Amoxicillin Himox®

℞

100 mg/mL Powder for Suspension (Oral Drops)
125 mg/5 mL Powder for Suspension
250 mg/5 mL Powder for Suspension
250 mg and 500 mg Capsule

ANTIBACTERIAL

FORMULATIONS

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

Each 5 mL reconstituted suspension contains:
Amoxicillin (as trihydrate) ..... 125 mg or 250 mg

Each capsule contains:
Amoxicillin (as trihydrate) ..... 250 mg or 500 mg

PRODUCT DESCRIPTIONS

Amoxicillin (Himox®) 100 mg/mL powder for suspension (oral drops), 125 mg/5 mL and 250 mg/5 mL powder for suspension are off-white to yellow powder for reconstitution into orange, sweet,fruit-flavored suspensions.
Amoxicillin (Himox®) 250 mg capsule is a hard gelatin capsule with white opaque cap and body.
Amoxicillin (Himox®) 500 mg capsule is a hard gelatin capsule with dark brown opaque cap and light orange opaque body.

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 susceptibility tests.

PHARMACOKINETICS

After oral administration, amoxicillin is stable in gastric acid and about 74-92% of a single oral dose of the drug is absorbed from the gastrointestinal (GI) tract of fasting adults. Peak serum concentrations (C_{max}) of amoxicillin are generally attained within 1-2 hours and serum concentrations are usually low and undetectable 6-8 hours later. Increasing the dose results in a corresponding increase in C_{max} and area under the serum concentration-time curves (AUC).

After oral administration of a single dose of amoxicillin 250 or 500 mg, the C_{max} were 3.5-5 or 5.5-11 mcg/mL, respectively. In a study in healthy, fasting adults who received a single oral dose of amoxicillin 500 mg, the mean serum drug concentrations were 3.3, 6.7, 9.3, 5.8, and 0.6 mcg/mL at 30 minutes, 1 hour, 2 hours, 3 hours, and 4 hours, respectively, after the dose.

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:
  - Upper and lower respiratory tract infections including ear, nose and throat infections (e.g., acute otitis media)
  - Gastrointestinal tract infections
  - Genitourinary tract infections
  - Skin and skin structure infections
  - Bone infections (e.g., osteomyelitis)
  - Gall bladder / Biliary tract infections
  - *Helicobacter pylori* infections (in combination with other drugs)
  - Lyme Disease
  - Dental abscess (as an adjunct to surgical management)
- As prophylaxis for endocarditis: For the prevention of bacteremia, associated with procedures such as dental extraction in patients at risk of developing bacterial endocarditis
- Step down treatment for severe infections due to susceptible organisms, initially given intravenous antimicrobial therapy.

DOSAGE AND ADMINISTRATION

Amoxicillin may be given orally without regard to meals.

Usual Adult Dose: 250 mg to 500 mg every 8 hours or 500 mg every 12 hours, depending on the type and severity of infection.

- **Maximum Dose:** 6 g/day in divided doses. An adult dose of 3 g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent respiratory tract infection.

Recommended Adult Dose for Specific Infections:

Indication	Oral Amoxicillin Dose in Adults
Ear, nose, throat, genitourinary tract, skin and skin structure infections	• **Mild to Moderate:** 250 mg every 8 hours or 500 mg every 12 hours • **Severe:** 500 mg every 8 hours
Lower respiratory tract infections (LRTI)	**Mild to Moderate or Severe:** 500 mg every 8 hours
*Helicobacter pylori to reduce the risk of recurrent duodenal ulcer**	• **Triple therapy regimen:** - Amoxicillin 1 g + clarithromycin 500 mg + omeprazole 20 mg, all given every 12 hours for 10 days • **Dual therapy regimen** (in whom resistance to clarithromycin is known or suspected): - Amoxicillin 1 g + lansoprazole 30 mg, each given every 8 hours for 14 days
Lyme Disease	• **For isolated erythema chronicum migrans:** 4 g/day • **For generalized manifestations:** 6 g/day
Endocarditis prophylaxis for dental procedures	2 g as a single dose 30 to 60 minutes before procedure

* Amoxicillin is used in conjunction with a proton pump inhibitor (e.g., omeprazole, lansoprazole) and another antibiotic (e.g., clarithromycin, metronidazole) - See respective product label for complete prescribing information.

Usual Pediatric Dose:

- **Neonates and infants ≤ 3 months:** 20 to 30 mg/kg body weight/day in divided doses every 12 hours
- **Infants >3 months and Children <40 kg:** 25 to 50 mg/kg body weight/day in divided doses every 8 hours or every 12 hours.

Recommended Pediatric Dose for Specific Infections:

Indication	Oral Amoxicillin Dose for Infants >3 months and Children <40 kg	
	Mild to Moderate Infection	**Severe Infection**
Ear, nose, throat, genitourinary tract, 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
LRTI	45 mg/kg body weight /day in divided doses every 12 hours	45 mg/kg body weight /day in divided doses every 12 hours

For Endocarditis Prophylaxis for Dental Procedures in Children: 50 mg/kg body weight as a single dose given 30 to 60 minutes before procedure.

Patients with Renal Impairment:

Creatinine clearance (mL/min)	Adults and Children ≥ 40 kg	Children < 40 kg*
> 30	No adjustment necessary	No adjustment necessary
10-30	250 mg or 500 mg every 12 hours	15 mg/kg body weight/day in divided doses every 12 hours
< 10	250 mg or 500 mg every 24 hours	15 mg/kg body weight given as a single daily dose
Adult patients undergoing hemodialysis should receive 250 mg or 500 mg of amoxicillin every 24 hours, depending on the severity of infection, and should receive an additional dose of the drug during and after each dialysis period.		

*In the majority of cases, parenteral therapy will be preferred.

Usual Duration of Treatment:

- **For most infections:** 5 to 14 days, depending on the type and severity of infection. Continue treatment for at least 48 to 72 hrs after the patient becomes asymptomatic or after evidence of bacterial eradication has been continued.
- **For β-hemolytic streptococcal infections:** At least 10 days to prevent rheumatic fever or glomerulonephritis.
- **For Lyme Disease:** At least 12 days
- Frequent bacteriologic and clinical appraisal is necessary during treatment of chronic urinary tract infections and maybe required for several months after therapy has been completed.

Or, as prescribed by a physician.

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.
125 mg/5 mL or 250 mg/5 mL powder for suspension, 60 mL	36 mL	
125 mg/5 mL or 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 in a dry place at temperatures not exceeding 30°C. Protect from light
Keep the products out of sight and reach of children.

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

AVAILABILITY

Amoxicillin (Himox®) 100 mg/mL Powder for Oral Drops in bottle of 10 mL
Amoxicillin (Himox®) 125 mg/ 5mL Powder for Oral Suspension in bottles of 60 mL and 105 mL
Amoxicillin (Himox®) 250 mg/ 5mL Powder for Oral Suspension in bottles of 60 mL and 105 mL
Amoxicillin (Himox®) 500 mg capsule in box of 100's (in flex foil)
Amoxicillin (Himox®) 250 mg capsule in box of 100's (in flex foil)

Manufactured by
ASIAN ANTIBIOTICS, INC.
No. 130 Pioneer Street
Mandaluyong City, Philippines for
UNILAB, Inc.
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Metro Manila, Philippines
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Trusted Quality Healthcare

Reg. IPOPHIL