Clavodar®

دار الدواء
Dar Al Dawa

Amoxicillin/Clavulanic Acid

TWICE DAILY

DESCRIPTION:
Clavodar® is an oral antibacterial combination consisting of the semisynthetic antibiotic amoxicillin and the ß-lactamase inhibitor, clavulanic acid.

PHARMACOLGY:
Amoxicillin is a semisynthetic antibiotic with a broad spectrum of bactericidal activity against many gram-positive and gram-negative microorganisms. Clavulanic acid is a ß-lactam, structurally related to the penicillins, which possesses the ability to inactivate a wide range of ß-lactamase enzymes commonly found in microorganisms resistant to penicillins and cephalosporins.

INDICATIONS:
Clavodar® is indicated in the treatment of the following infections:
- Lower Respiratory Tract Infections–caused by ß-lactamase-producing strains of *Haemophilus influenzae* and *Moraxella (Branhamella) catarrhalis*.
- Otitis Media–caused by ß-lactamase-producing strains of *Haemophilus influenzae* and *Moraxella (Branhamella) catarrhalis*.
- Sinusitis–caused by ß-lactamase-producing strains of *Haemophilus influenzae* and *Moraxella (Branhamella) catarrhalis*.
- Skin and Skin Structure Infections–caused by ß-lactamase-producing strains of *Staphylococcus aureus, Escherichia coli* and *Klebsiella* spp.
- Urinary Tract Infections–caused by ß-lactamase-producing strains of *Escherichia coli, Klebsiella* spp. and *Enterobacter* spp.

Because amoxicillin has greater *in vitro* activity against *Streptococcus 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 **Clavodar®**.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of **Clavodar®** and other antibacterial drugs, **Clavodar®** should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

CONTRAINDICATIONS:
Clavodar® 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 the drug.

SIDE EFFECTS:
Clavodar® is generally well tolerated.
The following adverse reactions have been reported for ampicillin class antibiotics:
- Gastrointestinal: Diarrhea, nausea, vomiting, indigestion, gastritis, stomatitis, glossitis, black "hairy" tongue, mucocutaneous candidiasis, enterocolitis and hemorrhagic/pseudomembranous colitis.
- Hypersensitivity Reactions: Skin rashes, pruritus, urticaria, angioedema, serum sickness-like reactions (urticaria or skin rash accompanied by arthritis, arthralgia, myalgia and frequently fever), erythema multiforme (rarely Stevens-Johnson syndrome), acute generalized exanthematous pustulosis and an occasional case of exfoliative dermatitis (including toxic epidermal necrolysis) have been reported. Serious and occasional fatal hypersensitivity (anaphylactic) reactions can occur with oral penicillin.
- Liver: A moderate rise in AST (SGOT) and/or ALT (SGPT) has been noted in patients treated with ampicillin class antibiotics but the significance of these findings is unknown. Hepatic dysfunction, including increases in serum transaminases (AST and/or ALT), serum bilirubin and/or alkaline phosphatase,* has been infrequently reported. The histologic findings on liver biopsy have consisted of predominantly cholestatic, hepatocellular or mixed cholestatic-hepatocellular changes. On rare occasions, deaths have been reported. These have generally been cases associated with serious underlying diseases or concomitant medications.
- Renal: Interstitial nephritis and hematuria have been reported rarely.
- Hemic and Lymphatic Systems: Anemia, including hemolytic anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia and agranulocytosis have been reported during therapy with penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. A slight thrombocytosis was noted in less than 1% of the patients treated with the drug. There have been reports of increased prothrombin time in patients receiving the drug and anticoagulant therapy concomitantly.
- Central Nervous System: Agitation, anxiety, behavioral changes, confusion, convulsions, dizziness, insomnia, and reversible hyperactivity have been reported rarely.
- Miscellaneous: Tooth discoloration has been reported very rarely in children.

WARNINGS AND PRECAUTIONS:
- Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. If an allergic reaction occurs, **Clavodar®** 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 **Clavodar®**, 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.
- **Clavodar®** should be used with caution in patients with evidence of hepatic dysfunction. Hepatic toxicity associated with the use of **Clavodar®** is usually reversible. On rare occasions, deaths have been reported. These have generally been cases associated with serious underlying diseases or concomitant medications.
- While **Clavodar®** 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 **Clavodar®** 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.
- Information for Patients: Patients should be counseled that antibacterial drugs including **Clavodar®**, should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When **Clavodar®** is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may: (1) decrease the effectiveness of the immediate treatment, and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by **Clavodar®** or other antibacterial drugs in the future.
- Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have not been performed to evaluate carcinogenic potential. The mutagenic potential of the drug was investigated *in vitro* and *in vivo*. All were negative apart from the in vitro assay where weak activity was found at very high, cytotoxic concentrations. It was found that oral doses of up to 1200 mg/kg/day (5.7 times the maximum human dose) have no effect on fertility and reproductive performance in rats.
- Teratogenic effects. Pregnancy (Category B): This drug should be used during pregnancy only if clearly needed.
- Drug/Laboratory Test Interactions: Oral administration of **Clavodar®** 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 Benedict's Solution or Fehling's Solution. Since this effect may also occur with amoxicillin and therefore **Clavodar®**, it is recommended that glucose tests based on enzymatic glucose oxidase reactions be used.
- Labor and Delivery: Oral ampicillin class antibiotics are generally poorly absorbed during labor. However, it is not known whether the use of the drug in humans during labor or delivery has immediate or delayed adverse effects on the fetus, prolongs the duration of labor, or increases the likelihood that forceps delivery or other obstetrical intervention or resuscitation of the newborn will be necessary.
- Nursing Mothers: Ampicillin class antibiotics are excreted in the milk; therefore, caution should be exercised when **Clavodar®** is administered to a nursing woman.

DRUG INTERACTIONS:
- Probenecid decreases the renal tubular secretion of amoxicillin. Concurrent use with **Clavodar®** may result in increased and prolonged blood levels of amoxicillin. Co-administration of probenecid cannot be recommended.
- 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. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperuricemia present in these patients. There are no data with **Clavodar®** and allopurinol administered concurrently.
- In common with other broad-spectrum antibiotics, **Clavodar®** may reduce the efficacy of oral contraceptives.
- 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 amoxicillin and therefore **Clavodar®**.

DOSAGE AND ADMINISTRATION:
Clavodar® may be taken without regard to meals; however, absorption of clavulanate potassium is enhanced when **Clavodar®** is administered at the start of a meal. To minimize the potential for gastro-intestinal intolerance, **Clavodar®** should be taken at the start of a meal.
Adults: The usual adult dose is one 625 mg tablet every 12 hours. For more severe infections and infections of the respiratory tract, the dose should be one 1 g tablet every 12 hours or one 625 mg tablet every 8 hours.
Patients with impaired renal function do not generally require a reduction in dose unless the impairment is severe. Severely impaired patients with a glomerular filtration rate of <30 ml/min. should not receive the 1 g tablet. Patients with a glomerular filtration rate of 10 to 30 ml/min. should receive 625 mg tablet every 12 hours. Patients with a less than 10 ml/min. glomerular filtration rate should receive 625 mg tablet every 24 hours. Hemodialysis patients should receive 625 mg tablet every 24 hours. They should receive an additional dose both during and at the end of dialysis.
Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.
Adults who have difficulty swallowing may be given the 200 mg/5 ml suspension or the 400 mg/5 ml suspension in place of the 1 g tablet.
Pediatric Patients: Neonates and infants aged < 12 weeks (3 months): Due to incompletely developed renal function affecting elimination of amoxicillin in this age group, the recommended dose of **Clavodar®** is 30 mg/kg/day divided q12h, based on the amoxicillin component. Clavulanate elimination is unaltered in this age group.
Patients aged 12 weeks (3 months) and older: The usual dose is 200 mg/5 ml or 400 mg/5 ml oral suspension every 12 hours. In case of otitis media*, sinusitis, lower respiratory tract infections and more severe infections: The recommended dose is 45 mg/kg/day every 12 hours. For less severe infections the dose should be 25 mg/kg/day every 12 hours.
Pediatric patients weighing 40 kg or more should be dosed according to the adult recommendations.
** Duration of therapy studied and recommended for acute otitis media is 10 days.*

OVERDOSAGE:
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 **Clavodar®**, 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.
Both amoxicillin and clavulanate are removed from the circulation by hemodialysis.

PRESENTATIONS:
Clavodar® 625 Tablets: Packs of 14 and 20 film coated tablets. Each tablet contains 500 mg Amoxicillin (as amoxicillin trihydrate) and 125 mg Clavulanic Acid (as potassium clavulanate).
Clavodar® 1 g Tablets: Packs of 14 film coated tablets. Each tablet contains 875 mg Amoxicillin (as amoxicillin trihydrate) and 125 mg Clavulanic Acid (as potassium clavulanate).
Clavodar® 200/28 Suspension: Bottle of 70 ml. Each 5 ml contains 200 mg Amoxicillin (as amoxicillin trihydrate) and 28.5 mg Clavulanic Acid (as potassium clavulanate).
Clavodar® 400/57 Forte Suspension: Bottle of 70 ml. Each 5 ml contains 400 mg Amoxicillin (as amoxicillin trihydrate) and 57 mg Clavulanic Acid (as potassium clavulanate).

STORAGE CONDITIONS:
Clavodar® tablets: Store in a dry place up to 25°C.
Clavodar® powder for suspension: Keep tightly closed and store in a dry place up to 25°C. After reconstitution, store in the refrigerator between (2-8)°C and discard unused portion after 7 days.

This is a medicament.
- *Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.*
- *Follow strictly the doctor's prescription, the method of use, and the instructions of the pharmacist who sold you the medicament.*
- *The doctor and the pharmacist are experts in medicine, its benefits and its risks.*
- *Do not, by yourself, interrupt the period of treatment prescribed.*
- *Do not repeat the same prescription without consulting your doctor.*

Keep medicament out of reach of children

Manufactured by Dar Al Dawa, Na'ur - Jordan

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