Pharmacode position may change as per Supplier's m/c requirement & additional small pharma code may appear on the front / back panel

AUROPENNZ P1530389

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AUROPENNZ POWDER FOR INJECTION

(Ampicillin and Sulbactam Powder for Injection)

AUROPENNZ POWDER FOR INJECTION 1.5g

Description:

Before reconstitution: White to off-white crystalline powder filled in 30 mL clear glass tubular vial, stoppered with 20 mm grey colour bromo butyl rubber stopper and sealed with 20 mm dark green color flip-off aluminium seal.

After reconstitution: The solid dissolves completely leaving no visible residue as undissolved matter. The constituted solution is not less clear than an equal volume of the purified water contained in similar vial and examined similar.

Each vial contains 1063mg Ampicillin Sodium equivalent to 1000mg Ampicillin and 547mg Sulbactam Sodium equivalent to 500mg Sulbactam.

AUROPENNZ POWDER FOR INJECTION 3.0g

Description:

Before reconstitution: White to off-white crystalline powder filled in 30 mL clear glass tubular vial stoppered with 20 mm grey colour bromo butyl rubber stopper and sealed with 20 mm White color flip-off aluminium seal.

After reconstitution: The solid dissolves completely, leaving no visible residue as undissolved matter.

Each vial contains 2126mg Ampicillin Sodium USP equivalent to 2000mg Ampicillin and 1094mg Sulbactam Sodium USP equivalent to 1000mg Sulbactam.

Pharmacodynamic

Biochemical studies with cell-free bacterial systems have shown sulbactam to be an irreversible inhibitor of most important beta-lactamases that occur in penicillin-resistant organisms. While sulbactam's antibacterial activity is mainly limited to Neisseriaceae, the potential for sulbactam sodium in 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 beta-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.

Sulbactam sodium/ampicillin sodium IM/IV is effective against a wide range of Grampositive and Gram-negative bacteria including: *Staphylococcus aureus* and *epidermidis* (including penicillin-resistant and some methicillin-resistant strains); *streptococcus pneumoniae, Streptococcus faecalis* and other *Streptococcus* species; *Haemophilus influenzae* and *parainfluenzae* (both beta-lactamase positive and negative strains); *Branhamella catarrhalis*, anaerobes, including *Bacteroides fragilis* and related species; *Escherichia Coli, Klebsiella* species, *Proteus* species (both indole-positive and indole negative), *Morganelli morganii, Citrobacter* species, *Enterobacter* species, *Neisseria meningitides* and *Neisseria gonorrhoeae*.

Pharmacokinetic

Sulbactam sodium/ampicillin sodium IM/IV diffuses readily into most body tissues and fluids in the 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 intravenous or intramuscular administration and both components have a half life of approximately 1 hour. Most of the sulbactam sodium/ampicillin sodium IM/IV is axcreted unchanged in the urine.

Indications

Sulbactam sodium/ampicillin sodium IM/IV is indicated 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 septicemia; skin, soft tissue, bone and joint infections and ganococcal infections.

Sulbactam sodium/ampicillin sodium IM/IV may also be administered peri-operatively to reduce the incidence of post-operative wound infections in patients undergoing abdominal or pelvic surgery, in which peritoneal contamination may be present. In termination of pregnancy or cesarean section, sulbactam sodium/ampicillin sodium IM/IV may be used prophylactically to reduce post-operative sepsis.

Recommended Dose

Sulbactam sodium/ampicillin sodium IM/IV can be administered by either intravenous or intramuscular routes. The following dilutions may be used:

Total dosage (g)	Equivalent dosage of sulbactamam-picillin (g)	Package	Diluent volume (ml)	Maximum final concentration (mg/ml)
1.5	0.5-1.0	30 ml	3.2	125-250
3.0	10.-2.0	30 ml	6.4	125-250

For intravenous administration, sulbactam sodium/ampicillin sodium IM/IV should be reconstituted with sterile water for injection or any compatible solution. To ensure complete dissolution, allow foaming to dissipate in order to visually inspect. The dose can be given by bolus injection over a minimum of 3 minutes or can be used in greated dilutions as an intravenous infusion over 15-30 minutes.

Sulbactam sodium/ampicillin sodium parenteral may also be administered by deep intramuscular injection; if pain is experienced, 0.5% sterile solution for injection of lignocaine hydrochloride anhydrous may be used for reconstitution of the powder.

Use in Adults

The usual dosage range of sulbactam sodium/ampicillin sodium IM/IV is 1.5g to 12g per day in divided doses every 6 or 8 hours up to a maximum daily dosage of sulbactam of 4g. Less severe infections may be treated on an every 12 hours schedule.

Severity of infection	Daily dose of sulbactam sodium/ampicillin sodium IM/ IV(g)
Mild	1.5 to 3 (0.5+1 to 1+2)
Moderate	Up to 6 (2+4)
Severe	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 to 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 1500mg of sulbactam sodium/ampicillin sodium IM/IV contains approximately 115mg (5mmol) of sodium.

For the prophylaxis of surgical infections, 1.5-3 g of sulbactam sodium/ampicillin sodium IM/IV should be given at induction of anesthesia, 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 sulbactam sodium/ampicillin sodium IM/IV is indicated. In treatment of uncomplicated gonorrhea, sulbactam sodium/ampicillin sodium IM/IV can be given as a single dose of 1.5g. Concomitant probenecid 1.0g orally should be administered in order to prolong plasma concentrations of sulbactam and ampicillin.

Use in children, infants and neonates

The dosage of sulbactam sodium/ ampicillin sodium IM/IV 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 tor 8 hours in accordance with the usual practice for ampicillin.

In neonates during the first week of life (especially preterms), 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 hours.

Use in patients with 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 sulbactam sodium/ ampicillin sodium IM/IV in such patients should be administered less frequently in accordance with the usual practice for ampicillin.

Directions for Reconstitution

Intramuscular injection

1.5 g strength should be reconstituted with 3.2 mL of diluent.

Diluents for Intramuscular Injection

1. Sterile water for injection USP
2. 0.5% Lidocaine Hydrochloride Injection USP
3. 2% Lidocaine Hydrochloride Injection USP

Intravenous infusion

Primary diluent: Sterile water for injection

1.5g strength should be reconstituted with 3.2 mL Primary diluent

Secondary diluents for Intravenous infusion

The above solutions are further diluted with one of the following secondary diluent

1. Sterile water for injection
2. 0.9% sodium chloride injection
3. 5% dextrose injection
4. Lactated Ringer's solution
5. 5% dextrose in 0.45% saline
6. 10% invert sugar

Reconstitute the vial with one the diluents, shake well to get clear solution and use immediately.

Route of Administration

For Intramuscular and Intravenous.

Contraindication

The use of Ampicillin and Sulbactam is contraindicated in individuals with a history of an allergic reaction to any pencillins.

Warning and Precautions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on pencillin therapy including sulbactam sodium/ampicillin sodium IM/IV.

A/s: 210 x 300 mm ■ Black Booklet Size: 35 x 60 mm

AUROBINDO Packaging Development	Product Name: Auropennz Powder For Injection	Component: Leaflet	Item Code: P1530389	Date & Time: 14.02.2022 & 3.10 PM
	Customer / Country: Malaysia - Tender	Version No.: 00	Reason Of Issue: Revision	Reviewed / Approved by
Team Leader: Sravan	Dimensions: 210 x 300 mm	No. of Colours : 01		
Initiator: Saikanth		30389		
Artist: Vision Graphic Designers	Pharmacode: 30389			
Additional Information : Supersede Item Code: P1520425				Sign / Date

These reactions are more apt to occur in individuals with a history of pencillin 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 a pencillin, careful inquiry should be made concerning previous hypersensitivity reactions to pencillins, 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, intravenous steroids and airway management including intubation, should also be administered as indicated.

As with any antibiotic preparation, constant observation for signs of growth of nonsusceptible organisms, including fungi, is essential. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including sulbactam sodium/ampicillin sodium, 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*.

C.difficile produces toxin A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C.difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD has been reported to occur over two months after the administration of antibacterial agents.

As with any potent systemic agent, it is advisable to check periodically for organ system dysfunction during extended therapy; this includes renal, hepatic and hematopoietic systems. This is particularly important in neonates, especially when premature and other infants.

Since infectious mononucleosis is viral in origin, sulbactam sodium/ampicillin sodium IM/IV developed a skin rash, should not be used in its treatment.

A high percentage of patients with mononucleosis who received ampicillin have a skin rash.

Interaction 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.

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): Bacteriostatic drugs 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 penicillins 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 reagent, Fehling reagent, and Clinitest. 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. This effect may also occur with sulbactam sodium/ampicillin sodium IM/IV.

Incompatibilities
Sulbactam sodium/ampicillin sodium IM/IV and aminoglycosides 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 intramuscular route of administration. A small number of patients may develop phlebitis or an injection-site reaction after intravenous administration.

Blood and Lymphatic System Disorders: anemia, hemolytic anemia, thrombocytopenia, eosinophilia and leucopenia 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 disorder: nausea, vomiting, diarrhea, enterocolitis and pseudomembranous colitis.

Hepatobiliary disorder: bilirubinemia, abnormal hepatic function and jaundice.

Immune System Disorders: Anaphylactoid reaction and anaphylactic shock

Investigations: Transient elevations of ALT(SGPT) and AST(SGOT) transaminases

Nervous System Disorders: rare reports of convulsions

Renal and Urinary Disorder: rare reports of interstitial nephritis

Skin and Subcutaneous tissue Disorders: rash, itching, other skin reactions, rare reports of Stevens-Johnson syndrome, epidermal necrolysis and erythema multi forme Adverse reactions associated with the use of ampicillin alone may be observed with sulbactam sodium/ampicillin sodium IM/IV.

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 CFS 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 elimination of the drug from the body if overdosage occurs in patients with impaired renal function.

Storage Condition
Store in a dry place below 30°C
After reconstitution: Use immediately and discard the remaining solution.

Shelf life
36 months

Presentation :
Auropennz Powder For Injection is supplies in 30ml vial individually and in pack of 10 vials & 20 vials of 1.5g or 3.0g and each accompanied with package insert.

AUROBINDO
Manufactured by:
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