Ampicillin and Sulbactam for Injection USP
3 g / Vial
For IM/IV use

Composition :
Each vial contains:
Ampicillin sodium USP
Eq. to anhydrous Ampicillin……..2gm
Sulbactam Sodium USP
Eq. to anhydrous Sulbactam……..1 gm

Pharmacodynamics :
Ampicillin/sulbactam is a combination of a β-lactam antibiotic and a β-lactamase inhibitor. Ampicillin works by binding to penicillin-binding proteins (PBPs) to inhibit bacterial cell wall synthesis. This causes disruption of the bacterial cell wall and leads to bacterial cell death. However, resistant pathogens may produce β-lactamase enzymes that can inactivate ampicillin through hydrolysis. This is prevented by the addition of sulbactam, which binds and inhibits the β-lactamase enzymes. It is also capable of binding to the PBP of Bacteroides fragilis and Acinetobacter spp., even when it is given alone. The activity of sulbactam against Acinetobacter spp. seen in in-vitro studies makes it distinctive compared to other β-lactamase inhibitors, such as tazobactam and clavulanic acid.

Pharmacokinetics :
The addition of sulbactam to ampicillin enhances the effects of ampicillin. This increases the antimicrobial activity by 4- to 32-fold when compared to ampicillin alone. Ampicillin is a time-dependent antibiotic. Its bacterial killing is largely related to the time that drug concentrations in the body remain above the minimum inhibitory concentration (MIC). The duration of exposure will thus correspond to how much bacterial killing will occur. Various studies have shown that, for maximum bacterial killing, drug concentrations must be above the MIC for 50-60% of the time for the penicillin group of antibiotics. This means that longer durations of adequate concentrations are more likely to produce therapeutic success. However, when ampicillin is given in combination with sulbactam, regrowth of bacteria has been seen when sulbactam levels fall below certain concentrations. As with many other antibiotics, under-dosing of ampicillin/sulbactam may lead to resistance.
Ampicillin/sulbactam has poor absorption when given orally. The two drugs have similar pharmacokinetic profiles that appear unchanged when given together. Ampicillin and sulbactam are both hydrophilic antibiotics and have a volume of distribution (Vd) similar to the volume of extra-cellular body water. The volume that the drug distributes throughout in healthy patients is approximately 0.2 liters per kilogram of body weight. Patients on hemodialysis, elderly patients, and pediatric patients have shown a slightly increased volume of distribution. Using typical doses, ampicillin/sulbactam has been shown to reach desired levels to treat infections in the brain, lungs, and abdominal tissues. Both agents have moderate protein binding, reported at 38% for sulbactam and 28% for ampicillin. The half-life of ampicillin is approximately 1 hour, when used alone or in combination with sulbactam; therefore it will be completely eliminated from a healthy person in around 5 hours. It is eliminated primarily by the urinary system, with 75% excreted unchanged in the urine. Only small amounts of each drug were found to be excreted in the bile. Ampicillin/sulbactam should be given with caution in infants less than a week old and premature neonates. This is due to the underdeveloped urinary system in these patients, which can cause a significantly increased half-life for both drugs. Based on its elimination, ampicillin/sulbactam is typically given every 6 to 8 hours. Slowed clearance of both drugs has been seen in the elderly, renal disease patients, and critically ill patients on renal replacement therapy. Reduced clearance has been seen in both pediatric and post-operative patients. Adjustments in dosing frequency may be required in these patients due to these changes

Indication :
Ampicillin and Sulbactam for Injection, USP is indicated for the treatment of infections due to susceptible strains of the designated microorganisms in the conditions listed below.
Skin and Skin Structure Infections caused by beta-lactamase producing strains of Staphylococcus aureus ,[2] Escherichia coli ,[2] Klebsiella spp. [2] (including K. pneumoniae [2]) , Proteus mirabilis , [2] Bacteroides fragilis , [2] Enterobacter spp.,[2] and Acinetobacter calcoaceticus .[2]
Intra-Abdominal Infections caused by beta-lactamase producing strains of Escherichia coli, Klebsiella spp. (including K. pneumoniae[2]), Bacteroides spp. (including B. fragilis), and Enterobacter spp.[2]
Gynecological Infections caused by beta-lactamase producing strains of Escherichia coli,[2] and Bacteroides spp.[2] (including B. fragilis[2]).
Efficacy for this microorganism in this organ system was studied in fewer than 10 infections.
While Ampicillin and Sulbactam for Injection USP is indicated only for the conditions listed above, infections caused by ampicillin susceptible organisms are also amenable to treatment with Ampicillin and Sulbactam for Injection USP due to its ampicillin content. Therefore, mixed infections caused by ampicillin-susceptible organisms and beta-lactamase producing organisms susceptible to Ampicillin and Sulbactam for Injection USP should not require the addition of another antibacterial.

Dosage & Administration :
The recommended adult dose of ampicillin/sulbactam is 1.5 grams (1g ampicillin sodium plus 0.5g sulbactam sodium) to 3.0 grams (2g ampicillin sodium plus 1g sulbactam sodium) every six hours. In pediatric patients, the dose is based on body weight and is recommended at 300 mg per kilogram of body weight per day. This total daily dose is to be divided into equal amounts to be given every six hours. In patients with decreased kidney function, the dosing frequency may need to be reduced.
Ampicillin and Sulbactam for Injection USP may be administered by either the intravenous or the intramuscular routes.
For the intravenous administration, the dose can be given by slow intravenous injection over at least 10-15 minutes or can also be delivered, in greater dilutions with 50–100 mL of a compatible diluent as an intravenous infusion over 15–30 minutes.
Ampicillin and Sulbactam may be administered by deep intramuscular injection.
The recommended adult dosage of Ampicillin and Sulbactam for Injection USP is 1.5 g (1 g ampicillin as the sodium salt plus 0.5 g sulbactam as the sodium salt) to 3 g (2 g ampicillin as the sodium salt plus 1 g sulbactam as the sodium salt) every six hours. This 1.5 to 3 g range represents the total of ampicillin content plus the sulbactam content of Ampicillin and Sulbactam for Injection USP, and corresponds to a range of 1 g ampicillin/ 0.5 g sulbactam to 2 g ampicillin/1 g sulbactam. The total dose of sulbactam should not exceed 4 grams per day.
Pediatric Patients 1 Year of Age or Older: The recommended daily dose of Ampicillin and Sulbactam for Injection USP in pediatric patients is 300 mg per kg of body weight administered via intravenous infusion in equally divided doses every 6 hours. This 300 mg/kg/day dosage represents the total ampicillin content plus the sulbactam content of Ampicillin and Sulbactam for Injection USP, and corresponds to 200 mg ampicillin/100 mg sulbactam per kg per day.

Method of administration:
Ampicillin; sulbactam is administered intravenously or intramuscularly.
Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit.
Ampicillin; sulbactam 1.5 g corresponds to 1 g ampicillin and 0.5 g sulbactam, while ampicillin; sulbactam 3 g corresponds to 2 g ampicillin and 1 g sulbactam.

Contraindications :
The use of Ampicillin and Sulbactam for Injection USP is contraindicated in individuals with a history of hypersensitivity reactions (e.g. anaphylaxis or Steven-Johnson syndrome) to ampicillin, sulbactam or to other beta-lactam antibacterial drugs.
Ampicillin and Sulbactam for Injection USP is contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with Ampicillin and Sulbactam for Injection USP.

Warning and Precaution:
Hypersensitivity
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. these reactions are more apt to occur in individuals with a history of penicillin hypersensitivity and/ or hypersensitivity reactions to multiple allergens.
Hepatotoxicity
Hepatic dysfunction, including hepatitis and cholestatic jaundice has been associated with the use of Ampicillin and sulbactam for injection. Hepatic toxicity is usually reversible; however, deaths have been reported. Hepatic function should be monitored at regular intervals in patients with hepatic impairment.
Clostridium difficile Associated Diarrhea: Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Ampicillin and Sulbactam, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

PRECAUTIONS
General: A high percentage of patients with mononucleosis who receive ampicillin develop a skin rash. Thus, ampicillin class antibacterials should not be administered to patients with mononucleosis. In patients treated with Ampicillin and Sulbactam for Injection the possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur ,the drug should be discontinued and/or appropriate therapy instituted.
Prescribing Ampicillin and Sulbactam for Injection in the absence of 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.

Use in Pregnancy
Pregnancy Category B: Reproduction studies have been performed in mice, rats, and rabbits at doses up to ten (10) times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Ampicillin and Sulbactam. 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.
Labor and Delivery: Studies in guinea pigs have shown that intravenous administration of ampicillin decreased the uterine tone, frequency of contractions, height of contractions, and duration of contractions.
Nursing Mothers: Low concentrations of ampicillin and sulbactam are excreted in the milk; therefore, caution should be exercised when Ampicillin and Sulbactam for Injection is administered to a nursing woman.
Pediatric Use: The safety and effectiveness of Ampicillin and Sulbactam have been established for pediatric patients one year of age and older for skin and skin structure infections as approved in adults.

Effects on ability to drive and use machines :
Adverse effects on the ability to drive or operate machinery have not been observed.

Drug Interaction & Incompatibilities :
Probenecid decreases the renal tubular secretion of ampicillin and sulbactam. Concurrent use of probenecid with Ampicillin and Sulbactam for Injection USP may result in increased and prolonged blood levels of ampicillin and sulbactam. 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 the hyperuricemia present in these patients. There are no data with Ampicillin and Sulbactam for Injection and allopurinol administered concurrently. Ampicillin and Sulbactam for Injection USP and aminoglycosides should not be reconstituted together due to the in vitro inactivation of aminoglycosides by the ampicillin component of Ampicillin and Sulbactam for Injection USP

Side Effects :
Adult Patients: Ampicillin and Sulbactam is generally well tolerated. The following adverse reactions have been reported.

Local Adverse Reactions
Pain at I.M. injection site – 16%
Pain at I.V. injection site – 3%
Thrombophlebitis – 3%
Phlebitis – 1.2%

Systemic Adverse Reactions
The most frequently reported adverse reactions were diarrhea in 3% of the patients and rash in less than 2% of the patients.
Additional systemic reactions reported in less than 1% of the patients were: itching, nausea, vomiting, candidiasis, fatigue, malaise, headache, chest pain, flatulence, abdominal distension, glossitis, urine retention, dysuria, edema, facial swelling, erythema, chills, tightness in throat, substernal pain, epistaxis and mucosal bleeding.
Pediatric Patients: Available safety data for pediatric patients treated with Ampicillin and Sulbactam demonstrate a similar adverse events profile to those observed in adult patients. Additionally, atypical lymphocytosis has been observed in one pediatric patient receiving Ampicillin and Sulbactam.
Adverse Laboratory Changes
Adverse laboratory changes without regard to drug relationship that were reported during clinical trials were:
Hepatic: Increased AST (SGOT), ALT (SGPT), alkaline phosphatase, and LDH.
Hematologic: Decreased hemoglobin, hematocrit, RBC, WBC, neutrophils, lymphocytes,platelets and increased lymphocytes, monocytes, basophils, eosinophils, and platelets.
Blood Chemistry: Decreased serum albumin and total proteins.
Renal: Increased BUN and creatinine.
Urinalysis: Presence of RBCs and hyaline casts in urine.
Postmarketing Experience
In addition to adverse reactions reported from clinical trials, the following have been identified during post-marketing use of Ampicillin and sulbactam for injection or other products containing ampicillin. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made.
Blood and Lymphatic System Disorders: Hemolytic anemia, thrombocytopenic purpura, and agranulocytosis have been reported. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. Some individuals have developed positive direct Coombs Tests during treatment with Ampicillin and sulbactam for injection, as with other beta-lactam antibacterials.
Gastrointestinal Disorders: Cholestatic hepatitis, cholestasis, hyperbilirubinemia, jaundice, abnormal hepatic function, gastritis, stomatitis, black "hairy" tongue and Clostridium difficile associated diarrhea.
General Disorders and Administration Site Conditions: Injection site reaction
Immune System Disorders: Serious and fatal hypersensitivity (anaphylactic) reactions.
Nervous System Disorders: Convulsion
Renal and Urinary Disorders: Tubulointerstitial nephritis
Skin and Subcutaneous Tissue Disorders: Toxic epidermal necrolysis, Stevens-Johnson syndrome, and acute generalised exanthematous pustulosis (AGEP), urticaria, erythema multiforme, and exfoliative dermatitis.

Overdosage:
Neurological adverse reactions, including convulsions, may occur with the attainment of high CSF levels of beta-lactams. Ampicillin may be removed from circulation by hemodialysis. The molecular weight, degree of protein binding and pharmacokinetics profile of sulbactam suggest that this compound may also be removed by hemodialysis.

Storage :
Store below 30°C. Protect from light & moisture.

Presentation :
20ml Vial

Keep out of reach of children.

Prescription only medicine

RemDcion
Healthcare International
Navi Mumbai, India.

AMSLT21

RemDcion Healthcare International	**Component:** Leaflet	**Code:** AMS/LT/21	**Version:** 01
	Colour: **Black**		
	GSM: 54 gsm Maplitho Paper **Dimension:** 100 x 280 mm		
Product: Ampicillin & Salbactum 3.0 g for Injection	Date: 27.08.21	Approved	