Ceftazidime

Onetazid

1 g Powder for Injection (IM/IV)

ANTIBACTERIAL (Cephalosporin)

℞

FORMULATION:
Each vial contains:
Ceftazidime, USP (as pentahydrate)
Equivalent to
Anhydrous Ceftazidime 1g

PRODUCT DESCRIPTION:
White crystalline powder, filled in clear glass sealed vials.

PHARMACODYNAMICS:
Pharmacotherapeutic group: Anti-bacterials for systemic use. Third-generation cephalosporins.

Mechanism of action
Ceftazidime inhibits bacterial cell wall synthesis following attachment to penicillin binding proteins (PBPs). This results in the interruption of cell wall (peptidoglycan) biosynthesis, which leads to bacterial cell lysis and death.

PK/PD relationship
For cephalosporins, the most important pharmacokinetic-pharmacodynamic index correlating with *in vivo* efficacy has been shown to be the percentage of the dosing interval that the unbound concentration remains above the minimum inhibitory concentration (MIC) of Ceftazidime for individual target species (i.e. %T>MIC).

Mechanism of Resistance
Bacterial resistance to Ceftazidime may be due to one or more of the following mechanisms:
• hydrolysis by beta-lactamases. Ceftazidime may be efficiently hydrolysed by extended-spectrum beta-lactamases (ESBLs), including the SHV family of ESBLs and AmpC enzymes that may be induced or stably derepressed in certain aerobic Gram-negative bacterial species.
• reduced affinity of penicillin-binding proteins for Ceftazidime.
• outer membrane impermeability, which restricts access of Ceftazidime to penicillin binding proteins in Gram-negative organisms.
• bacterial efflux pumps.

PHARMACOKINETICS:
Absorption
After intramuscular administration of 500 mg and 1 g of ceftazidime, peak plasma levels of 18 and 37 mg/L respectively are achieved rapidly. Five minutes after intravenous bolus injection of 500 mg, 1 g or 2 g, plasma levels are 46, 87 and 170 mg/L, respectively. The kinetics of ceftazidime are linear within the single dose range of 0.5 to 2 g following intravenous or intramuscular dosing.

Distribution
The serum protein binding of Ceftazidime is low at about 10%. Concentrations in excess of the MIC for common pathogens can be achieved in tissues such as bone, heart, bile, sputum, aqueous humour, synovial, pleural and peritoneal fluids. Ceftazidime crosses the placenta readily, and is excreted in the breast milk. Penetration of the intact blood-brain barrier is poor, resulting in low levels of Ceftazidime in the CSF in the absence of inflammation. However, concentrations of 4 to 20 mg/L or more are achieved in the CSF when the meninges are inflamed.

Biotransformation
Ceftazidime is not metabolised.

Elimination
After parenteral administration plasma levels decrease with a half-life of about 2 hrs. Ceftazidime is excreted unchanged into the urine by glomerular filtration; approximately 80 to 90 % of the dose is recovered in the urine within 24 hrs. Less than 1 % is excreted via the bile.

INDICATIONS:
For the treatment of suspected or documented susceptible *Pseudomonas aeruginosa* infections, and infections due to susceptible aerobic, gram-positive organisms, including lower respiratory tract, skin, soft tissue, abdominal, bone and joints, and urinary tract infections.

INSTRUCTION FOR RECONSTITUTION:
Ceftazidime may be used by IV, IM or infusion in 3-5 minutes.
Intramuscular Administration:
Dissolve drug in Sterile Water for Injection or Lidocaine hydrochloride solution (0.5% or 1%) with concentration approximate 250 mg/mL.
Intravenous Administration:
Dissolve drug in Sterile Water for Injection, Sodium chloride 0.9% or Dextrose 5% solution with concentration approximate 100 mg/mL.
Intravenously by infusion:
Dissolve drug in Sterile Water for Injection, Sodium chloride 0.9% or Dextrose 5% solution with concentration approximate 10 mg-20 mg/mL.

DOSAGE AND ADMINISTRATION:

Table 1: Adults and children ≥ 40 kg

Intermittent Administration	
Infection	Dose to be administered
Broncho-pulmonary infections in cystic fibrosis	100 mg to 150 mg/kg/day every 8 h, maximum 9 g per day[1]
Febrile neutropenia	2 g every 8 h
Nosocomial pneumonia	
Bacterial meningitis	
Bacteraemia*	
Bone and joint infections	1-2 g every 8 h
Complicated skin and soft tissue infections	
Complicated intra-abdominal infections	
Peritonitis associated with dialysis in patients on CAPD	
Complicated urinary tract infections	1-2 g every 8 h or 12 h
Peri- operative prophylaxis for transurethral resection of prostate (TURP)	1 g at induction of anaesthesia, and a second dose at catheter removal
Chronic suppurative otitis media	1 g to 2 g every 8 h
Malignant otitis externa	
Continuous infusion	
Infection	Dose to be administered
Febrile neutropenia	Loading dose of 2 g followed by a continuous infusion of 4 to 6 g every 24 h
Nosocomial pneumonia	
Broncho-pulmonary infections in cystic fibrosis	
Bacterial meningitis	
Bacteraemia*	
Bone and joint infections	
Complicated skin and soft tissue infections	
Complicated intra-abdominal infections	
Peritonitis associated with dialysis in patients on CAPD	
[1]In adults with normal renal function 9 g/day has been used without adverse effects. *When associated with, or suspected to be associated with, any of the infections.	

Table 2: Children < 40 kg

Infants and toddlers >2 months and children <40 kg	Infection	Usual dose
Intermittent Administration		
	Complicated urinary tract infections	100 mg-150 mg/kg/day in three divided doses, maximum 6 g/day
	Chronic suppurative otitis media	
	Malignant otitis externa	
	Neutropenic children	150 mg/kg/day in three divided doses, maximum 6 g/day
	Broncho-pulmonary infections in cystic fibrosis	
	Bacterial meningitis	
	Bacteraemia*	
	Bone and joint infections	100 mg –150 mg/kg/day in three divided doses, maximum 6 g/day
	Complicated skin and soft tissue infections	
	Complicated intra-abdominal infections	
	Peritonitis associated with dialysis in patients on CAPD	
Continuous Infusion		
	Febrile neutropenia	Loading dose of 60-100 mg/kg followed by a continuous infusion 100-200 mg/kg/day, maximum 6 g/day
	Nosocomial pneumonia	
	Broncho-pulmonary infections in cystic fibrosis	
	Bacterial meningitis	
	Bacteraemia*	
	Bone and joint infections	
	Complicated skin and soft tissue infections	
	Complicated intra-abdominal infections	
	Peritonitis associated with dialysis in patients with CAPD	
Neonates and infants < 2 months	Infection	Usual dose
Intermittent Administration		
	Most infections	25-60 mg/kg/day in two divided doses[1]
[1]In neonates and infants < 2 months, the serum half life of ceftazidime can be three to four times that in adults. *Where associated with, or suspects to be associated with, any of the infections listed in section 4.1.		

CONTRAINDICATIONS:
Hypersensitivity to Penicillin or Cephalosporins.

WARNINGS:
Hypersensitivity
As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported. In case of severe hypersensitivity reactions, treatment with Ceftazidime must be discontinued immediately and adequate emergency measures must be initiated.

Pseudomembranous colitis
Antibacterial agent-associated colitis and pseudomembranous colitis have been reported with nearly all antibacterial agents, including Ceftazidime, and may range in severity from mild to life-threatening.

Renal function
Concurrent treatment with high doses of cephalosporins and nephrotoxic medicinal products such as aminoglycosides or potent diuretics (e.g., furosemide) may adversely affect renal function.

Overgrowth of non-susceptible organisms
Prolonged use may result in the overgrowth of non-susceptible organisms (e.g., *Enterococci*, fungi) which may require interruption of treatment or other appropriate measures. Repeated evaluation of the patient's condition is essential.

PRECAUTIONS:
Patients with known hypersensitivity to penicillins.
Patients with a personal or familial history of allergy such as bronchial asthma, rash and urticaria.
Patients with severe renal dysfunction
The elderly, patients with malnutrition, and those with disorder of general condition (Since vitamin K deficiency may occur, observe closely).
- Use in pregnancy and nursing mothers.
Because safety to pregnant women is not established, this drug should be used in these only if clearly needed.
Low concentrations of Ceftazidime are excreted in human milk. Caution should be exercised when it is administered to a nursing woman.

PREGNANCY AND LACTATION:
Use with caution.

Elderly: Decrease dose in case of renal impairment.

DRUG INTERACTIONS:
With aminoglycoside or diuretic: Risk of nephrotoxicity.
Chloramphenicol causes antagonistic effect with Ceftazidime, therefore, concomitant use of these medications should be avoided.

ADVERSE DRUG REACTIONS:
Gastrointestinal: diarrhea, abdominal pain, vomiting and nausea.
Hypersensitivity: rash, urticaria, pruritis, Stevens Johnson Syndrome
Shock: may occur, especially in patients, who show hypersensitivity with this drug.
Hepatic: Slightly increase in SGOT, SGPT and alkaline phosphatase
Renal: Slight increase in serum creatinine
Central nervous system: headache or dizziness
Hematology: Leukopenia, thrombocytopenia, eosinophilia, prolongation of prothrombin time (rarely)
Other: candidiasis, vaginitis

OVERDOSE AND TREATMENT:
Overdose can lead to neurological sequelae including encephalopathy, convulsions and coma.
Symptoms of overdose can occur if the dose is not reduced appropriately in patients with renal impairment. Serum levels of ceftazidime can be reduced by haemodialysis or peritoneal dialysis.

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.
Seek medical attention immediately at the first sign of any adverse drug reaction.

KEEP ALL MEDICINES OUT OF CHILDREN'S REACH.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C. Protect from light and moisture.

AVAILABILITY:
USP Type I Clear and Colorless vial x 10 mL, Box of 1's

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