# PRECTUM- 4.5GM. INJECTION

FOR I.V. USE ONLY

## Composition:

Each Vial Contains:
Piperacillin Sodium U.S.P.
Eq. Piperacillin 4gm.
Tazobactam Sodium
Eq. to Tazobactam 0.5gm.

## MECHANISM OF ACTION :

Piperacillin is an extended spectrum semi-synthetic penicillin group of drug. It exerts bactericidal activity by inhibiting septum formation and cell wall synthesis of susceptible bacteria. In vitro, piperacillin is active against a variety of Gram+ve and Gram-ve 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 varies in its ability to inhibit penicillinases. Tazobactam does not induce chromosomally-mediated β-lactamases at tazobactam concentrations achieved with the recommended dosage regimen.

## PHARMACOLOGY :

### Pharmacodynamics :

Piperacillin is a penicillin beta-lactam antibiotic used in the treatment of bacterial infections caused by susceptible bacteria usually gram+ve, organisms. The name "penicillin" can either refer to several variants of penicillin available, or to the group of antibiotics derived from the penicillins. Piperacillin has in vitro activity against gram-positive and gram-negative aerobic and anaerobic bacteria. The bactericidal activity of Piperacillin results from the inhibition of cell wall synthesis and is mediated through Piperacillin binding to penicillin binding proteins (PBPs). Piperacillin is stable against hydrolysis by a variety of beta-lactamases, including penicillinases and cephalosporinases and extended spectrum beta-lactamases.

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 penicillinases and cephalosporinases. It varies in its ability to inhibit penicillinases..

### Pharmacokinetics :

**Absorption :** Peak plasma concentrations of piperacillin and tazobactam are attained immediately after completion of an intravenous infusion. The plasma concentration, following a 30-minute infusion of Piperacillin and Tazobactam, were similar to those attained when equivalent doses of piperacillin were administered alone. Steady-state plasma concentrations of Piperacillin and Tazobactam were similar to those attained after the first dose due to the short half-lives of Piperacillin and Tazobactam.

**Metabolism :** Piperacillin is metabolized to a minor microbiologically active desethyl metabolite. Tazobactam is metabolized to a single metabolite that lacks pharmacological and antibacterial activities.

**Distribution :** 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 like uterus, ovary, and fallopian tube and bile.

**Excretion :** Following single or multiple Piperacillin and Tazobactam doses to healthy subjects, the plasma half-life is ranged from 0.7 to 1.2 hours and was unaffected by dose or duration of infusion.

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 in the urine. Because Piperacillin is excreted by the biliary route as well as by the renal route, it can be used safely in appropriate dosage in patients with severely restricted kidney function.

Tazobactam and its metabolite are eliminated primarily by renal excretion with 80% of the administered dose as unchanged drug and the remainder as the single metabolite. Piperacillin, Tazobactam and desethyl piperacillin are also secreted into the bile.

## INDICATIONS AND USAGE :

Piperacillin/Tazobactum combination is indicated in moderate to severe infections caused by piperacillin-resistant but Piperacillin/Tazobactum susceptible micro organisms, beta lactamase producing strains likely -

1. Appendicitis (complicated by rupture or abscess) and peritonitis caused by piperacillin- resistant, beta-lactamase producing strains of E. coli.
2. Uncomplicated and complicated skin and structure infections.
3. Postpartum endometritis or pelvic inflammatory disease caused by piperacillin- resistant, beta-lactamase producing strains of E. coli.
4. Community- acquired pneumonia (moderate severity only) caused by piperacillin- resistant, beta-lactamase producing strains of H. influenza.
5. Nosocomial pneumonia (moderate to severe) caused by piperacillin- resistant, beta- lactamase producing strains.
6. Septicemia and meningitis caused by Piperacillin/Tazobactum susceptible pathogens.

## CONTRAINDICATION :

History of allergic reactions to any of the penicillins, cephalosporins or beta-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 Tazobactum. Pseudomembranous colitis has been reported with nearly all antibacterial agents, including piperacillin/ tazobactam and may range in severity from mild to life- threatening.

## DRUG INTERACTION :

Drug interactions between piperacillin/tazobactam and aminoglycosides, probenecid, vancomycin, heparin, vecuronium and methotrexate has been observed.

## PRECAUTIONS :

**General**: Bleeding manifestations, emergence of resistant organisms that might cause super infections, neuromuscular excitability or convulsions and fever and rash in cystic fibrosis patients.

**Pregnancy** (**Teratogenic effects** - Pregnancy Category B.) - Animal reproduction studies have failed to demonstrate a risk to the fetus. There are, however, no adequate and well controlled studies with the Piperacillin / Tazobactam combination or with piperacillin or tazobactam alone in pregnant women.

**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 injection is administered to a nursing woman.

**Paediatric Use:** Safety and efficacy in pediatrics patients have not been established.

**Geriatric Use**: Patients over 65 years are not at an increased risk of developing adverse effects solely because of age. However, dosage should be adjusted in the presence of renal insufficiency. In general, dose selection to an elderly patient should be cautions, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function because 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.

## ADVERSE REACTIONS :

Adverse events reported in >1% patients were diarrhea, headache, constipation, nausea, insomnia, rash, vomiting, dyspepsia, purities, stool changes, fever, agitation, pain, moniliasis, hypertension, dizziness, abdominal pain, chest pain, edema, anxiety, and rhinitis, 90% of the adverse events reported were mild to moderate in severity end transient in nature.
**Injection site reaction** - Pain and inflammation, thrombophlebitis and edema are adverse local reactions that were reported, irrespective of relationship to therapy with piperacillin and tazobactam for injection.

## OVER DOSAGE :

Patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure).
Treatment should be supportive and symptomatic according the patient's clinical presentation Excessive serum concentrations of either piperacillin or tazobactam may be reduced by hemodialysis.

## DOSAGE AND ADMINISTRATION :

**Adult :** Dose of Piperacillin / tazobactam in intra-abdominal Infection, peritonitis, skin or soft tissue infection, endometritis, pelvic inflammatory disease, pneumonia, aspiration pneumonia, bacteremia, deep neck infection, febrile neutropenia, joint infection, osteomyelitis, pyelonephritis, urinary tract infection is 4.5gm. I.V. every 8 hourly.

Prectum should be administered by intravenous infusion over 30 minutes.

**Pediatric Patients :** For pediatric patients between 2 months and 9 months of age is 80 mg piperacillin/10 mg tazobactam per kg. of body weight, every 8 hours. Pediatric patients weighing over 40 kg and with normal renal function should receive the adult dose. There are no dosage recommendations for Piperacillin/ Tazobactam in pediatric patients with impaired renal function.

**Nosocomial Pneumonia :** Initial presumptive treatment of patients with nosocomial pneumonia should start with a dosage of 4.5 g every six hours plus an aminoglycoside, totaling 18.0 g (16.0 g piperacillin/2.0 g

tazobactam). Treatment with the aminoglycoside should be continued in patients from whom Pseudomonas aeruginosa is isolated. If Pseudomonas aeruginosa is not isolated, the aminoglycoside may be discontinued at the discretion of the treating physician.

Due to the in vitro inactivation of the aminoglycoside by beta-lactam antibiotics, Prectum and the aminoglycoside are recommended for separate administration. Prectum and the aminoglycoside should be reconstituted, diluted, and administered separately when concomitant therapy with aminoglycosides is indicated.

**Dosing range :** Prectum 4.5 gm. Intra venous 6-8hourly , should not to exceed 18 g/day.

**Duration of therapy :** The usual duration of therapy of Prectum is from seven to ten days. However, the recommended duration of Prectum in nosocomial pneumonia is 7 to 14 days.

In all conditions, the duration of therapy should be guided by the severity of the infection and the patient's clinical and bacteriological progress.

**UNUSED RECONSTITUTED SOLUTION** :
Use entire reconstituted solution promptly. Discard unused portion after 24 hours if stored at room temperature (20°C to 25°C) or after 48 hours if stored at refrigerated temperature (2°C to 8°C).

Reconstituted solution must be inspected visually for particulate matter and discoloration prior to and during administration.

**COMOETIBLE RECONSITUTION DIALUENTS** :
0.9% Sodium Chloride for Injection, Sterile Water for Injection, Dextrose 5% Bacteriostatic Saline/Parabens, Bacteriostatic Water/Parabens, Bacteriostatic Saline/Benzyl Alcohol.

Reconstituted Prectum solution should be further diluted in a compatible intravenous solution. Maximum recommended volume per dose of Sterile Water for Injection is 50 ml. Prectum should not be mixed with other drugs in a syringe or infusion bottle since compatibility has not been established.

## PRESENTATION :

1 vial of 4.5 gm. Piperacillin / Tazobactam with 20ml. sterile water for injection in a carton.