



AMPICILLIN for Injection

USP

ANTIBIOTIC

ACTIONS AND CLINICAL PHARMACOLOGY

Ampicillin has a broad spectrum of bactericidal activity against many gram-positive and gram-negative aerobic and anaerobic bacteria. It acts through the inhibition of cell wall mucopeptide biosynthesis during the stage of active multiplication.

INDICATIONS AND CLINICAL USE

The treatment of infections due to susceptible gram-negative organisms (including strains of *Shigellae*, *S. typhosa* and other *salmonellae*, *E. coli*, *H. influenzae*, and *P. mirabilis*) and susceptible gram-positive organisms [including streptococci, pneumococci, and non-beta-lactamase (penicillinase) producing staphylococci].

CONTRAINDICATIONS

A history of allergic reactions to penicillins or cephalosporins.

WARNINGS

Before therapy, inquiry as to past penicillin or other allergies, is essential as reactions occur more frequently in hypersensitive persons. During therapy, if allergic or anaphylactic reactions occur, discontinue treatment and initiate usual measures, i.e., antihistamines, pressor amines or corticosteroids. During long term therapy, renal, hepatic, and hematopoietic functions should be checked periodically. Candidiasis and other superinfections may occur, especially in debilitated and malnourished patients, or those with low resistance to infection due to corticosteroids, immunosuppressors or irradiation.

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The passage of any penicillin from blood into brain is facilitated by inflamed meninges and during cardiopulmonary bypass. In the presence of such factors and particularly in the presence of renal failure when high serum concentrations can be attained, central nervous system adverse effects including myoclonus, convulsive seizures and depressed consciousness can be expected. Although this complication has not been reported with ampicillin, it should be anticipated.

PRECAUTIONS

The safety of this drug in pregnancy has not been established.

ADVERSE REACTIONS

Gastrointestinal Disturbances

Glossitis, stomatitis, black "hairy" tongue, nausea, vomiting, diarrhea, enterocolitis and pseudomembranous colitis. (These reactions are usually associated with oral administration.)

Hypersensitivity Reactions

Erythematous maculopapular rashes have been reported fairly frequently: urticaria, erythema multiforme, and a few cases of exfoliative dermatitis have been observed. Anaphylaxis is the most serious reaction usually associated with parenteral administration.

Urticaria, other skin rashes, and serum sickness-like reactions may be controlled with antihistamines, and if necessary, systemic corticosteroids. Serious anaphylactic reactions require the immediate use of epinephrine, oxygen and i.v. corticosteroids. In cases of infectious mononucleosis, where ampicillin has been administered, an extremely high incidence of generalized rash has been reported.

Hepatic

A mild transitory elevation of serum glutamic oxaloacetic transaminase (SGOT) in individuals receiving large (2 to 4 times the recommended dose) and often repeated i.m. injections. Evidence indicates that glutamic oxaloacetic transaminase (SGOT) is released at the site of i.m. injection of ampicillin sodium and that the presence of the enzyme in the blood does not necessarily indicate liver involvement.

Hematologic Disturbances

Anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia and agranulocytosis have been reported. These are usually reversible on discontinuation of the drug, and are believed to be hypersensitivity phenomena.

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SYMPTOMS AND TREATMENT OF OVERDOSAGE

The treatment of overdose would likely be needed only in patients with severely impaired renal function.

DOSAGE AND ADMINISTRATION

Dosage

Infections of the ear, nose, throat and lower respiratory tract:

Adults: 250 to 500 mg every 6 hours.

Children: 25 to 50 mg/kg/day in equally divided doses at 6 hour intervals.

Infections of the gastrointestinal tract and of the genitourinary tract:

Adults: 500 mg every 6 hours.

Children: 50 mg/kg/day in equally divided doses at 6 hour intervals.

Larger doses may be required for stubborn or severe infections. The children's dosages are intended for individuals whose weights will not result in calculated dosage greater than that recommended for adults.

In the treatment of chronic urinary tract and intestinal tract infections, frequent bacteriological and clinical appraisal is necessary. Smaller doses than those recommended above should not be used; higher rinses may be needed at times. In stubborn infections, therapy may be required for several weeks. It may be necessary to continue clinical and/or bacteriological follow-up for several months after cessation of therapy.

Treatment should be continued for a minimum of 48 to 72 hours beyond the time that the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. A minimum of 10 days treatment is recommended for any infection caused by beta-hemolytic streptococci.

In gonorrhea therapy, serologic tests for syphilis should be performed initially and monthly for 3 months.

Reconstituted Solutions

ASEPTIC TECHNIQUES SHOULD BE USED.

Use Sterile Water for Injection as the only diluent.

Reconstituted solutions should be used within one hour when kept at controlled room temperature between 15 °C and 30 °C, since the potency may decrease significantly. Protect reconstituted solutions from freezing.

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Intramuscular: Using Sterile Water for Injection, Ampicillin for Injection, USP may be reconstituted as follows (see Table 1):

Table 1: Reconstitution for Intramuscular Use

<u>Vial Size</u>	<u>Diluent Added</u>	<u>Approximate Withdrawable Volume</u>	<u>Approximate Concentration Per mL</u>
250 mg	0.9 mL	1 mL	250 mg
500 mg	1.8 mL	2 mL	250 mg
1 g	3.4 mL	4 mL	250 mg
2 g	6.8 mL	8 mL	250 mg

Direct intravenous use: Use Sterile Water for Injection. Add 5 mL to the 250 mg or 500 mg vial, withdraw contents, and administer slowly over a period of 3 to 5 minutes. Add 7.4 mL to the 1 g vial and withdraw the entire contents (see Table 2). Inject slowly over a period of at least 10 to 15 minutes. **CAUTION:** More rapid administration may result in convulsive seizures.

Table 2: Reconstitution for Intravenous Use

<u>Vial Size</u>	<u>Diluent Added</u>	<u>Approximate Withdrawable Volume</u>	<u>Approximate Concentration Per mL</u>
250 mg	5 mL	5 mL	50 mg
500 mg	5 mL	5 mL	100 mg
1 g	7.4 mL	8 mL	125 mg
2 g	10 mL	11 mL	180 mg

Intravenous Infusion: Reconstitute the 1g or 2 g vial with 7.4 mL or 10 mL respectively, of Sterile Water for Injection prior to dilution to the desired volume with one of the i.v. solutions listed below. Stability studies at concentrations of 2 mg/mL and 30 mg/mL in various i.v. solutions, indicate the drug will lose less than 10% activity at room temperature (between 15 °C and 30 °C) for the time periods stated (see Table 3). Unused portions should be discarded after the time period indicated.

Table 3

<u>Diluent</u>	<u>Concentration</u>	<u>Stability Periods</u>
Isotonic Sodium Chloride	30 mg/mL	8 hours
5% Dextrose in Water	2 mg/mL	4 hours
5% Dextrose in 0.4% Sodium Chloride Solution	2 mg/mL	4 hours
10% Invert Sugar in Water	2 mg/mL	4 hours
M/6 Sodium Lactate Solution	30 mg/mL	8 hours

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The drug concentration and the rate and volume of infusion should be adjusted so that the total dose of ampicillin is administered before the drug loses its stability in the solution in use.

Parenteral products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

COMPOSITION

Each vial of Ampicillin for Injection contains 250 mg, 500 mg, 1 g, or 2 g of ampicillin as the sodium salt. Each gram of ampicillin sodium contains approximately 60 mg or approximately 6% sodium.

STABILITY AND STORAGE RECOMMENDATIONS

Store the dry powder at controlled room temperature between 15 °C and 30 °C.

AVAILABILITY OF DOSAGE FORMS

Ampicillin for Injection is supplied as a dry powder in vials containing 250 mg, 500 mg, 1 g and 2 g of ampicillin as ampicillin sodium.



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