

Amsubac 1.5 g Injection - Malaysia Pack Insert

Open Length 370 (L) x 140(H) mm

58 GSM White Print Paper, Colour Black

Ref. specification No.FD/LT/3OT9307/002/0124

AMSUBAC 1.5 g Injection

Ampicillin 1000mg and Sulbactam 500mg

Product Name
AMSUBAC 1.5 g Injection

Product Description
White powder in clear colorless glass vial for injection. A clear and colorless solution after reconstituted.

Composition
Each vial contains :
Ampicillin sodium USP equivalent to Ampicillin 1000mg
Sulbactam sodium USP equivalent to Sulbactam 500mg

Pharmacodynamics
Biochemical studies with cell-free bacterial systems have shown sulbactam to be an irreversible inhibitor of most important β-lactamases that occur in penicillin-resistant organisms. It possesses significant antibacterial activity only against Neisseriaceae, *Acinetobactercalcoaceticus*, *Bacteroides* sp, *Branhamella catarrhalis* and *Pseudomonas cepacia*. The potential for sulbactam sodium preventing the destruction of penicillins and cephalosporins by resistant organisms was confirmed in whole organism studies using resistant strains, in which sulbactam sodium exhibited marked synergistic effects with penicillins and cephalosporins. Since sulbactam also binds to some penicillin-binding proteins, some sensitive strains are rendered more susceptible to the combination than to the β-lactam antibiotic alone.

The bactericidal component of the combination is ampicillin which, like benzyl penicillin, acts against sensitive organisms during the stage of active multiplication by the inhibition of biosynthesis of cell wall mucopeptide.

Ampicillin & Sulbactam Injection is effective against a wide range of gram-positive and gram-negative bacteria including: *Staphylococcus aureus* and *S.epidermidis* (including penicillin-resistant and some methicillin-resistant strains); *Streptococcus pneumoniae*, *Streptococcus faecalis* and other *Streptococcus* sp; *Haemophilus influenzae* and *parainfluenzae* (both β-lactamase-positive and -negative strains); *Branhamella catarrhalis*; anaerobes, including *Bacteroides fragilis* and related species; *Escherichia coli*, *Klebsiella* sp, *Proteus* sp (both indole-positive and indole-negative), *Morganella morganii*, *Citrobacter* sp and *Enterobacter* sp, *Neisseria meningitidis* and *Neisseria gonorrhoeae*.

Pharmacokinetics
Sulbactam sodium and ampicillin sodium diffuses readily into most body tissues and fluids in human. Penetration into brain and spinal fluid is low except when meninges are inflamed. High concentrations of sulbactam and ampicillin are achieved in the blood following IV or IM administration and both components have a half-life of approximately 1 hour. Most of the sulbactam sodium and ampicillin sodium is excreted unchanged in the urine.

Indication
For infections caused by susceptible microorganisms, typical indications are upper and lower respiratory tract infections including sinusitis, otitis media and epiglottitis; bacterial pneumonias; urinary tract infections and pyelonephritis; intra-abdominal infections including peritonitis, cholecystitis, endometritis and pelvic cellulitis; bacterial septicaemia; skin, soft tissue, bone and joint infections and gonococcal infections.

Ampicillin sodium & Sulbactam sodium may also be administered preoperatively to reduce the incidence of postoperative wound infections in patients undergoing abdominal or pelvic surgery, in which peritoneal contamination may be present. In termination of pregnancy or caesarean section, Ampicillin sodium & Sulbactam sodium may be used prophylactically to reduce postoperative sepsis.

Recommended Dosage
Ampicillin sodium & Sulbactam sodium can be administered by either IV or IM routes. The following dilutions may be used: See Table 1.

Table 1.				
Total Dosage (g)	Equivalent Dosage of Sulbactam Ampicillin (g)	Package	Diluent Volume (mL)	Maximum Final Concentration (mg/mL)
0.75	0.25-0.5	10-mL vial	1.6	125-250
1.5	0.5-1	20-mL vial	3.2	125-250
3	1-2	20-mL vial	6.4	125-250

For IV administration, Ampicillin sodium & Sulbactam sodium should be reconstituted with sterile water for injection or any compatible solution. To ensure complete dissolution, allow foaming to dissipate to permit visual inspection. The dose can be given by bolus injection over a minimum of 3 min or can be used in greater dilutions as an IV infusion over 15-30 min. Ampicillin sodium & Sulbactam sodium parenteral may also be administered by deep IM injection; if pain is experienced, 0.5% sterile solution for injection of lignocaine HCl anhydrous may be used for reconstitution of the powder.

Adults:
The usual dosage range of Ampicillin sodium & Sulbactam sodium is 1.5-12 g/day in divided doses every 6 or 8 hours up to a maximum daily dosage of sulbactam of 4 g. Less severe infections may be treated on an every-12-hr schedule. (See Table 2.)

Table 2.	
Severity of Infection	Daily Dose of Ampicillin & Sulbactam IM/IV (g)
Mild Moderate Severe	1.5 to 3 (0.5+1 to 1+2) up to 6 (2+4) up to 12 (4+8)

More or less frequent dosing may be indicated depending on the severity of the illness and the renal function of the patient. Treatment is usually continued until 48 hours after pyrexia and other abnormal signs have resolved. Treatment is normally given for 5-14 days, but the treatment period may be extended or additional ampicillin may be administered in severely ill cases.

In treating patients on restricted sodium intake, it should be noted that 1500 mg of Ampicillin sodium & Sulbactam sodium contains approximately 115 mg (5 mmol) of sodium.

For the prophylaxis of surgical infections, 1.5-3 g of Ampicillin sodium & Sulbactam sodium should be given at induction of anaesthesia, which allows sufficient time to achieve effective serum and tissue concentrations during the procedure. The dose may be repeated every 6-8 hours; administration is usually stopped 24 hours after the majority of surgical procedures, unless a therapeutic course of Ampicillin sodium & Sulbactam sodium is indicated.

In the treatment of uncomplicated gonorrhea, Ampicillin sodium & Sulbactam sodium can be given as a single dose of 1.5 g. Concomitant probenecid 1 g orally should be administered in order to prolong plasma concentrations of sulbactam and ampicillin.

Children, Infants, Neonates:
The dosage of Ampicillin sodium & Sulbactam sodium for most infections in children, infants and neonates is 150 mg/kg/day (corresponding to sulbactam 50 mg/kg/day and ampicillin 100 mg/kg/day). In children, infants and neonates, dosing is usually every 6 or 8 hrs in accordance with the usual practice for ampicillin. In neonates during the 1st week of life (especially pre-terms), the recommended dose is 75 mg/kg/day (corresponding to 25 mg/kg/day sulbactam and 50 mg/kg/day ampicillin) in divided doses every 12 hrs.

Renal Impairment:
In patients with severe impairment of renal function (creatinine clearance ≤30 mL/min), the elimination kinetics of sulbactam and ampicillin are similarly affected and hence the plasma ratio of one to the other will remain constant. The dose of Ampicillin sodium & Sulbactam sodium in such patients should be administered less frequently in accordance with the usual practice for ampicillin.

Prepared by	Checked by	Reviewed by		Approved by
AM (RNG)	E / IC - Production	DGM (NCM)	DGM (RPS)	DGM (MVS)

Incompatibilities

For IV administration, Ampicillin sodium & Sulbactam sodium should be reconstituted with sterile water for injection or any compatible solution. To ensure complete dissolution, allow foaming to dissipate to permit visual inspection. The dose can be given by bolus injection over a minimum of 3 min or can be used in greater dilutions as an IV infusion over 15-30 min. Sulbactam sodium/ampicillin sodium parenteral may also be administered by deep IM injection; if pain is experienced, 0.5% sterile solution for injection of lignocaine HCl anhydrous may be used for reconstitution of the powder.

Contraindications

The use of Ampicillin sodium & Sulbactam sodium is contraindicated in individuals with a history of hypersensitivity reactions to any of the penicillins.

Warnings and Precautions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy including sulbactam sodium/ampicillin sodium IM/IV. These reactions are more apt to occur in individuals with a history of penicillin hypersensitivity and/or hypersensitivity reactions to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before therapy with penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins and other allergens. If an allergic reaction occurs, the drug should be discontinued and the appropriate therapy instituted.

Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, IV steroids and airway management, including intubation, should be administered as indicated. As with any antibiotic preparation, constant observation for signs of overgrowth of nonsusceptible organisms, including fungi, is essential. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

A high percentage of patients with mononucleosis who receive ampicillin develop a skin rash. Thus, ampicillin mononucleosis who receive ampicillin develop a skin rash. In patients treated with Ampicillin sodium & Sulbactam sodium, the possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving Pseudomonas or Candida), the drug should be discontinued and/or appropriate therapy instituted.

Interactions with Other Medicaments

Allopurinol: The concurrent administration of allopurinol and ampicillin substantially increases the incidence of rashes in patients receiving both drugs as compared with patients receiving ampicillin alone.

Aminoglycosides: Mixing ampicillin with aminoglycosides *in vitro* has resulted in substantial mutual inactivation; if these groups of antibacterials are to be administered concurrently, they should be administered at separate sites at least 1 hour apart (see Incompatibilities). Anticoagulants: Parenteral penicillins can produce alterations in platelet aggregation and coagulation tests. These effects may be additive with anticoagulants.

Bacteriostatic drugs (chloramphenicol, erythromycin, sulfonamides and tetracyclines) may interfere with the bactericidal effect of penicillins; it is best to avoid concurrent therapy. Estrogen-containing Oral Contraceptives: There have been case reports of reduced oral contraceptive effectiveness in women taking ampicillin, resulting in unplanned pregnancy. Although the association is weak, patients should be given the option to use an alternate or additional method of contraception while taking ampicillin.

Methotrexate: Concurrent use with penicillin has resulted in decreased clearance of methotrexate and in methotrexate toxicity. Patients should be closely monitored. Leucovorin dosages may need to be increased and administered for longer periods of time.

Probenecid: Probenecid decreases renal tubular secretion of ampicillin and sulbactam when used concurrently; this effect results in increased and prolonged serum concentrations, prolonged elimination half-life, and increased risk of toxicity.

Laboratory Test Interactions: False positive glycosuria may be observed in urinalysis using Benedict's reagent, Fehling's reagent and Clinitest. Following administration of ampicillin to pregnant women, a transient decrease of plasma concentration of total conjugated estriol, estriol-glucuronide, conjugated estrone and estradiol has been noted. This effect may also occur with sulbactam sodium/ampicillin sodium IM/IV. Incompatibilities:Sulbactam sodium/ampicillin sodium IM/IV should be reconstituted and administered separately, due to the *in vitro* inactivation of aminoglycosides by any of the aminopenicillins.

Pregnancy and Lactation

Animal reproduction studies have revealed no evidence of impaired fertility or harm to the fetus due to sulbactam and ampicillin. Sulbactam crosses the placental barrier. Safety for use in pregnancy and lactation has not been established.

Side Effects

As with other parenteral antibiotics, the principal side effect observed is injection site pain, especially associated with the IM route of administration. A small number of patients may develop phlebitis or an injection site reaction, after IV administration.

Blood and Lymphatic System:

Anaemia, hemolytic anaemia, thrombocytopenia, eosinophilia and leukopenia have been reported during therapy with sulbactam sodium/ampicillin sodium. These reactions are reversible on discontinuation of therapy and are believed to be sensitivity reactions.

Gastrointestinal:

The most common were nausea, vomiting, diarrhoea, enterocolitis, and pseudomembranous colitis.

Hepatobiliary Disorders: Bilirubinemia, abnormal hepatic function and jaundice.

Immune System: Anaphylactoid reaction and anaphylactic shock.

Nervous System: Rare reports of convulsions.

Renal and Urinary Systems: Rare reports of interstitial nephritis.

Skin and Subcutaneous Tissue:

Rash, itching and other skin reactions, rare reports of Stevens-Johnson syndrome, epidermal necrolysis and erythremamultiforme.

Hepatic:

Transient elevations of ALT (SGPT) and AST (SGOT) transaminases. Adverse reactions associated with the use of ampicillin alone may be observed with Ampicillin & Sulbactam.

Symptoms and Treatment of Overdose

Limited information is available on the acute toxicity of ampicillin sodium and sulbactam sodium in humans. Overdosage of the drug would be expected to produce manifestations that are principally extensions of the adverse reactions reported with the drug. The fact that high CSF concentrations of β -lactam antibiotics may cause neurologic effects, including seizures, should be considered. Because ampicillin and sulbactam are both removed from the circulation by hemodialysis, these procedures may enhance the elimination of the drug from the body if overdosage occurs in patients with impaired renal function.

Presentation

1 vial or 10 vials are packed in a folded paper box.

Storage Condition

Store below 30°C.

Shelf Life

36 months from the date of manufacture if kept as recommended. Balance solution should be discarded.

Registration number

AMSUBAC 1.5 g Injection - MAL09111742AZ
BRU22033199P

Name and Address of Manufacturer

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Date of revision of package insert

30th January 2024

30T9307/002/0124