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CLAVICIN-XR

Amoxicillin & Clavulanate Potassium ER Tablets 1000mg & 62.5mg

Composition :
Each film coated tablet contains :
Amoxicillin Trihydrate USP
equivalent to Amoxicillin.............1000 mg
Clavulanate Potassium USP
equivalent to Clavulanic acid...... 62.5 mg
Excipients.................................. q.s.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of CLAVICIN XR (amoxicillin/clavulanate potassium) and other antibacterial drugs. CLAVICIN XR should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria

Description : CLAVICIN XR is an oral antibacterial combination consisting of the semisynthetic antibiotic amoxicillin (present as amoxicillin trihydrate) and the B-lactamase inhibitor clavulanate potassium (the potassium salt of clavulanic acid). Amoxicillin is an analog of ampicillin,derived from the basic penicillin nucleus 6-aminopenicillanic acid. The amoxicillin trihydrate molecular formula is $C_{16}H_{19}N_3O_5S\text{-}3H_2O$ and the molecular weight is 419.45. Clavulanic acid is produced by the fermentation of Streptomyces clavuligerus. It is a B-lactam structurally related to the penicillins and possesses the ability to inactivate a wide variety of B-lactamase by blocking the active sides of these enzymes. Clavulanic acid is particularly active against the clinically important plasmid-medicated B-lactamase frequently responsible for transferred drug resistance to penicillin and cephalosporins. The clavulanate potassium molecular formula is $C_8H_8KNO_5$,and the molecular weight is 237.25.

CLINICAL PHARMACOLOGY : Amoxicillin and clavulanate potassium are well absorbed from the gastrointestinal tract after oral administration of CLAVICIN XR . CLAVICIN XR is an extended-release formulation which provides sustained plasma concentrations of amoxicillin. Amoxicillin systematic exposure achieved with CLAVICIN XR is similar to that produced by the oral administration of equivalent doses of amoxicillin alone. Absorption of amoxicillin is decreased in the fasted state. CLAVICIN XR is not recommended to be taken with high-fat meal,because clavulanate absorption is decreased. The half-life of amoxicillin after the oral administration of CLAVICIN XR is approximately 1.3 hours, and that of clavulanate is approximately 1.0 hour. Clearance of amoxicillin is predominantly renal, with approximately 60% to 80% of the dose being excreted unchanged in urine, whereas clearance of clavulanate has both a renal (30% to 50%) and a non-renal component. Concurrent administration of probenecid delays amoxicillin excretion but does not delay renal excretion of clavulanate. Neither component in CLAVICIN XR is highly protein-bound; clavulanate has been found to be 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.

Microbiology: Amoxicillin is semisynthetic antibiotic with a broad spectrum of bactericidal activity against many gram-positive and gram-negative microorganisms. Amoxicillin is,however, susceptible to degradation by B-lactamases. and therefore, its spectrum of activity does not include organisms which produce these enzymes. Clavulanic acid is B-lactam,structurally related to penicillin,which posseses the ability to inactivate a wide range of B-lactamase enzymes commonly found in microorganisms resistant to penicillins and cehalosporins. In particular,it has good activity against the clinically important plasmid-medicated B-lactamases frequently found responsible for transferred drug resistance.

DRUG INTERACTIONS : Probenecid decreases the renal tubular secretion of amoxicillin. Concurrent use with CLAVICIN XR may result in increased and prolonged blood levels of amoxicillin. Coadministration of probebecid cannot be recommended. In common with other broad-spectrum antibiotics. CLAVICIN XR may reduce the efficacy of oral contraceptives. Carcinogenesis, Mutagenesis, impairment of Fertility: Long term studies in animals have not been performed to evaluate carcinogenic potential. The mutagenic potential of CLAVICIN XR was investigated in vitro with an Ames test, a human lymphocyte cytogenetic assay, a yeast test, and a mouse lymphoma forward mutation assay, and in vivo with mouse micronucleus tests and a dominant lethal test. All were negative apart from the in vitro mouse lymphoma assay, where weak activity was found at very high, cytotoxic concentrations. CLAVICIN XR at oral doses of up to 1,200mg/kg/day (1.9 times the maximum human dose of amoxicillin and 15 times the maximum human dose of clavulanate based on body surface area) was found to have no effect on fertility and reproductive performance in rats dosed with a 2:1 ratio formulation of amoxicillin: clavulanate.

Nursing Mothers : Ampicillin-class antibiotics are excreted in the milk;therefore,caution should be exercised when CLAVICIN XR is administered to a nursing woman.

Pediatric Use : Safely and effectiveness in pediatric patients younger than 16 years have not been established.

Geriatric Use : The drug is known to be substantially excreted by the kidney, and the risk of dose-dependent 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, it may be useful to monitor renal function.

ADVERSE REACTIONS : The following adverse reactions have been reported for ampicillin-class antibiotics:

Gastrointestinal : Diarrhea,nausea,vomiting,indigestion,gastritis,stomatitis,glossitis,black "hairy" tongue, muccocutaneous candidiasis, enterocolitis, and hemorrhagic/psuedomembranous colitis. Onset of psuedomembranous colitis symptoms may occur during or after antibiotic treatment.

Hypersensitivity Reactions : Skin rashes, pruritus, urticaria, angeoedema, serum sickness like reactions (urticaria or skin rash accompanied by arthritis, arthralgia, mylagia, and frequently fever), erythema multiforme (rarely Stevens-Johnson syndrome), acute generalized exanthematous pustulosis, hypersensitivity vasculitis, and an 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 hepatitis and cholestatic jaundice, increases in serum transaminases (AST and/or ALT), serum bilirubin, and/ alkaline phosphatase, has been infrequently reported with CLAVICIN XR .

Renal: Interstitial nephritis and hematuria have been reported rarely. Crystalluria has also been reported.

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. There have been reports of increased prothrombin time in patients receiving CLAVICIN XR and anticoagulant therapy concomitantly. The clavulanic acid component of CLAVICIN XR protects amoxicillin from degradation by B-lactamase enzymes and effectively extends the antibiotic spectrum of amoxicillin to include many bacteria normally resistant to amoxicillin and other B-lactam antibiotics.

INDICATIONS AND USAGE : CLAVICIN XR Extended Release Tablets are indicated for the treatment of patients with community-acquired pneumonia or acute bacterial sinusitis due to confirmed, or suspected β-lactamase-producing
pathogens (i.e. H. influenzae, M. catarrhalis,H.paraininfluenzae,K. pneumonia, or methicillin-susceptible S. pneumoniae with reduced susceptibility to penicillin (i.e. penicillin MICs = 2 mcg/mL). CLAVICIN XR is not indicated for the treatment of infections due to S. pneumoniae with penicillin MICs ≥4 mcg/mL. Data for the treatment of infections due to S. pneumoniae with penicillin MICs ≥4 mcg/mL. To reduce the development of drug-resistant bacteria and maintain the effectiveness of CLAVICIN XR and other antibacterial drugs, CLAVICIN XR should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting 6 or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

MODE OF ADMINISTRATION:
Clavicin XR is for oral use.

CONTRAINDICATIONS : CLAVICIN XR 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 treatment with amoxicillin/clavulanate potassium.
CLAVICIN XR is contraindicated in patients with severe renal impairment (creatinine clearance <30mL/min.)
and in hemodialysis patients.

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.
CLAVICIN XR should be used with caution in patients with evidence of hepatic dysfunction.
Hepatic toxicity associated with the use of amoxicillin/clavulanate potassium is usually reversible.

PRECAUTIONS : While amoxicillin/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 if therapy is for longer than the drug is approved for administration.
CLAVICIN XR should be taken every 12 hours with a meal or snack to reduce the possibility of gastrointestinal upset.

Central Nervous System : Agitation, anxiety, behavioral changes, confusion, convulsions, dizziness, headache, insomnia, and reversible hyperactivity have been reported rarely.

Miscellaneous : Tooth discoloration (brown), yellow, or gray staining) has been rarely reported. Most reports occurred in pediatric patients. Discoloration was reduced or eliminated with brushing or dental cleaning in most cases.

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.

DOSAGE AND ADMINISTRATION : CLAVICIN XR should be taken at start of the meal to enhance the absorption of amoxicillin and to minimize the potential for gastrointestinal intolerance. Absorption of the amoxicillin component is decreased when CLAVICIN XR is taken on an empty stomach.
The recommended dose of CLAVICIN XR is 4,000 mg/250 mg daily according to the following table:

Mild to Moderate infection	1 tablets q 12h
Moderate to severe infection	2 tablets q 12h

Tablets of amoxicillin + Clavulanate potassium IR(250 mg or 500 mg) can not be used to provide the same dosage as CLAVICIN XR Extended Released Tablets. This is because CLAVICIN XR contains 62.5 mg of clavulanic acid, while the Amoxicillin + Clavulanate potassium tablets contain 125 mg clavulanic acid. In addition, the Extended Release tablet provides an extended time course of plasma amoxicillin and concentrations compared to immediate- release Tablets. Thus , two Amoxicillin + Clavulanate Potassium 500-mg tablets are not equivalent to one CLAVICIN XR tablet.

Geriatric Use : No dosage adjustment is required for the elderly.

STORAGE : Store below 25° C. Protect from light.

PRESENTATION : CLAVICIN XR tablets Alu-Alu Blister of 10 tablets packed in a monocarton.

A Product of :
Strides
Strides Pharma Science Limited
Strides House, Bilekahalli, Bannerghatta Road,
Bangalore – 560076, Karnataka, India.

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230 x 160 mm

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CMO - ARTWORK DETAIL LABEL

		MFG. LOCATION	MORSEF PHARMACEUTICALS PVT. LTD.		
PRODUCT	CLAVIVIN-XR 1000 mg + 62.5 mg Tablets				
BUYER/COUNTRY	French Africa	COMPONENT	Pack Insert		
DIMENSION	230mm x 160 mm			PACK	--------
NEW ITEM CODE	1041012	OLD ITEM CODE	1038540		
COLOUR SHADES	Black			No. of Colours	1
Change Control No.	[illegible]			Artwork Version	[illegible]