receiving mycophenolatemofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid (MPA) of approximately 50% has been reported following commencement of oral amoxycillin 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 mycophenolatemofetil 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.

USE IN PREGNANCY AND LACTATION:
Pregnancy: Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Limited data on the use of amoxycillin/clavulanic acid during pregnancy in humans do not indicate an increased risk of congenital malformations. Use should be avoided during pregnancy, unless considered essential by the physician.
Lactation: Both substances are excreted into breast milk. An effect of clavulanic acid on the breast-fed infant is not known. Consequently, diarrhoea and fungal infection of the mucous membranes are possible in the breast-fed infant, so that breast-feeding might have to be discontinued. Amoxycillin/clavulanic acid should only be used during breast-feeding after benefit/risk assessment by the physician.

ADVERSE EFECTS:
The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and vomiting.The following terminologies have been used in order to classify the occurrence of undesirable effects. Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000), Not known (cannot be estimated from the available data).
Infections and infestations: Mucocutaneouscandidosis: Common; Overgrowth of non-susceptible organisms: Not known
Blood and lymphatic system disorders: Reversible leucopenia (including neutropenia): Rare; Thrombocytopenia: Rare; Reversible agranulocytosis: Not known; Haemolyticanaemia: Not known; Prolongation of bleeding time and prothrombin time: Not known
Immune system disorders: Angioneuroticoedema: Not known; Anaphylaxis: Not known; Serum sickness-like syndrome: Not known; Hypersensitivity vasculitis: Not known.
Nervous system disorders: Dizziness: Uncommon; Headache: Uncommon; Convulsions: Not known; Aseptic meningitis: Not known.
Vascular disorders: Thrombophlebitis: Rare.
Gastrointestinal disorders: Diarrhoea: Common; Nausea: Uncommon; Vomiting: Uncommon
Indigestion: Uncommon; Antibiotic-associated colitis: Not known.
Hepatobiliary disorders: Rises in AST and/or ALT5: Uncommon; Hepatitis: Not known; Cholestatic jaundice: Not known.
Skin and subcutaneous tissue disorders: Skin rash: Uncommon; Pruritus: Uncommon; Urticaria: Uncommon; Erythema multiforme: Rare; Stevens-Johnson syndrome: Not known; Toxic epidermal necrolysis: Not known; Bullous exfoliative-dermatitis: Not known; Acute generalisedexanthemouspustulosis (AGEP): Not known.
Renal and urinary disorders: Interstitial nephritis: Not known; Crystalluria: Not known.

OVERDOSAGE:
Symptoms: Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. Amoxycillin 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.
Amoxycillin has been reported to precipitate in bladder catheters, predominantly after intravenous administration of large doses. A regular check of patency should be maintained.
Treatment: Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance. Amoxycillin/clavulanic acid can be removed from the circulation by haemodialysis.

STORAGE:
Protect from light at a temperature not exceeding 25°C. Do not freeze. Keep out of the reach of children.
CAUTION: Do not use if reconstituted solution contains visible solid particles.

PRESENTATION:
Combipack of one vial and one 20 ml ampoule of Sterile Water for Injection.

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