AMOXICILLIN

PEDIAMOX®

Antibacterial (Penicillin)

℞

100 mg/mL Powder for Suspension (Oral Drops)
250 mg/5 mL Powder for Suspension

FORMULATIONS
Each mL reconstituted suspension (oral drops) contains:
Amoxicillin (as trihydrate) ..... 100 mg
Each 5 mL reconstituted suspension contains:
Amoxicillin (as trihydrate) ..... 250 mg

PRODUCT DESCRIPTIONS
Amoxicillin (Pediamox®) 100 mg/mL Powder for Suspension (Oral Drops) and **Amoxicillin (Pediamox®) 250 mg/5mL Powder for Suspension** are off-white to yellow powder for reconstitution into orange, sweet, fruit-flavored suspensions.

PHARMACODYNAMICS
Amoxicillin exerts its bactericidal activity by interfering with the bacterial cell wall synthesis. Peptidoglycan is a heteropolymeric structure that provides the cell wall with mechanical stability. The final stage of peptidoglycan synthesis involves the completion of the cross-linking when the terminal glycine residue of the pentaglycine bridge is linked to the fourth residue of the pentapeptide. The transpeptidase that catalyzes this step is inhibited by penicillins. As a result, the bacterial cell wall is weakened, the cell swells, and then ruptures. Amoxicillin is readily hydrolyzed by the staphylococcal penicillinase.

ANTIMICROBIAL SPECTRUM OF ACTIVITY
Amoxicillin is a broad spectrum aminopenicillin antibiotic that is structurally related to ampicillin. It is rapidly bactericidal against susceptible organisms during the stage of active multiplication. Amoxicillin is ineffective in most staphylococcal infections since it is destroyed by β-lactamase.
Amoxicillin is active *in vitro* and in clinical infections against most strains of the following microorganisms:

Aerobic Gram-positive	Aerobic Gram-negative
Enterococcus faecalis *Staphylococcus* spp* (β-lactamase-negative strains only) *Streptococcus pneumoniae* *Streptococcus* spp. (α- and β-hemolytic strains only)	*Escherichia coli* (β-lactamase-negative strains only) *Haemophilus influenzae* (β-lactamase-negative strains only) *Proteus mirabilis* (β-lactamase-negative strains only)
Helicobacter	
Helicobacter pylori	

*Staphylococci which are susceptible to amoxicillin but resistant to methicillin/oxacillin should be considered as resistant to amoxicillin.
The following microorganisms are generally sensitive to amoxicillin *in vitro*:

Gram-positive	Gram-negative
Clostridium spp. *Corynebacterium* spp. *Bacillus anthracis* *Listeria monocytogenes*	*Salmonella* spp. *Shigella* spp. *Bordetella pertussis* *Brucella* spp. *Neisseria gonorrheae* *Neisseria meningitidis* *Pasteurella septica* *Leptospira* spp. *Fusobacterium* spp. *Vibrio cholerae*
Other Microorganism	
Borrelia burgdorferi	

It is suggested to carry out susceptibity tests.

PHARMACOKINETICS
Amoxicillin is stable in the presence of gastric acid and is rapidly absorbed after oral administration.

In children 4 to 45 months old given amoxicillin oral suspension 15 mg/kg daily, the serum drug concentrations ranged from 2.4-8.5, 1.9-11.3, 1.7-6.4, 0.17-1.9, and 0.14-3.3 mcg/mL at 30 minutes, 1 hour, 2 hours, 4 hours, and 6 hours, respectively, after a dose.

Oral absorption of amoxicillin is delayed in neonates compared with absorption in children and adults. After oral administration of a single dose of amoxicillin in neonates, the C_{max} is generally attained within 3-4.5 hours compared with 1-2 hours in children and adults.

The apparent volume of distribution of amoxicillin ranges from 0.267 to 0.315 L/kg in adults with normal renal function. Amoxicillin is generally distributed into ascitic, synovial, and pleural fluids, middle ear effusions, bronchial and maxillary sinus secretions, sputum, and tonsils. It is also distributed into the liver, lungs, gallbladder, prostate, and muscle. Low concentrations of the drug are also attained in saliva, sweat and tears. Amoxicillin is distributed into bile in varying amounts. If biliary obstruction is not present, amoxicillin concentration in bile is generally 1-30 times greater than concurrent serum concentrations of the drug. As with other penicillins, only negligible amounts of amoxicillin have been detected in aqueous humor. Minimal drug concentrations are attained in cerebrospinal fluid (CSF) of patients with uninflamed meninges; higher concentrations may be attained when meninges are inflamed.

Amoxicillin readily crosses the placenta and is distributed into human milk in low concentrations. Amoxicillin concentrations in cord blood are reportedly 25-33% of concurrent maternal serum concentrations. About 17-20% of the drug is bound to serum proteins. As with other penicillins, amoxicillin is excreted by renal tubular secretion and to a lesser extent by glomerular filtration. Small amounts of the drug are also excreted in feces and bile. About 19-33% of the drug is excreted in urine as penicilloic acid, which is a microbiologically inactive metabolite.

Serum concentration of amoxicillin is generally higher and serum half-life ($t_{1/2}$) is longer in neonates than in older children or adults. In general, the serum $t_{1/2}$ of the drug is inversely proportional to birthweight, gestational age and chronologic age. This appears to result from immature mechanisms for renal tubular secretion of the drug. The serum $t_{1/2}$ of amoxicillin is about 3.7 hours in full-term neonates, and 0.9-1.9 hours in infants and children.

Amoxicillin is removed by hemodialysis. Only minimal amounts appear to be removed by peritoneal dialysis.

INDICATIONS
For the treatment of the following infections caused by susceptible microorganisms:
- Ear, nose, throat, genitourinary tract infections
- Uncomplicated skin and skin structure infections
- Acute otitis media
- Lower respiratory tract infections

DOSAGE AND ADMINISTRATION
Recommended Oral Dosing Regimen:
- Neonates and infants <3 months: 20-30 mg/kg body weight/day in divided doses every 12 hours
- Infants >3 months and Children < 40 kg : 25-50 mg/kg body weight/day in divided doses every 8 hours or every 12 hours

Usual Duration of Treatment:
5 to 14 days depending on severity and type of infection
Or, as prescribed by a physician.

Oral Dosing Regimen for Specific Infections

Type of Infection	Oral Dose for Infants > 3 months and Children < 40 kg	
	Mild to Moderate Infection	Severe Infection
Ear, nose, throat, genitourinary tract, or skin and skin structure infections	25 mg/kg body weight/day in divided doses every 12 hours or 20 mg/kg body weight/day in divided doses every 8 hours	45 mg/kg body weight/day in divided doses every 12 hours or 40 mg/kg body weight/day in divided doses every 8 hours
Acute otitis media	80-90 mg/kg body weight/day in divided doses every 12 hours	80-90 mg/kg body weight/day in divided doses every 12 hours
Lower respiratory tract infections	45 mg/kg body weight/day in divided doses every 12 hours	45 mg/kg body weight/day in divided doses every 12 hours

Directions for Reconstitution:

Amoxicillin Dosage Format and Pack size	Volume of Distilled Water to be Added	Directions
100 mg/mL powder for suspension (oral drops), 10 mL	6 mL	Tap the bottle several times to loosen the powder before reconstitution. Add the required amount of distilled water in two portions, replace the bottle cap and shake vigorously after each addition until all contents are evenly suspended. Keep bottle tightly closed. Shake well before use.
250 mg/ 5 mL powder for suspension, 60 mL	36 mL	
250 mg/ 5 mL powder for suspension, 105 mL	63 mL	
Store for not more than 7 days at 25°C - 30°C or not more than 14 days under refrigeration (2°C - 8°C). Protect from light.		

CONTRAINDICATIONS
- Known hypersensitivity to penicillins or cephalosporins, or any component of the product.
- Patient with infectious mononucleosis since amoxicillin is likely to cause a maculopapular rash.

WARNINGS AND PRECAUTIONS
- 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 hypersensitivity reactions to multiple allergens.
  Careful inquiry should be made concerning previous hypersensitivity to penicillins, cephalosporins or other drugs before initiating therapy with amoxicillin. If an allergic reaction occurs, the drug should be discontinued and appropriate therapy instituted.
  Serious anaphylactoid reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should also be administered as indicated.
- *Clostridium difficile*-associated diarrhea (CDAD) and colitis have been reported with the use of nearly all antibacterial agents, including amoxicillin, and may range in severity from mild to life threatening. It is important to consider this diagnosis in patients who present with diarrhea following administration of antibacterial agents.
- During administration of high doses of amoxicillin, it is recommended to maintain adequate fluid intake and urinary output in order to reduce the possibility of crystalluria associated with amoxicillin therapy.
- In patients with renal impairment, the dose of amoxicillin should be adjusted based on the degree of impairment.
- As with any potent drug, periodic assessment of organ system functions, including renal, hepatic, hematopoietic, is recommended during prolonged therapy.
- Prescribing amoxicillin 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.
- As with other antibacterial drugs, long term or repeated use may result in overgrowth of non-susceptible organisms, including fungi.

INTERACTIONS WITH OTHER MEDICAMENTS
- **Allopurinol:** An increased incidence of skin rashes reportedly occurs in hyperuricemic patients who are concomitantly receiving allopurinol and amoxicillin compared with those receiving amoxicillin or allopurinol alone.
- **Anticoagulants:** Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.
- **Bacteriostatic agents (e.g., Chloramphenicol, macrolides, sulfonamides, and tetracyclines):** These antibacterial agents may interfere with the bactericidal effects of penicillin. This has been demonstrated *in vitro*; however, the clinical significance of this interaction is not well documented.
- **Beta-lactamase Inhibitors:** *In vitro* and *in vivo* studies indicate that the combination of amoxicillin with clavulanic acid or sulbactam results in a synergistic bactericidal effect against many strains of β-lactamase-producing bacteria.
- **Digoxin:** Concurrent administration with amoxicillin may result in increased absorption of digoxin.
- **Methotrexate:** Concomitant use of penicillins (e.g., amoxicillin) may decrease the renal clearance of methotrexate, presumably by inhibiting renal tubular secretion of the drug. Increased serum concentrations of methotrexate, resulting in GI or hematologic toxicity, have been reported. Careful monitoring is recommended during concomitant therapy.
- **Oral Contraceptives:** As with other antibiotics, amoxicillin may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral estrogen/progesterone contraceptives.
- **Probenecid:** Concurrent use of amoxicillin and probenecid may result in increased and prolonged blood levels of amoxicillin.

Interference with Laboratory Tests:
- High urine concentrations of ampicillin may result in false-positive reactions when testing for the presence of glucose in urine using Clinitest®, Benedict's solution, Since the effect may also occur with amoxicillin, it is recommended that glucose tests based on enzymatic glucose oxidase reactions (e.g., Clinistix®) be used.
- Administration of ampicillin to pregnant women may result in a transient decrease in plasma concentrations of total conjugated estriol, estriol-glucuronide, conjugated estrone, and estradiol, This effect may also occur with amoxicillin.
- Amoxicillin may interfere with protein testing when colorimetric methods are used.

STATEMENT ON USAGE FOR HIGH RISK GROUPS
Pregnancy: (Pregnancy Category B). The safety of amoxicillin during pregnancy has not been definitely established. However, amoxicillin has been administered to pregnant women, particularly in the treatment of urinary tract infections, without evidence of adverse effects to the fetus.
Lactation: Since amoxicillin is distributed into human milk and may lead to sensitization of the infant, the drug should be used with caution when breastfeeding.
Children: Neonates and young infants have incompletely developed renal function which may result in delayed elimination of amoxicillin. Dosing of amoxicillin should be modified in pediatric patients 12 weeks old or younger (≤ 3 months old) [see **Dosage and Administration**]
Elderly: Since elderly patients are more likely to have decreased renal function, care should be taken in dose selection.
Renal Impairment: The doses and/or frequency of amoxicillin administration should be modified in response to the degree of renal impairment, severity of infection, and susceptibility of the causative organisms [see **Dosage and Administration**]

UNDESIRABLE EFFECTS
As with other penicillins, it may be expected that untoward reactions will be related to sensitivity phenomena. They are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins and cephalosporins and in those with a history of allergy, asthma, hay fever or urticaria.

The following adverse reactions have been reported with the use of amoxicillin:

Dermatologic / Hypersensitivity Reactions: Anaphylaxis (usually associated with the parenteral dosage form), serum sickness-like reactions (urticaria or skin rash accompanied by arthritis, arthralgia, myalgia, and frequently fever); severe allergic reactions including angioedema; exanthema, acute and generalized exanthematous pustulosis (AGEP), bullous and exfoliative dermatitis, erythematous maculopapular rashes, erythema multiforme, hypersensitivity vasculitis, mucocutaneous/oral and vaginal candidiasis, pruritus, Stevens-Johnson syndrome, toxic epidermal necrolysis

GI: Nausea, vomiting, diarrhea, black "hairy" tongue, CDAD and colitis (during or following discontinuance of amoxicillin); hemorrhagic colitis; acute, transient enterocolitis with severe abdominal pain and bloody diarrhea, but without evidence of CDAD and colitis; glossitis, stomatitis, epigastric distress, gastritis, flatulence, soft stools, loss of appetite/anorexia, enanthemas/sore mouth or tongue, dry mouth, taste disturbances

Nervous System: Agitation, anxiety, behavioral changes, confusion, convulsions (at extremely high doses), dizziness, reversible hyperactivity, hyperkinesia, insomnia
When penicillin reaches a high concentration in the CSF, neurotoxic symptoms consisting of myoclonia, convulsive seizures and depressed consciousness may occur. Unless drug administration is discontinued or its dosage reduced, the syndrome may progress to coma and death.

Hemic and Lymphatic System: Anemia, including hemolytic anemia; agranulocytosis, abnormal platelet aggregation, eosinophilia, leukopenia, neutropenia, prolongation of bleeding time, prothrombin time and activated partial thromboplastin time (APTT); thrombocytopenia, thrombocytopenic purpura

Hepatic: A moderate rise in aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT); transient increases in serum alkaline phosphatase and lactate dehydrogenase levels; hepatic dysfunction including cholestatic jaundice, hepatic cholestasis and acute cytolytic hepatitis

Renal: Acute interstitial nephritis, crystalluria

Other Adverse Effects: Tooth discoloration (brown, yellow, or gray staining) mostly in pediatric patients. In most cases, discoloration was reduced or eliminated with brushing or dental cleaning.

OVERDOSE AND TREATMENT
Clinical features of amoxicillin overdosage may include allergic reactions and GI effects such as nausea, vomiting and diarrhea. Symptomatic treatment with attention to water/electrolyte balance is recommended.

Crystalluria, in some cases leading to renal failure, has been observed after amoxicillin overdosage in adults and children. Adequate fluid intake and diuresis should be maintained to reduce the risk of amoxicillin crystalluria.

Interstitial nephritis resulting in oliguric renal failure has also been reported in a small number of patients after overdose with amoxicillin.

Renal impairment appears to be reversible with cessation of drug administration. High blood levels may occur more readily in patients with impaired renal function because of decreased renal clearance of amoxicillin.

Amoxicillin may be removed from circulation by hemodialysis.

STORAGE CONDITIONS
Store at temperatures not exceeding 30°C, Protect from light.
Keep the products out of sight and reach of children.

AVAILABILITY
Amoxicillin (Pediamox®) 100 mg/mL Powder for Suspension (Oral Drops) in amber bottle of 10mL
Amoxicillin (Pediamox®) 250 mg/5mL Powder for Suspension in amber bottles of 60mL and 105mL

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

DATE OF REVISION OF PACKAGE INSERT: August 2018 (IN 10-065 PED)
DATE OF FIRST AUTHORIZATION (DR-X9100): December 2000
DATE OF FIRST AUTHORIZATION (DR-X8346): February 2001

ADVERSE DRUG REACTION REPORTING STATEMENT
For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph **AND** Unilab at (+632) 858-1000 or productsafety@unilab.com.ph. By reporting undesirable effects, you can help provide more information on the safety of this medicine.

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