PRESCRIBING INFORMATION

[Pr] Ampicillin Sodium for Injection BP

250 mg, 500 mg, 1 g and 2 g

(As ampicillin sodium)

Antibiotic

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CANADA

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Table of Contents

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	All Non medicinal Ingredients
Parenteral	Powder for injection 250 mg, 500 mg, 1 g and 2 g	*see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

Ampicillin Sodium for Injection BP is indicated for 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 penicillin or cephalosporins.

WARNINGS AND PRECAUTIONS

General: A high percentage of patients with infectious mononucleosis or lymphatic leukemia who receive ampicillin develop a skin rash, and the drug should not be administered to such patients. In most cases, the rash is maculopapular, pruritic, and generalized. Prolonged use of antibiotics may promote overgrowth of nonsusceptible organisms. Should superinfections occur, appropriate measures should be taken.

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.

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.

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; uriticaria, erythema multiforme, and a few cases of exfoliative dermatitis have been observed. Anaphylaxis is the most serious reaction usually associated with parenteral administration.

Note: Uriticaria, 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.

Renal: Interstitial nephritis has been reported.

Ototoxicity: Ampicillin may be ototoxic when given i.v. in very high doses.

Hepatic: A mild transitory elevation of serum glutamic oxaloacetic transaminase (SGOT) in individuals receiving large (2 to 4 times recommended dose) and often repeated i.m. injections.

Evidence indicates that serum glutamic oxaloacetic transaminase (SGOT) is released at the site of i.m. injection of sodium ampicillin and that the presence of the enzyme in the blood does not necessarily indicate liver involvement.

Hematologic Disturbances: Anemia, thrombocytopenia, thrombocytopenic purpura, hemorrhagic diathesis, eosinophilia, leukopenia and agranulocytosis have been reported rarely in association with ampicillin therapy. These reactions are usually reversible on discontinuation of the drug and are believed to be hypersensitivity phenomena.

DRUG INTERACTIONS

Drug Interactions: The concurrent administration of allopurinol and ampicillin increases substantially the incidence of rashes in patients receiving both drugs as compared to patients receiving ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to

allopurinol or to hyperuricemia present in these patients. Ampicillin and aminoglycosides should not be reconstituted together due to the in vitro inactivation of the aminoglycosides by the ampicillin.

Drug/Laboratory Test Interactions: Following administration of ampicillin to pregnant women, a transient decrease in plasma concentration of total conjugated estriol, estriol glucuronide, conjugated estrone and estradiol has been noted.

With high urine concentrations of ampicillin, false-positive urinary glucose reactions may occur if copper reduction methods are used. Therefore, it is recommended that glucose tests based on enzymatic glucose oxidase reactions be employed.

Pregnancy: Animal studies with ampicillin have shown no teratogenic effects. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Lactation: Ampicillin is excreted in trace amounts in human milk. Therefore, caution should be exercised when ampicillin is administered to a nursing mother.

Use in Elderly: There are no known specific precautions for the use of ampicillin in the elderly.

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 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 doses 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 Group A betahemolytic streptococci. In gonorrhea therapy, serologic tests for syphilis should be performed initially and monthly for 3 months.

Administration:

Reconstitution:

Reconstituted Solutions: Use sterile water for injection as the only diluent.

I.M. Use: Using sterile water for injection, reconstitute as follows:

Vial Size (mg)	Volume of Diluent Added (mL)	Withdrawable Volume (mL)	Nominal Concentration (mg/mL)
250	1.9	2.0	125
500	1.8	2.0	250
1000	3.5	4.0	250

Withdraw the entire contents and use immediately after reconstitution.

Direct I.V. Use: Use sterile water for injection, reconstitute as follows:

Vial Size (mg)	Volume of Diluent Added (mL)	Withdrawable Volume (mL)	Nominal Concentration (mg/mL)
250	1.9	2.0	125
500	1.8	2.0	250

For direct intravenous administration, the product should be diluted to a concentration of 50 mg/mL with Sterile Water for Injection and administered by slow injection (three to four minutes).

Withdraw the entire contents and use immediately after reconstitution.

I.V. Infusion: Use sterile water for injection for initial dilution of the 1 g and 2 g vials, and reconstitute as follows:

Vial Size (g)	Volume of Diluent Added (mL)	Withdrawable Volume (mL)	Nominal Concentration (mg/mL)
1	3.5	4.0	250
2	6.8	8.0	250

Withdraw the entire contents and use immediately after reconstitution.

Parenteral Products: Stability studies on ampicillin sodium, 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 (22°C) for the time periods stated when the drug is added to the following infusion fluids:

Isotonic sodium chloride:	(30 mg/mL)	8 hours
5% dextrose in water:	(2 mg/mL)	0 hours
5% dextrose in 0.4% sodium chloride solution:	(2 mg/mL)	0 hours

IM/Direct IV Use: Entire contents should be withdrawn and the dose injected over a period of 3-5 minutes.

IV Infusion: Entire contents should be withdrawn and the dose injected over a period of at least 10-15 minutes.

CAUTION: More rapid administration may result is convulsive seizures. The solution must be used immediately after reconstitution.

OVERDOSAGE

The treatment of overdosage would likely be needed only in patients with severely impaired renal function. In case of overdosage, discontinue medication, treat symptomatically and institute supportive measures as required. In patients with renal function impairment, ampicillin class antibiotics can be removed by hemodialysis but not by peritoneal dialysis.

For management of a suspected drug overdose, contact your regional Poison Control Centre immediately.

ACTION 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.

STORAGE AND STABILITY

Store at room temperature (15°C to 25°C). Reconstituted solutions should be used immediately after reconstitution.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage form	**Powder for Injection**			
Strength	**250 mg**	**500 mg**	**1 g**	**2 g**
Description	White to off-white powder filled in 10 ml clear glass vials, stoppered with grey bromo butyl rubber stoppers and sealed with aluminium seals having taxim red coloured polypropylene disc.	White to off-white powder filled in 10 ml clear glass vials, stoppered with grey bromo butyl rubber stoppers and sealed with aluminium seals having violet coloured polypropylene disc.	White to off - white powder filled in 15 mL clear glass vials, stoppered with grey bromo butyl rubber stoppers and sealed with aluminium seals having grey coloured polypropylene disc.	White to off-white powder filled in 20 ml clear glass vials, stoppered with grey bromo butyl rubber stoppers and sealed with aluminium seals having yellow coloured polypropylene disc.
Composition	Each vial contains 282.50 mg of Ampicillin Sodium equivalent to 250 mg of Ampicillin. **Non-medicinal Ingredients:** water for injection	Each vial contains 564.90 mg of Ampicillin Sodium equivalent to 500 mg of Ampicillin. **Non-medicinal Ingredients:** water for injection	Each vial contains 1.13 g of Ampicillin Sodium equivalent to 1 g of Ampicillin. **Non-medicinal Ingredients:** water for injection	Each vial contains 2.26 g of Ampicillin Sodium equivalent to 2 g of Ampicillin. **Non-medicinal Ingredients:** water for injection
Packaging	10 mL clear glass vial. The available pack sizes are 10 x 10 Vials each.	10 mL clear glass vial. The available pack sizes are 10 x 10 Vials each.	15 mL clear glass vial. The available pack sizes are 10 x 10 Vials each.	20 mL clear glass vial. The available pack sizes are 10 x 10 Vials each.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

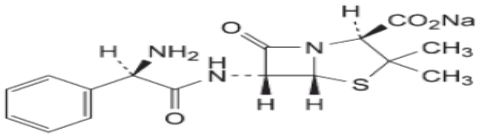
Drug Substance

Proper name: Ampicillin Sodium

Chemical name: Sodium (2S,5R,6R)-6-[[(2R)-2-amino-2-phenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate.

Molecular formula and molecular mass: $C_{16}H_{18}N_3NaO_4S$, 371.4 g/mol

Structural formula:



Physicochemical properties: A White or almost white powder hygroscopic.

REFERENCES:

- Prescribing information - Ampicillin Sodium for Injection USP. Teva Canada Limited., Date of Revision: April 29, 2014.