F3872D-Phl

CO-AMOXICLAV

COMOXI DS

312.5 mg per 5 mL Powder for Suspension

ANTIBACTERIAL

℞

FORMULATION:

Each 5 mL (1 teaspoonful) reconstituted suspension contains:

Amoxicillin (as trihydrate) USP ..... 250 mg

Clavulanic Acid (as Potassium clavulanate) BP ..... 62.5 mg

Product complies USP specifications.

PRODUCT DESCRIPTION:

Comoxi DS is available as white powder, when reconstituted gives an off-white to cream color suspension with raspberry flavour.

PHARMACOLOGICAL PROPERTIES:

Pharmacodynamic properties:

Microbiology

Amoxicillin is a semi-synthetic antibiotic with broad spectrum of antibacterial activity against many Gram-positive and Gram-negative micro-organisms.

Clavulanic acid is a β-lactam, structurally related to the penicillin, which 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 beta-lactamases frequently responsible for transferred drug resistance. The formulation of Amoxicillin and Clavulanic acid in Co-Amoxiclav (Comoxi DS) protects Amoxicillin from degradation by β-lactamase enzymes and effectively extends the antibacterial spectrum of amoxicillin to include many bacteria normally resistant to Amoxicillin and other β-lactam antibiotics. Thus, Co-Amoxiclav (Comoxi DS) possesses the distinctive properties of a broad spectrum antibiotic and a β-lactamase inhibitor.

Pharmacokinetic properties:

Absorption: Amoxicillin and Clavulanate Potassium are well absorbed form the gastrointestinal tract after oral administration of Co-Amoxiclav (Comoxi DS). This can be given without regards to meals.

Distribution: The half-life of Amoxicillin after the oral administration of Co-Amoxiclav (Comoxi DS) is 1.3 hours that of Clavulanic Acid is 1.0 hour.

Metabolism: Neither a component in Co-Amoxiclav (Comoxi DS) is highly protein-bound; clavulanic acid has been found to be approximately 25% bound to human serum and amoxicillin approximately 18% bound.

Elimination: The main route of elimination of the drug is through urine. Amoxicillin diffuses readily into most body tissues and fluids with exception of the brain and spinal fluid.

INDICATIONS:

It is used for urinary tract infections due to susceptible organisms; Otitis media or sinusitis due to resistant microorganisms; e.g. *H.influenzae, S.pneumoniae, M. catarrhalis;* Lower respiratory tract skin infections due to susceptible organisms; and Polymicrobial infections with mixed aerobic and anaerobic such as diabetic foot, gynaecological infections, intra-abdominal infections.

DOSAGE AND ADMINISTRATION:

Adults and children ≥ 40 kg: One 500 mg/125 mg dose taken three times a day.

Children < 40 kg: 20 mg/5 mg/kg/day to 60 mg/15 mg/kg/day given in three divided doses.

Children may be treated with Co-Amoxiclav tablets, suspensions or pediatric sachets. Children aged 6 years and below should preferably be treated with Co-Amoxiclav suspension or pediatric sachets.

Elderly: No dose adjustment is considered necessary.

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

Renal impairment: Dose adjustments are based on the maximum recommended level of amoxicillin.

No adjustment in dose is required in patients with creatinine clearance (CrCl) greater than 30 ml/min.

Adults and children ≥ 40 kg	
CrCl: 10-30 ml/min	500 mg/125 mg twice daily
CrCl < 10 ml /min	500 mg/125 mg once daily
Haemodialysis	500 mg/125 mg every 24 hours, plus 500 mg/125 mg during dialysis, to be repeated at the end of dialysis (as serum concentrations of both amoxicillin and clavulanic acid are decreased)
Children < 40 kg	
CrCl: 10-30 ml/min	15 mg/3.75 mg/kg twice daily (maximum 500 mg/125 mg twice daily).
CrCl < 10 ml /min	15 mg/3.75 mg/kg as a single daily dose (maximum 500 mg/125 mg).
Haemodialysis	15 mg/3.75 mg/kg per day once daily. Prior to haemodialysis 15 mg/3.75 mg/kg. In order to restore circulating drug levels, 15 mg/3.75 mg per kg should be administered after haemodialysis.

CONTRAINDICATIONS:

Co-Amoxiclav (Comoxi DS) is contraindicated in patients with a history of allergic reactions to any penicillin. It is also contraindicated in patients with a previous history of Co-Amoxiclav-associated cholestatic Jaundice/Hepatic dysfunction.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

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. THERE HAVE BEEN REPORTS OF INDIVIDUALS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY THAT HAVE EXPERIENCED SEVERE REACTIONS WHEN TREATED WITH CEPHALOSPORINS. BEFORE INITIATING THERAPY WITH CO-AMOXICLAV (COMOXI DS), CAREFULLY INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLIN, CEPHALOSPORINS OR OTHER ALLERGENS. IF AN ALLERGIC REACTION OCCURS, CO-AMOXICLAV (COMOXI DS) SHOULD BE DISCONTINUED AND THE APPROPRIATE THERAPY INSTITUTED. SERIOUS ANAPHYLACTIC REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE. OXYGEN, INTRAVENOUS STEROID AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, SHOULD ALSO BE ADMINISTERED AS INDICATED.

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 normalized ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If Co-administration is necessary, the prothrombin time or international normalized ratio should be carefully monitored with the addition or withdrawal of amoxicillin. 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 amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin but not of clavulanic acid.
Mycophenolate mofetil: In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid (MPA) 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. Therefore, a change in the dose of mycophenolate mofetil 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.

ADVERSE EFFECTS:
Undesirable effects, as with amoxicillin, are uncommon and mainly of mild and transitory nature.
Gastrointestinal reactions: diarrhoea, indigestion, nausea, vomiting and candidiasis. Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis) has been reported rarely. Nausea, although uncommon, is more often associated with higher oral dosages. If gastrointestinal side effects occur with oral therapy, they may be reduced by taking Co-Amoxiclav Powder for Suspension at the start of meals. As with other antibiotics, the incidence of gastrointestinal reactions may be raised in children under
two years. Superficial tooth discolouration has been reported rarely, mostly with suspension, it can usually be removed by brushing.
Genito-urinary effects: vaginal itching, soreness and discharge may occur.
Hepatic effects: moderate and asymptomatic rises in AST and/or ALT and alkaline phosphates have been reported occasionally. Hepatitis and cholestatic jaundice have been reported rarely. These hepatic reactions have been reported more commonly with Co-Amoxiclav Powder for Suspension than any other penicillins. After Co-Amoxiclav Powder for Suspension hepatic reactions have been reported more frequently in males and elderly patients, particularly over 65 years. The risk increases with duration of treatment longer than 14 days. These reactions have been rarely reported in children. Signs and symptoms usually occur during or shortly after treatment but in some cases may occur until several weeks after treatment has ended. Hepatic reactions are usually reversible but they may be severe and very rarely, deaths have been reported.
Hypersensitivity reactions: urticartical and erythematous rashes sometimes occur. Rarely erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis and bullous exfoliative dermatitis, serum sickness-like syndrome and hypersensitivity vasculitis have been reported. Treatment should be discontinued if one of these disorders occur. In common with other β-lactam antibiotics angioedema and anaphylaxis have been reported, interstitial nephritis can occur rarely.
Haematological effects: as with other β-lactam transient leucopenia, thrombocytopenia and haemolytic anaemia have been reported rarely. Prolongation of bleeding time and prothrombin time has also been reported rarely (see interaction with other medicaments and other forms of interaction section).
Central Nervous System (CNS) effect: CNS effects have been seen very rarely. These include: reversible hyperactivity, dizziness, headache and convulsions. Convulsions may occur with impaired renal function or in those receiving high doses.
Renal and urinary tract disorders: Crystalluria has been reported very rarely.

REPORTING OF SUSPECTED ADVERSE REACTIONS
To allow continued monitoring of the benefit/ risk balance of the medicinal product, reporting of suspected adverse reaction is necessary. Healthcare professionals are encouraged to report any suspected adverse reactions, directly to the importer/ distributor and/or to FDA: www.fda.gov.ph. Patients are advised to seek immediate medical attention at the first sign/s of adverse reactions.

OVERDOSAGE AND TREATMENT:
Following overdosage, patients have experienced primarily gastrointestinal symptoms including stomach and abdominal pain, vomiting, and diarrhoea. Rash, hyperactivity, or drowsiness has also been observed in a small number of patients. In case of overdose, discontinue Co-Amoxiclav (Comoxi DS), treat symptomatically and institute supportive measures as required.

DIRECTION FOR RECONSTITUTION:
60 mL bottle: Tap bottle to loosen the powder. Add 52mL distilled waterand shake vigorously.
90 mL bottle: Tap bottle to loosen the powder. Add 77mL distilled water and shake vigorously.

Once reconstituted the suspension must be stored in refrigerator (at temperatures between 2° C - 8° C) and be discarded after 7 days.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

AVAILABILITY
Amber Glass Bottle x 60 mL; and 90 mL (Box of 1's) with 30ml plastic measuring cup.

Manufactured by:
MACTER INTERNATIONAL LTD.
E-40/A, S.I.T.E., Karachi, Pakistan

Imported and Distributed by:
SAHAR INTERNATIONAL TRADING, INC.
354 Aguirre Ave. Phase III, BF Homes
Parañaque City
SAHAR

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