RACIBAC
(Piperacillin / Tazobactam)
For Injection U.S.P.

4.5g, 2.25g
I.V. Powder for Injection

رِسی بیک
(پیپریسیلین/ٹیزوبیکٹم)
انجکشن یو۔ایس۔پی۔
۴.۵ گرام
۲.۲۵ گرام
صرف ریدی استعمال کے لئے

QUALITATIVE AND QUANTITATIVE COMPOSITION
RACIBAC for Injection U.S.P. 2.25g:
Each vial contains: Piperacillin Sodium U.S.P. equivalent to Piperacillin.....2g
Tazobactam Sodium equivalent to Tazobactam U.S.P. 0.25g
To be reconstituted with 10mL Sterile Water for Injection.
Each vial contains 4.70 mmol (108 mg) of sodium.
RACIBAC for Injection U.S.P. 4.5g:
Each vial contains: Piperacillin Sodium U.S.P. equivalent to Piperacillin.....4g
Tazobactam Sodium equivalent to Tazobactam U.S.P. 0.5g
To be reconstituted with 20mL Sterile Water for Injection.
Each vial contains 9.44mmol (217mg) sodium.

DESCRIPTION
RACIBAC (piperacillin and tazobactam) for Injection is antibacterial combination products consisting of the semisynthetic antibacterial piperacillin sodium and the β-lactamase inhibitor tazobactam sodium for intravenous administration.

CLINICAL PHARMACOLOGY
Mechanism of Action: Piperacillin, a broad spectrum, semisynthetic penicillin exerts bactericidal activity by inhibition of both septum and cell wall synthesis. Tazobactam, a beta-lactam structurally related to penicillins, is an inhibitor of many beta-lactamases, which commonly cause resistance to penicillins and cephalosporins but it does not inhibit AmpC enzymes or metallo beta- lactamases. Tazobactum extends the antibiotic spectrum of piperacillin to include many beta-lactamase producing bacteria that have acquired resistance to piperacillin alone. **Pharmacodynamics:** The pharmacodynamic parameter for piperacillin/tazobactam that is most predictive of clinical and microbiological efficacy is time above Minimum Inhibitory Concentration (MIC). **Pharmacokinetics: Absorption:** The peak piperacillin and tazobactam concentrations after 4g / 0.5g administered over 30 minutes by intravenous infusion are 298 μg/ml and 34 μg/ml respectively. **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/Tazobactam is widely distributed in tissue and body fluids including intestinal mucosa, gallbladder, lung, bile and bone. Mean tissue concentrations are generally 50 to 100% of those in plasma. **Metabolism:** Piperacillin is metabolized to a minor microbiologically active desethyl metabolite. Tazobactam is metabolized to a single metabolite that lacks pharmacological and antibacterial activities. **Elimination:** Piperacillin and tazobactam are eliminated by the kidney via glomerular filtration and tubular secretion. Piperacillin is excreted rapidly as unchanged drug with 68% of the administered dose appearing in the urine. Tazobactam and its metabolite are eliminated primarily by renal excretion with 80% of the administered dose appearing as unchanged drug and the remainder as the single metabolite. Piperacillin, tazobactam, and desethyl piperacillin are also secreted into the bile.

INDICATIONS AND USAGE
RACIBAC is a combination product consisting of a penicillin class antibacterial, piperacillin, and a β-lactamase inhibitor, tazobactam, indicated for the treatment of patients with moderate to severe infections caused by susceptible isolates of the designated bacteria in the following conditions: Intra-Abdominal Infections, Uncomplicated and complicated skin and skin structure infections, Female Pelvic Infections, Community and hospital acquired pneumonia (moderate severity only), Nosocomial pneumonia (moderate to severe), septicemia, Complicated infections involving the urinary-tract, infections in neutropenic patients.

CONTRAINDICATIONS
- Hypersensitivity to the active substances or any other penicillin-antibacterial agent.- History of acute severe allergic reaction to any other beta-lactam active substances (e.g. cephalosporin, monobactam or carbapenem).

INTERACTIONS
Non-depolarizing muscle relaxants: Piperacillin when used concomitantly with vecuronium has been implicated in the prolongation of the neuromuscular blockade of vecuronium. Due to their similar mechanisms of action, it is expected that the neuromuscular blockade produced by any of the non-depolarizing muscle relaxants could be prolonged in the presence of piperacillin.
Oral anticoagulants: During simultaneous administration of heparin, oral anticoagulants and other substances that may affect the blood coagulation system including thrombocyte function, appropriate coagulation tests should be performed more frequently and monitored regularly.
Methotrexate: Piperacillin may reduce the excretion of methotrexate; therefore, serum levels of methotrexate should be monitored in patients to avoid substance toxicity. **Probenecid:** As with other penicillins, concurrent administration of probenecid and piperacillin/tazobactam produces a longer half-life and lower renal clearance of piperacillin and tazobactam; however peak plasma concentrations of either active substance is unaffected. **Aminoglycosides:** Piperacillin, either alone or with tazobactam, did not significantly alter the pharmacokinetics of tobramycin in subjects with normal renal function and with mild or moderate renal impairment. The inactivation of tobramycin and gentamicin by piperacillin has been demonstrated in patients with severe renal impairment. **Effects on laboratory tests:** Non enzymatic methods of measuring urinary glucose may lead to false positive results, as with other penicillins. Therefore, enzymatic urinary glucose measurement is required under piperacillin/tazobactam therapy. A number of chemical urine protein measurement methods may lead to false-positive results. Protein measurement with dip sticks is not affected.

USE IN SPECIFIC POPULATION
Pregnancy: Piperacillin/Tazobactam should only be used during pregnancy if clearly indicated i.e. only if the expected benefit outweighs the possible risks to the pregnant woman and fetus. **Breast feeding:** Women who are breast feeding should be treated only if the expected benefit outweighs the possible risks to the woman and child. **Pediatric Use:** Safety and efficacy in pediatric patients less than 2 months of age have not been established. **Geriatric use:** Dosage should be adjusted in the presence of renal impairment. **Renal patients:** In patients with creatinine clearance ≤ 40mL/min and dialysis patients (hemodialysis and Continuous Ambulatory Peritoneal Dialysis (CAPD)), the intravenous dose of RACIBAC should be reduced to the degree of renal function impairment. **Patients with Cystic Fibrosis:** As with other semisynthetic penicillins, piperacillin therapy has been associated with an increased incidence of fever and rash in cystic fibrosis patients.

PRECAUTIONS
Hypersensitivity Adverse Reactions: If patients develop a skin rash they should be monitored closely and RACIBAC discontinued if lesions progress. **Hematologic Adverse Reactions:** If bleeding manifestations occur, RACIBAC should be discontinued and appropriate therapy instituted. The leukopenia/-neutropenia associated with RACIBAC administration appears to be reversible and most frequently associated with prolonged administration. **Central Nervous System Adverse Reactions:** 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). **Nephrotoxicity in Critically Ill Patients:** Combined use of piperacillin/tazobactam and vancomycin may be associated with an increased incidence of acute kidney injury. **Electrolyte Effects:** RACIBAC contains a total of 2.84 mEq (65 mg) of Na+ (sodium) per gram of piperacillin in the combination product. This should be considered when treating patients requiring restricted salt intake as high doses may lead to hypernatremia (owing to sodium content of preparations). **Clostridium difficile Associated Diarrhea:** Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including RACIBAC, and may range in severity from mild diarrhea to fatal colitis. If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against C. difficile may need to be discontinued. **Development of Drug Resistant Bacteria:** Prescribing RACIBAC in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of development of drug-resistant bacteria.

ADVERSE REACTIONS

Common: Diarrhea, nausea, vomiting, rash including maculopapular rash, anemia, candidal superinfection, constipation, headache, insomnia. **Uncommon:** Leukopenia, neutropenia, thrombocytopenia, hypersensitivity, hypotension, thrombophlebitis, phlebitis, Jaundice, dyspepsia, stomatitis, Alanine aminotransferase increased, aspartate aminotransferase increased, Pruritus, urticaria, Blood creatinine increased, Pyrexia, injection site reactions. **Rare:** Hemolytic anemia, purpura, epistaxis, bleeding time prolonged, eosinophilia, Anaphylactic/ anaphylactoid reaction (including shock), Flushing, Abdominal pain, pseudomembranous colitis, Hepatitis, blood bilirubin increased, blood alkaline phosphatase increased, gammaglutamil transferase increased, Erythema multiforme, dermatitis bullous, exanthema, Arthralgia, myalgia, Tubulonterstitial nephritis, renal failure, Chills. **Very rare:** Agranulocytosis, pancytopenia, activated partial thromboplastin time prolonged, Coombs' direct test positive, pancytopenia, thrombocythemia, Hypokalemia, blood glucose decreased, blood albumin decreased, blood protein total decreased, Stevens-Johnson-Syndrome, toxic epidermal necrolysis, Blood urea increased, epistaxis, pneumonia eosinophilic, thrombocytosis.

DOSAGE AND ADMINISTRATION

Hospital-acquired pneumonia | Septicaemia | Complicated infections involving the urinary tract| Complicated infections involving the skin | Complicated infections involving the soft-tissues| Nosocomial Pneumonia: RACIBAC should be administered by intravenous infusion over 30 minutes.

Adult: 4.5 g every 8 hours; increased if necessary to 4.5 g every 6 hours, increased frequency may be used for severe infections. The usual duration of RACIBAC treatment is from 7 to 10 days. **Pediatric:** By intravenous infusion: Neonate: 90 mg/kg every 8 hours, child: 1 month–11 years: 90 mg/kg every 6–8 hours (max. per dose 4.5 g every 6 hours), child 12–17 years: 4.5 g every 8 hours; increased if necessary to 4.5 g every 6 hours, increased frequency may be used for severe infections. **Nosocomial Pneumonia:** Initial presumptive treatment of patients with nosocomial pneumonia should start with RACIBAC at a dosage of 4.5 g every six hours plus an aminoglycoside, totaling 18.0 g (16.0 g piperacillin/2.0 g tazobactam). The recommended duration of RACIBAC treatment for nosocomial pneumonia is 7 to 14 days. Treatment with the aminoglycoside should be continued in patients from whom P. aeruginosa is isolated. **Infections in neutropenic patients:** By intravenous infusion: Adult: 4.5 g every 6 hours, child: 90 mg/kg every 6 hours (max. per dose 4.5 g). Complicated intra-abdominal infections: By intravenous infusion: Child 2–11 years: 112.5 mg/kg every 8 hours (max. per dose 4.5g), child 12–17 years: 4.5 g every 8 hours; increased if necessary to 4.5 g every 6 hours, in-creased frequency may be used for severe infections. **Unlicensed use:** Not licensed for use in children under 12 years (except for children 2–12 years with neutro-penia and complicated intra-abdominal infections). **Renal Impairment:** Adults: In patients with renal impairment (creatinine clearance ≤ 40 mL/min) and dialysis patients (hemodialysis and CAPD), the intravenous dose of RACIBAC should be reduced to the degree of actual renal function impairment. The recommended daily doses of RACIBAC for patients with renal impairment are as follows:

Table: Recommended Dosing of RACIBAC in Patients with Normal Renal Function and Renal Impairment (As total grams piperacillin/tazobactam)

Renal Function (creatinine clearance, mL/min)	All Indications (except nosocomial pneumonia) Nosocomial Pneumonia	Nosocomial Pneumonia
>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

* Creatinine clearance for patients not receiving hemodialysis
** 0.75 g (0.67 g piperacillin/0.08 g tazobactam) should be administered following each hemodialysis session on hemodialysis days

RACIBAC (0.67 g piperacillin/0.08 g tazobactam) should be administered following each dialysis period on hemodialysis days. No additional dosage of RACIBAC is necessary for CAPD patients.

Child under 12 years: 78.75mg/kg (max. 4.5g) every 8 hours if estimated glomerular filtration rate less than 50mL/minute/1.73m2. Child 12-18 years: max. 4.5g every 8 hours if estimated glomerular filtration rate 20-40mL/minute/1.73m2; max. 4.5g every 12hours if estimated glomerular filtration rate less than 20mL/minute/1.73m2.

Directions for Administration: For intravenous infusion, give intermittently in Glucose 5% or Sodium chloride 0.9%. Reconstitute initially (2.25 g in 10 mL, 4.5 g in 20 mL) with water for injections, or glucose 5%, or sodium chloride 0.9%, then dilute to 50–150mL with infusion fluid; give over 30 minutes.

Compatible Reconstitution Diluents for Pharmacy and Single Dose Vials: 0.9% sodium chloride for injection Sterile water for injection Dextrose 5% Bacteriostatic saline/parabens Bacteriostatic water/parabens.

Compatible Intravenous Solutions for Pharmacy and Single Dose Vials: 0.9% sodium chloride for injection sterile water for injection Dextran 6% in saline Dextrose 5%. Maximum recommended volume per dose of sterile water for injection is 50 mL. RACIBAC should not be mixed with other drugs in a syringe or infusion bottle since compatibility has not been established. RACIBAC is not chemically stable in solutions that contain only sodium bicarbonate and solutions that significantly alter the pH. RACIBAC should not be added to blood products or albumin hydrolysates. Due to the in vitro inactivation of aminoglycosides by piperacillin, RACIBAC and aminoglycosides are recommended for separate administration. RACIBAC and aminoglycosides should be reconstituted, diluted, and administered separately when concomitant therapy with aminoglycosides is indicated.

OVERDOSAGE:

Symptoms: There have been post-marketing reports of overdose with piperacillin/tazobactam. The majority of those events experienced including nausea, vomiting, and diarrhoea, have also been reported with the usual recommended doses. Patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure). **Treatment:** In the event of an overdose, piperacillin/tazobactam treatment should be discontinued. No specific antidote is known. Treatment should be supportive and symptomatic according to the patient's clinical presentation. Excessive serum concentrations of either piperacillin or tazobactam may be reduced by haemodialysis.

INSTRUCTIONS:

Dosage as directed by the physician or see package insert for full prescribing information. **Prior to reconstitution:** Store at 20°C-25°C, excursions permitted to 15°C-30°C. Protect from sunlight and moisture. **After reconstitution:** Discard unused portions after storage for 24 hours at 20°C-25°C or after storage for 48 hours at refrigerated temperature (2°C to 8°C). Avoid freezing and injection should not be used if container is leaking, solution is cloudy or it contains un-dissolved particles. Keep all medicines out of the reach of children.

PRESENTATION

RACIBAC (Piperacillin/Tazobactam) for injection U.S.P. 2.25g is available in glass vial with 10ml sterile water for injection & insert.

RACIBAC (Piperacillin/Tazobactam) for injection U.S.P. 4.5g is available in glass vial with 20ml sterile water for injection & insert.

علامات/طریقہ استعمال:
ربی بیک کمپونڈ آف ازوبیکٹم سے حساسیت رکھنے والے مریضوں میں ربی بیک کا استعمال ممنوع ہے۔

مضر اثرات:
دست، متلی، اُلٹی، خون کی کمی، رگڑ، بخار کی کمی، سر درد، قبض۔

احتیاطی تدابیر:
پیراسیلین یا فیزوبیکٹم سے حساسیت رکھنے والے مریضوں میں ربی بیک کا استعمال ممنوع ہے۔
حاملہ خواتین اور دودھ پلانے والی مائیں ضرورت پڑنے کے پیش نظر صرف ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
بچے، بزرگ اور گردوں کے امراض میں مبتلا مریض صرف ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
سوڈیم کی موجودگی کے پیش نظر سوڈیم کنٹرولڈ ڈایبیٹ کے مریض ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:
خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
سلوشن بنانے سے پہلے ۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر رکھیں، محفوظ رکھنے کی ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔
روشنی اور نمی سے محفوظ رکھیں۔

سلوشن بنانے کے بعد:
تیار شدہ سلوشن کو ۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر ۲۴ گھنٹے اور ریفریجریٹر میں ۲ سے ۸ ڈگری سینٹی گریڈ پر ۴۸ گھنٹے تک محفوظ رکھا جا سکتا ہے۔
انجکشن میں کوئی غیر اصل پڑیہ شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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