TIZID

(CEFTAZIDIME) USP

INJECTION

PRESENTATION

Tizid (Ceftazidime) for Injection is supplied as a white to faintly yellow powder in vials containing 250mg, 500mg and 1g ceftazidime (as pentahydrate) with sodium carbonate (118mg per gram of Ceftazidime).

Each pack includes one ampoule of distilled water for preparation. On the addition of water of injection, **Tizid** (Ceftazidime) dissolves with effervescence to produce a solution for injection. Solutions of ceftazidime range in color from light yellow to amber, depending on the diluent and volume used.

USES: Ceftazidime is a bactericidal cephalosporin antibiotic which is resistant to most beta-lactamases and is active against a wide range of Gram-positive and Gram-negative bacteria. **Tizid** (Ceftazidime) is indicated for the treatment of single or multiple infections caused by susceptible organisms. **Tizid** (Ceftazidime) because of its broad antibacterial spectrum may be used alone as empirical therapy. However, it may be used in combination with an aminoglycoside or most other betalactam antibiotics. It may also be used with an antibiotic against anaerobes when the presence of Bacteriodes fragillis is suspected.

MAJOR INDICATIONS

- **Severe Infection** e.g. septicaemia, bacteraemia, peritonitis, meningitis Infections in immunosuppressed patients with heamatologic or solid malignancies, infections in patients in intensive care, e.g. infected bums.
- **Respiratory Tract Infections** e.g. pneumonia, bronchopneumonia, empyeme, lung abscess and lung infections in cystic fibrosis.
- **Ear, Nose & Throat Infection** e.g. Otistis media, sinusitis, malignant otitis extema and others.
- **Urinary tract infections**, e.g. acute and chronic pyelonephritis, prostatitis, cystitis, renal abscess and infections associated with bladder and renal stones.
- **Skin & Soft Tissue Infections,** erysipelas, abscesses, cellulites, infected bums wounds, skin ulcers.
- **Gastrointestinal Biliary and Abdominal Infections,** e.g. cholecystitis, empyema of gall bladder, intra-abdominal abscesses, peritonitis, post-partum and pelvic inflammatory conditions.
- **Bone & Joint Infections,** e.g. Osteitis, osteomylitis, septic arthritis, infected bursitis.
- **Dialysis Infections** associated with haemo and peritoneal dialysis and with continuous ambulatory peritoneal dialysis (CAPD).
- **Prophylaxis:** Prostatic surgery (transurethral resection).

MODE OF ACTION

Tizid (Ceftazidime) is a bactericidal antibiotic. It inhibits bacterial cell wall synthesis.

SPECTRUM

A wide range of pathogenic strains and isolates associated with hospital acquired as well as community acquired infections are susceptible to **Tizid** (Ceftazidime) in vitro including strains resistant to gentamicin and other aminoglycosides. Ceftazidime is highly stable to most clinically important beta-lactamases produced by both Gram-positive and Gram-negative organisms; therefore it is active against many ampicillin and cephalothin-resistant strains. In vitro the activities of ceftazidime and aminoglycosides in combination are additive. There is evidence of synergy in some strains. This property may be important in the treatment of febrile neutropenic patients.

Ceftazidime is active in vitro against the following organisms:

GRAM-NEGATIVE

- E-Coli
- Klebsiella spp (including K. Pneumoniae).
- Proteus mirabillis.
- Proteus vulgaris.
- Morgenela morgani (formerly Proteus morgani).
- Proteus rettgen.
- Pseudomonas spp (including P.Aeruginosa)
- Providencia spp.
- Enterobacter spp.
- Citrobacter spp.
- Serratia spp.
- Salmonella spp.
- Shigella spp.
- Yersinia enlerocolitica.
- Pasteurella multocida.
- Acinabacter spp.
- Neisseria gonorrhoeae.
- Neisseria meringitidis.
- Haemophilus influenzae (including ampicillin-resistant strains).
- Haemophilus parainfluenzae (including ampicillin-resistant strains).

GRAM-POSITIVE

- Staphylococcus aureus (methicillin-sensitive strains).
- Micrococcus spp.
- Streptococcus pyogenes (Group A beta-haemolytic streptococcus).
- Streptococcus Group B (Strepagalactae).
- Streptococcus pneumoniae.
- Streptococcus mitis
- Streptococcus spp (excluding Entecooccus, Streptococcus Faecalis)

ANAEROBIC STRAINS

- Peptococcus spp.
- Peptostreptococuus spp.
- Streptococcus spp.
- Propionibacterium spp.
- Clostridium perfringens
- Clostridium perfringens
- Fusobacterium spp.
- Bacteriodes spp. (many strains of B. fragilis are resistant)

NOTE: Cefazidime is not active in vitro against Methicillin resistant Staphyioccoci. Streptococcus faecalist and many other enterococci, Clostridium difficile. Listeria monocytogenes and Campylobacter species.

DOSAGE RECOMMENDATIONS

Tizid (Ceftazidime) is to be used by the parenteral route, the dosage depends upon the severity, sensitivity, site and type of infection and upon the age, weight and renal function of the patient.

1. ADULTS: 1-6 g/day in 2 or 3 divided doses by IV or IM Injection Urinary tract and less severe infections - 500mg or 1g every 12 hours. Most infections -1g every 8 hours or 2g every 12 hours very servers infections particularly in immunocompromised patients including those with neutropenia -2g every 8 or 12 hours. Fibrocystic adults with Pseudomonal lung infections (with normal renal functions) 100-150mg/kg/day in 3 divided doses.

A. MAXIMUM DOSAGE

In adults with normal renal function 9g/day has been used without ill effect.

B. PROPHYLACTIC AGENT

When used as prophylactic agent in prostatic surgery 1g should be given at the induction of anesthesia. A second dose should be considered at the lime of catheter removal.

C. Use in elderly in view of the reduced clearance of Ceftazidime in acutely ill elderly patients, the daily dosage should not normally exceed 3g, especially in those over 80 years of age.

2.1. NEONATES (0-2 months): 25-60mg/kg/day in 2 divided doses. In neonates the serum half-life of Ceftazidime can be 3-4 times that in adults.

ii. INFANTS AND CHILDREN (>2 months): 30-100mg/kg/day m 2 or 3 divided doses. Doses up to 150mg/kg/day (maximum 6g/day) in three divided doses may be given to infected immunocompromised or fibrocystic children or children with meningitis.

DOSAGE IN RENAL IMPAIRMENT

Ceftazidime is excreted unchanged by the kidneys exclusively by glomerular filtration. Therefore in patients with impaired renal function the dosage should be reduced. An initial loading dose of 1g should be given. Maintenance doses should be based on GFR.

Recommended maintenance doses of Ceftazidime In renal Insufficiency in patients with less severe Infections:

Creatinine clearance (ml/min.)	Approx. Serum creatinine (mcmol/l) (mg/dl)	Recommended unit dose of ceftazidime (g)	Frequency of dosing (hourly)
>50	<150	-	Normal dosage
50-31	150 - 200 (1.7-2.3)	1.0	12
30-16	200 - 350 (2.3-4.0)	0.5	24
15-16	350 - 500 (4.0-5.6)	0.5	24

SEVERE INFECTIONS

In patients with severe infections the unit dose should be increased by 50% or the dosing frequency increased. In such patents the Ceftazidime serum level should not exceed 40mg/l.

In children the creatinine clearance should be adjusted for body surface area or lean body mass.

A. HAEMODIALYSIS the serum half-life during haemodialysis ranges from 3 to 5 hours. Following each haemodialysis period the maintenance dose of Ceftazidime recommended in the above table should be repeated.

B. PERITONEAL DIALYSIS Ceftazidime may be used in peritoneal dialysis and continuous ambulatory peritoneal dialysis (CAPD). In addition to intravenous use Ceftazidime can be incorporated into the dialysis fluid (usually 125 to 250mg for 2 liters of dialysis solution).

C. For patients in renal failure or continuous arteriovenous haemodialysis or high-flux haemo-filtration in intensive therapy Units: 1g daily either as a single dose or in divided doses. For low-flux haemo-filtration follow the dosage recommended under impaired renal function.

IMPAIRED HEPATIC FUNCTION: No adjustment in dosage for patients with hepatic dysfunction.

ADMINISTRATION: Tizid (Ceftazidime) may be given intravenously or by deep intramuscular injection.

INSTRUCTION FOR CONSTITUTION: All sizes of vials are supplied under reduced pressure. As the product dissolves, carbon dioxide is released and a positive pressure develops. Small bubbles of carbon dioxide in the constituted solution may be ignored.

PREPARATION OF SOLUTION

Vial Size		Amount of Diluent to be added (ml)	Approximate Concentration (mg/ml)
250mg	Intramuscular Intravenous	1.0 ml 2.5 ml	210 90
500mg	Intramuscular Intravenous	1.5 ml 5 ml	260 90
1g	Intramuscular Intravenous	3 ml 10 ml	260 90

Tizid (Ceftazidime) solutions may be given directly into the vein or Introduced Into the giving set/I.V. line if the patient is receiving Parenteral fluids.
Tizid (Ceftazidime) is compatible with most commonly used Intravenous fluids

1. Insert the syringe needles through the vial closure and inject the recommended volume of diluent.
2. Remove the needle and shake to dissolve. Carbon dioxide is released and a dear solution is obtained in about 1-2 minutes
3. Invert the vial with the syringe piston fully depressed and insert the needle into the solution.
4. Withdraw the total volume of solution into the syringe ensuring that the needle remains in the solution. Small bubbles of carbon dioxide may be disregarded.
5. Make the total volume in 2 steps

CONTRA-INDICATIONS
Patients with known hypersensitivity to Cephalosporin antibiotics.

WARNINGS: Before beginning treatment establish whether the patient has a history of hypersensitivity reactions to Ceftazidime cephalosporins, penicillin or other drugs. Special caution is necessary when giving Ceftazidime to patients who have previously show type 1 or immediate hypersensitivity reactions to penicillin. If an allergic reaction to Ceftazidime occurs discontinue the drug. Serious hypersensitivity reactions may require epinephrine adrenaline), hydrocortisone antihistamine or other emergency measures as clinically indicated.

PRECAUTION

1. Concurrent treatment with high doses of cephalosporins and nephrotoxic drugs such as aminoglycosides or potent diuretics (e.g. frusemide) may adversely after renal function. Clinical experience has shown that is not likely to be a problem with Ceftazidime at the recommended dose levels.
2. There is no evidence that Ceftazidime adversely affects renal function at normal therapeutic doses. Ceftazidime is eliminated via the kidney. Therefore the dosage should be reduced according to the degree of renal impairment. Neurological sequlae have occasionally been reported when the dose has not been reduced appropriately, (see dosage in impaired Renal Function)
3. Pregnancy: There is no experiment evidence of Embryopathic or teratogenic effects, but as with all drugs Ceftazidime should be administered with caution during the early months of pregnancy and early infancy. Use in pregnancy requires that the anticipated benefits be weighed against possible risks.
4. Lactation: Ceftazidime is excreted in human milk in small quantities and should be used with caution in nursing mothers.
5. Ceftazidime does not interfere with enzyme-based tests for glycosuria. Slight interference may be observed with copper reduction methods (Benedict's. Fehling's. Clinites). Ceftazidime does not interfere in the alkaline picrate assay for creatinine. A positive Coomb's test develops in about 5% of patients and may interfere with blood cross-matching.
6. As with other broad spectrum antibiotics, prolonged use may result in the overgrowth of non-susceptible organisms (e g. Candida. Enterococci) which may require interruption of treatment or appropriate measures. Repeated evaluation of the patient's Condition is essential.
7. Chloramphenicol is antagonistic in vitro with Ceftazidime and other cephalosporins. The clinical relevance of this finding is unknown, but if concurrent administration of Ceftazidime with chloramphenocol is proposed, the possibility of antagonism should be considered.

SIDE EFFECTS
Ceftazidime is generally well tolerated. Adverse reactions are Infrequent and include.
Local: Reported in fewer than 2% of patients, were phlebitis or trombophlebitis with IV administration, and/or inflammation after IM injection.
Hypersensitivity reaction: Reported in 2% of patients. Angloedema and anaphyiaxis (including bronchospasm and/or Hypotension) have been reported.
As with other cephalosporins, there have been rare reports of toxic epidermal necrolysis. Steven-Johnson Syndrome, and erythema Multiforme, with Ceftazidime therapy.
Gastrointestinal: Reported in fewer than 2% of patients were Diarrhoea, nausea, vomiting, abdominal pain, and very rarely oral Thrush or colitis. As with other cephalosoporins. colitis may be Associated with Clostridium defficile and may present as pseudomembranous colitis.
Genito-urinary: (fewer than 1%) Candidaiasis: vaginitis.
Central Nervous System: (fewer than 1%) include headache, dizziness, seizures, paraesthesia and bad taste. There have reports of neurological sequelae including tremor, myoctonia. convulsions, and encephalopathy in patients with renal impairment, in whom the dose of Ceftazidime has not been appropriately reduced.
Laboratory Test Changes: Transient changes noted during Ceftazidime therapy include eosinophilia. positive Coomb's tests, very rarely haemolytic anaemia, thrombocytosis and elevations in one or more of the hepatic enzymes. ALT (SGPT). AST (SGOT).
LDH. GGT and alkaline phosphatase.
As with some other cephalosporins, transient elevations of blood urea, blood urea nitrogen and/or serum creatinine have been observed occasionally. Very rarely transient leucopenia. neutropenia, granulocytosis, thromobocytopenia and lymphocytosis have been reported.
Others: In addition to the adverse reactions listed above the following unwanted affects and altered lab tests have been reported for cephalosporin - class antibiotics include: urticaria, colitis, renal dysfunction, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, hemorrhage, prolonged prothrombin time, false-positive test for glucose, elevated bilirubin and pancytopenia.

OVER-DOSAGE
Ceftazidime over dosage has occurred in patients with renal failure. Overdosage can lead to neurological sequelae including encephalopathy, convulsions and coma. Serum levels of Ceftazidime can be reduced by haemodialysis or peritoneal dialysis

PHARMACEUTICAL PRECAUTION

1. Vials of **Tizid** (Ceftazidime) for injection should be stored at a temperature below 25°C. Occasional storage at temperatures not higher than 30°C for up to 2 months is not detrimental to the product.
2. Protect unconstituted vials from light.
3. Solutions of Ceftazidime in water for injections or compatible fluids retain satisfactory potency for 18 hours at a temperature below 25°C or 7 days in a refrigerators
4. Compatibility: Ceftazidime is compatible with most commonly used intravenous fluids. Ceftazidime is less stable in Sodium Bicarbonate injection than in other intravenous fluids. It is not recommended as a diluent. Ceftazidime and aminoglycosides should not be mixed in the same giving set or syringe. Precipitation have been reported when vancomycin have been added to Ceftazidime in solution. Therefore, it would be prudent to flush giving sets and intravenous lines between administrations of these two agents.
5. Solutions range from light yellow to amber depending on concentration, diluent and storage conditions used Within the stated recommendations, product potency is not adversely affected by such color variations.
6. Ceftazidime at concentrations between 1 mg/ml and 40mg/ml is compatible with
0.9% Sodium Chloride Injection BP
M/6 Sodium Lactate Injection BP
Compound Sodium Lactate Injection BP (Hartmann's Solution)
5% Dextrose Injection BP
0.225% Sodium Chloride and 5% Dextrose Injection BP
0.45% Sodium Chloride and 5% Dextrose Injection BP
0.9% Sodium Chloride and 5% Dextrose Injection BP
0.18% Sodium Chloride and 4% Dextrose Injection BP
10% Dextrose Injection BP.
Dextran 40 Injection 10% in 0.9% Sodium Chloride Injection BP
Dextran 40 Injection 10% in 5% Dextrose Injection BP
Dextran 70 Injection 6% in 0.9% Sodium Chloride Injection BP
Dextran 70 Injection 6% in 5% Dextrose Injection BP
7. Ceftazidime at concentrations between 0.05mg/ml and 0.25mg/ml is compatible with intra peritoneal Dialysis Fluid (Lactate) BPC 1973.
8. Ceftazidime may be constituted for intramuscular use with 0.5% or 1% Lignocaine Hydrochloride Injection. Both components retain satisfactory potency when ceftazidime at 4mg/ml is admixed with.
Hydrocortisone (hydrocortisone sodium phosphate) 1 mg/ml in 0.9% Sodium Chloride Injection BP or 5% Dextrose Injection BP
Cefuroxime (cefuroxime sodium) 3mg/ml in 0.9% Sodium Chloride Injection BP.
Cloxacillin (cloxacillin sodium) 4mg/ml in 0.9% Sodium Chloride Injection BP
Heparin 10 IU/ml or 50 IU/ml in 0.9% Sodium Chloride Injection: Potassium Chloride 10mgEq/l or 40mgEq/l in 0.9% Sodium Chloride Injection BP
9. The contents of a 500mg vial of **Tizid** (Ceftizidime) for injection, constituted with 1.5ml water for injections, may be added to metronidazole injection (500mg in 100ml) and both retain their activity.
10. **Note:** Parenteral drug products should be inspected visually for particular matter before administration when even solution and container permit.

INSTRUCTIONS
Store at 15- 30°C. Protect from heat, light & moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.
NOTE:
For IM/IV use only. Effervescence occurs on addition of water for injection.

PRESENTATION
Vial containing 250mg, 500mg or 1g Ceftazidime (as Pentahydrate).

ٹائی زِڈ انجیکشن

(سیفٹازیڈیم) یو ایس پی

ہدایات: دوا کو 15-30° سینٹی گریڈ پر رکھیں۔ گرمی، روشنی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔
نوٹ: عضلاتی / وریدی استعمال کے لیے۔

STANDPHARM

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