suitable diluents Piperacillin and Tazobactam for Injection should be administered by intravenous infusion over 30 minutes. The usual total daily dose of Piperacillin and Tazobactam for Injection for adults is 3.375 g every six hours totaling 13.5 g (12 g piperacillin/1.5 g tazobactam).

Recommended Dosing of Piperacillin and Tazobactam in Patients with Normal Renal Function and Renal Insufficiency (As total grams piperacillin/tazobactam)

Renal Function (Creatinine Clearance, mL/min)	All Indication (except nosocomial pneumonia)	Nosocomial Pneumonia
* Creatinine clearance for patients not receiving hemodialysis ** 0.75 g should be administered following each hemodialysis session on hemodialysis days		
>40 mL/min	3.375 q 6 h	4.5 q 6 h
20–40 mL/min*	2.25 q 6 h	3.375 q 6 h
20 mL/min*	2.25 q 8 h	2.25 q 6 h
Hemodialysis**	2.25 q 12 h	2.25 q 8 h
CAPD	2.25 q 12 h	2.25 q 8 h

For patients on hemodialysis, the maximum dose is 2.25 g every twelve hours for all indications other than nosocomial pneumonia and 2.25 g every eight hours for nosocomial pneumonia. Since hemodialysis removes 30% to 40% of the administered dose, an additional dose of 0.75 g Piperacillin and Tazobactam should be administered following each dialysis period on hemodialysis days. No additional dosage of Piperacillin and Tazobactam is necessary for CAPD patients.

Drug Interactions

Aminoglycosides

The mixing of beta-lactam antibiotics with aminoglycosides *in vitro* can result in substantial inactivation of the aminoglycoside. The aminoglycoside should be reconstituted and administered separately The inactivation of aminoglycosides in the presence of penicillin-class drugs has been recognized.

Probenecid

Probenecid administered concomitantly with Piperacillin and tazobactam prolongs the half-life of piperacillin by 21% and of tazobactam by 71%.

Vancomycin

No pharmacokinetic interactions have been noted between Piperacillin and tazobactam and vancomycin.

Heparin

Coagulation parameters should be tested more frequently and monitored regularly during simultaneous administration of high doses of heparin, oral anticoagulants, or other drugs that may affect the blood coagulation system or the thrombocyte function.

Vecuronium

Piperacillin when used concomitantly with vecuronium has been implicated in the prolongation of the neuromuscular blockade of vecuronium.

ADVERSE REACTIONS

Local reactions: Phlebitis, pain , inflammation ,thrombophlebitis , erythemia ,deep vein thrombosis and oedema

Gastrointestinal :Diarrhea ,headache ,constipation, nausea , vomiting ,dyspepsia ,hyperbilirubinemia,cholestative hepatitis ,bloody diarrhea &rarely pseudomembranous colitis

Hypersensitivity Reaction: Anaphylactoid reactions,rash,pruritus,vesicular eruptions &positive Coombs tests.

Renal: Elevations of creatinine or BUN &rarely ,intestinal nephritis

C.N.S: Headache ,dizziness,fatigue .

Haematologic &Lymphatic :Reversible leucopenia ,neutropenia,thrombocytopenia &/or eosinophilia have been reported

Serum Electrolytes : Individuals with liver disease or individuals receiving cytotoxic therapy or diuretic were reported .Rarely to demonstrate a disease in serum potassium concentrate ions with high doses piperacillin .

Skeletal: Rarely ,prolonged muscle relaxation .

Other : Super-infection ,including candidiasis

* This drug may cause Hypokalemia or Bronchospasm as an adverse drug reaction

PRECAUTIONS General

Bleeding manifestations have occurred in some patients receiving β-lactam antibiotics, including piperacillin. These reactions have sometimes been associated with abnormalities of coagulation tests such as clotting time, platelet aggregation, and prothrombin time, and are more likely to occur in patients with renal failure. If bleeding manifestations occur, piperacillin and tazobactam for injection should be discontinued and appropriate therapy instituted.

As with other penicillins, patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure).

Piperacillin and Tazobactam is a monosodium salt of piperacillin and a monosodium salt of tazobactam and contains a total of 2.79 mEq (64 mg) of Na^+ per gram of piperacillin in the combination product. This should be considered when treating patients requiring restricted salt intake. Periodic electrolyte determinations should be performed in patients with low potassium reserves, and the possibility of hypokalemia should be kept in mind with patients who have potentially low potassium reserves and who are receiving cytotoxic therapy or diuretics.

As with other semisynthetic penicillins, piperacillin therapy has been associated with an increased incidence of fever and rash in cystic fibrosis patient

Pregnancy Piperacillin and tazobactam cross the placenta in humans. this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Piperacillin is excreted in low concentrations in human milk; tazobactam concentrations in human milk have not been studied. Caution should be exercised when piperacillin and tazobactam for injection is administered to a nursing woman.

Pediatric Use

Safety and efficacy in pediatric patients less than 2 months of age have not been established

Geriatric Use

Elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Overdose

Information of overdose of Piperacillin and tazobactam in humans is not available .Excessive serum levels of either Piperacillin and tazobactam may be reduced by haemodilasys .No specific antidote is not known . As with other penicillin's ,neuromuscular ,excitability or convulsions have occurred following large intravenous doses ,primarily in patients with impared renal function .In the case of monitor excitability or convulsions ,general supportive measures including administration of anticonvulsive agents (e.g diazepam or barbiturates) ,may be considered.

Storage : Store at controlled room temperature. protected from light. Do not freeze.

Improper storage may deteriorate the product.

Presentation: A white dry powder filled in clear glass vial

Manufactured by
AMERICAN REMEDIES
Care & Cure with Research
American Remedies Healthcare Pvt. Ltd.
(An ISO 9001:2015 Certified Company)
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ICO: American Remedies LLC, DE, USA

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

℞ Piperacillin & Tazobactam for Injection I.P.

AMERICAN

Pipracan

FOR I.V. use only
Composition
Each vial contains

Piperacillin Sodium (Sterile) I.P Eq. to anhydrous Piperacillin	4000 mg
Tazobactam Sodium (Sterile) I.P Eq. to Tazobactam	500mg

FOR I.V. use only
Composition
Each vial contains

Piperacillin Sodium (Sterile) I.P Eq. to anhydrous Piperacillin	2000 mg
Tazobactam Sodium (Sterile) I.P Eq. to Tazobactam	250mg

DESCRIPTION

Piperacillin and Tazobactam for injection is an injectable antibacterial combination product consisting of the semisynthetic antibiotic piperacillin sodium and the β-lactamase inhibitor tazobactam sodium for intravenous administration.

Piperacillin sodium is derived from D(-)-α-aminobenzyl-penicillin. The chemical name of piperacillin sodium is sodium (2*S*,5*R*,6*R*)-6-[(*R*)-2-(4-ethyl-2,3-dioxo-1-piperazine-carboxamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane- 2-carboxylate. The chemical formula is $C_{23}H_{27}N_5NaO_7S$ and the molecular weight is 539.5.

Tazobactam Sodium, a derivative of the penicillin nucleus, is a penicillanic acid sulfone. Its chemical name is sodium (2*S*,3*S*,5*R*)-3-methyl-7-oxo-3-(1*H*-1,2,3-triazol-1-ylmethyl)-4-thia- 1-azabicyclo[3.2.0]heptane-2-carboxylate-4,4-dioxide. The chemical formula is $C_{10}H_{11}N_4NaO_5S$ and the molecular weight is 322.3

Piperacillin/Tazobactam parenteral combination, is a white to off-white sterile, cryodesiccated powder consisting of piperacillin and tazobactam as their sodium salts packaged in glass vial

Microbiology

Piperacillin sodium exerts bactericidal activity by inhibiting septum formation and cell wall synthesis of susceptible bacteria. *In vitro*, piperacillin is active against a variety of gram-positive and gram-negative aerobic and anaerobic bacteria. Tazobactam sodium has little clinically relevant *in vitro* activity against bacteria due to its reduced affinity to penicillin-binding proteins. It is, however, a β -lactamase inhibitor of the Richmond-Sykes class III (Bush class 2b & 2b') penicillinases and cephalosporinases. It varies in its ability to inhibit class II and IV (2a & 4) penicillinases. Tazobactam does not induce chromosomally-mediated β-lactamases at tazobactam concentrations achieved with the recommended dosage regimen.

Piperacillin/tazobactam has been shown to be active against most strains of the following microorganisms both *in vitro* and in clinical infections

Aerobic and facultative gram-positive microorganisms:

Aerobic and facultative gram-negative microorganisms:

Gram-negative anaerobes:

Aerobic and facultative gram-positive microorganisms:

Aerobic and facultative gram-negative microorganisms:

Gram-positive anaerobes:

Gram-negative anaerobes:

Pharmacokinetics

Distribution :

Peak plasma concentrations of piperacillin and tazobactam are attained immediately after completion of an intravenous infusion of piperacillin and tazobactam for injection. Piperacillin plasma concentrations, following a 30-minute infusion of piperacillin and tazobactam for injection, were similar to those attained when equivalent doses of piperacillin were administered alone, with mean peak plasma concentrations of approximately 134 µg/mL, 242 µg/mL, and 298 µg/mL for the 2.25 g, 3.375 g, and 4.5 g piperacillin and tazobactam for injection, USP doses, respectively. The corresponding mean peak plasma concentrations of Tazobactam were 15 µg/mL, 24 µg/mL, and 34 µg/mL, respectively.

Metabolism &Excretion :

Piperacillin is metabolized to a minor microbiologically active desethyl metabolite. Tazobactam is metabolized to a single metabolite that lacks pharmacological and antibacterial activities. Both piperacillin and tazobactam are eliminated via the kidney by glomerular filtration and tubular secretion. Piperacillin is excreted rapidly as unchanged drug with 68% of the administered dose excreted in the urine. Tazobactam and its metabolite are eliminated primarily by renal excretion

with 80% of the administered dose excreted as unchanged drug and the remainder as the single metabolite. Piperacillin, tazobactam, and desethyl piperacillin are also secreted into the bile.

Both piperacillin and tazobactam are approximately 30% bound to plasma proteins. The protein binding of either piperacillin or tazobactam is unaffected by the presence of the other compound. Protein binding of the tazobactam metabolite is negligible.

Piperacillin and tazobactam are widely distributed into tissues and body fluids including intestinal mucosa, gallbladder, lung, female reproductive tissues (uterus, ovary, and fallopian tube), interstitial fluid, and bile. Mean tissue concentrations are generally 50% to 100% of those in plasma. Distribution of piperacillin and tazobactam into cerebrospinal fluid is low in subjects with non-inflamed meninges, as with other penicillins.

INDICATIONS

Piperacillin and Tazobactam for injection is indicated for the treatment of patients with moderate to severe infections caused by Piperacillin-resistant, Piperacillin/Tazobactam-susceptible, β-lactamase producing strains of the designated microorganisms in the specified conditions listed below:

ØAppendicitis (complicated by rupture or abscess) and peritonitis

ØUncomplicated and complicated skin and skin structure infections,

ØPostpartum endometritis or pelvic inflammatory disease

ØCommunity-acquired pneumonia

ØNosocomial pneumonia

CONTRAINDICATIONS

Piperacillin and Tazobactam for injection is contraindicated in patients with a history of allergic reactions to any of the penicillins, cephalosporins, or β-lactamase inhibitors.

WARNINGS

Serious And Occasionally Fatal Hypersensitivity (anaphylactic/anaphylactoid) Reactions (including Shock) Have Been Reported In Patients Receiving Therapy With Penicillins Including Piperacillin And Tazobactam These Reactions Are More Likely To Occur In Individuals With A History Of Penicillin Hypersensitivity Or A History Of Sensitivity To Multiple Allergens.. Before Initiating Therapy With Piperacillin And Tazobactam, Careful Inquiry Should Be Made Concerning Previous Hypersensitivity Reactions To Penicillins, Cephalosporins, Or Other Allergens. If An Allergic Reaction Occurs, Piperacillin And Tazobactam Should Be Discontinued And Appropriate Therapy Instituted.

Clostridium Difficile Associated Diarrhea (cdad) Has Been Reported With Use Of Nearly All Antibacterial Agents, Including Piperacillin And Tazobactam, 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.*

DOSAGE AND ADMINISTRATION

First reconstitute the contents of vial in 10/20 ml of sterile water for injection in 10/20 ml of .And futher diluted into