

INJEX

(Ceftazidime) Injection USP
250mg, 500mg and 1g

For IV or IM use

انجیکس

(سيفتازيڊيم) انجكشن يو ايس پي
250 ملي گرام، 500 ملي گرام اور 1 گرام

برائے وریدی یا عضلاتی استعمال

COMPOSITION

Injex Injection 250mg

Each vial contains:

Ceftazidime.....250mg

(As Ceftazidime Pentahydrate with Sodium Carbonate USP).

Finished Product Specs.: USP

Injex Injection 500mg

Each vial contains:

Ceftazidime.....500mg

(As Ceftazidime Pentahydrate with Sodium Carbonate USP).

Finished Product Specs.: USP

Injex Injection 1g

Each vial contains:

Ceftazidime.....1g

(As Ceftazidime Pentahydrate with Sodium Carbonate USP).

Finished Product Specs.: USP

DESCRIPTION

Ceftazidime is a semisynthetic, broad-spectrum, beta-lactam antibiotic for parenteral administration. Its molecular formula is $C_{22}H_{32}N_6O_{12}S_2$, representing a molecular weight of 636.6g/mol. Injex (Ceftazidime) Injection is a sterile, dry-powdered mixture of ceftazidime pentahydrate and sodium carbonate.

CLINICAL PHARMACOLOGY

Pharmacodynamics

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. 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 de-repressed 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.

Microbiological Susceptibility:

Gram-positive aerobes: *Streptococcus pyogenes*, *Streptococcus agalactiae*. Gram-negative aerobes: *Citrobacter koseri*, *Escherichia coli*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Neisseria meningitidis*, *Proteus mirabilis*, *Proteus* spp. (other), *Providencia* spp.

Pharmacokinetics

Absorption: After intramuscular administration of 500mg and 1g of ceftazidime, peak plasma levels of 18 and 37mg/L, respectively, are achieved rapidly. Five minutes after intravenous bolus injection of 500mg and 1g plasma levels are 46 and 7mg/L, respectively. The kinetics of ceftazidime are linear within the single dose range of 0.5 to 2g following intravenous or intramuscular dosing.

Distribution: The serum protein binding of ceftazidime is low at about 10%. Ceftazidime crosses the placenta readily, and is excreted in the breast milk. Penetration of the blood-brain barrier is poor, resulting in low levels of ceftazidime in the CSF in the absence of inflammation.

Metabolism: Ceftazidime is not metabolised.

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

Special Population

Renal impairment: Elimination of ceftazidime is decreased in patients with impaired renal function and the dose should be reduced.

Hepatic impairment: The presence of mild to moderate hepatic dysfunction had no effect on the pharmacokinetics of ceftazidime in individuals administered 2g intravenously every 8 hours for 5 days, provided renal function was not impaired.

Elderly: The reduced clearance observed in elderly patients was primarily due to

age-related decrease in renal clearance of ceftazidime. The mean elimination half-life ranged from 3.5 to 4 hours following single or 7 days repeat BID dosing of 2g IV bolus injections in elderly patients 80 years or older.

Paediatric population: The half-life of ceftazidime is prolonged in preterm and term neonates by 4.5 to 7.5 hours after doses of 25 to 30mg/kg. However, by the age of 2 months the half-life is within the range for adults.

THERAPEUTIC INDICATIONS

Ceftazidime is indicated for the treatment of the infections listed below in adults and children including neonates (from birth).

- Nosocomial pneumonia.
- Broncho-pulmonary infections in cystic fibrosis.
- Bacterial meningitis.
- Chronic suppurative otitis media.
- Malignant otitis externa.
- Complicated urinary tract infections.
- Complicated skin and soft tissue infections.
- Complicated intra-abdominal infections.
- Bone and joint infections.
- Peritonitis associated with dialysis in patients on CAPD.

Treatment of patients with bacteraemia that occurs in association with any of the infections listed above.

Ceftazidime may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection.

Ceftazidime may be used in the peri-operative prophylaxis of urinary tract infections for patients undergoing trans-urethral resection of the prostate (TURP). The selection of ceftazidime should take into account its antibacterial spectrum, which is mainly restricted to aerobic Gram negative bacteria.

Ceftazidime should be co-administered with other antibacterial agents whenever the possible range of causative bacteria would not fall within its spectrum of activity. Consideration should be given to official guidelines on the appropriate use of antibacterial agents.

DOSAGE AND ADMINISTRATION

The dosage of Ceftazidime is given in the table below.

	Intermittent Administration	
Infection	Adults and Children > 40kg	Infants & Toddlers > 2 months and Children < 40kg
Broncho-pulmonary infections in cystic fibrosis	100 to 150mg/kg/day every 8h. Maximum 9g per day	150mg/kg/day in three divided doses. Maximum 6g per day
Febrile neutropenia	2g every 8h	-
Nosocomial pneumonia		150mg/kg/day in three divided doses. Maximum 6g per day
Bacterial meningitis		
Bacteraemia		
Bone and joint infections	1-2g every 8h	100-150mg/kg/day in three divided doses. Maximum 6g per day
Complicated skin and soft tissue infections		
Complicated intra-abdominal infections		
Peritonitis associated with dialysis in patients on CAPD		
Complicated urinary tract infections	1-2g every 8h or 12h	150mg/kg/day in three divided doses. Maximum 6g per day
Peri-operative prophylaxis for transurethral resection of prostate (TURP)	1g at induction of anaesthesia, and a second dose at catheter removal	-
Chronic suppurative otitis media	1g to 2g every 8h	150mg/kg/day in three divided doses. Maximum 6g per day
Malignant otitis externa		
Continuous Infusion		
Infection	Adults and Children > 40kg	Infants & Toddlers > 2 months and Children < 40kg
Febrile neutropenia	Loading dose of 2g followed by a continuous infusion of 4 to 6g every 24h	Loading dose of 60-100mg/kg followed by a continuous infusion 100-200mg/kg/day. Maximum 6g per 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 on CAPD		

Special Population:

Paediatric population: The safety and efficacy of Ceftazidime administered as continuous infusion to neonates and infants of 2 months or younger has not been established. Elderly: In view of the age related reduced clearance of ceftazidime in elderly patients, the daily dose should not normally exceed 3g in those over 80 years of age. Hepatic impairment: Available data do not indicate the need for dose adjustment in mild or moderate liver function impairment. There are no study data in patients with severe hepatic impairment. Close clinical monitoring for safety and efficacy is advised. Renal impairment: Ceftazidime is excreted unchanged by the kidneys. 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 creatinine clearance.

Reconstitution:

After reconstitution, it is chemically and physically stable at 5°C to 25°C for 24 hours. After reconstitution, it should be used immediately, if not used immediately it should be stored at 2°C-8°C for no longer than 24 hours. See the chart below for Reconstitution information.

Vial Size	Route of Administration	Amount of Diluent to be added (ml)	Approximate Concentration (mg/ml)
250mg	IV	2.5	90
	IM	1.0	210
500mg	IV	5.0	96
	IM	1.5	294
1g	IV bolus	10.0	95
	IV Infusion	50.0	20
	IM	3.0	286

This product is for single use only. Any unused contents should be discarded.

CONTRAINDICATIONS

- Hypersensitivity to ceftazidime or to any other cephalosporin.
- History of severe hypersensitivity (e.g. anaphylactic reaction) to any other type of beta-lactam antibacterial agent (e.g. penicillins, monobactams and carbapenems).

ADVERSE REACTIONS

Infections and infestations:

Candidiasis (including vaginitis and oral thrush).

Blood and lymphatic system disorders:

Eosinophilia, thrombocytosis, neutropenia, leucopenia, thrombocytopenia, agranulocytosis, haemolytic anaemia and lymphocytosis.

Immune system disorders:

Anaphylaxis (including bronchospasm and/or hypotension).

Nervous system disorders:

Headache, dizziness, neurological sequelae and paraesthesia.

Vascular disorders:

Phlebitis or thrombophlebitis with intravenous administration.

Gastrointestinal disorders:

Diarrhoea, antibacterial agent associated diarrhoea and colitis, abdominal pain, nausea, vomiting and bad taste.

Hepatobiliary disorders:

Transient elevations in one or more hepatic enzymes and Jaundice.

Skin and subcutaneous tissue disorders:

Maculopapular or urticarial rash, pruritus, toxic epidermal necrolysis, stevens-johnson syndrome, erythema multiforme and angioedema.

Renal and urinary disorders:

Transient elevations of blood urea, blood urea nitrogen and/or serum creatinine, interstitial nephritis and acute renal failure.

General disorders and administration site conditions:

Pain and/or inflammation after intramuscular injection and fever.

DRUG INTERACTIONS

Interaction studies have only been conducted with probenecid and furosemide. Concurrent use of high doses with nephrotoxic medicinal products may adversely affect renal function. 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 chloramphenicol is proposed, the possibility of antagonism should be considered.

WARNINGS AND PRECAUTIONS

As with all beta-lactam antibacterial agents, serious and occasionally fatal hypersensitivity reactions have been reported with ceftazidime. In case of severe hypersensitivity reactions, treatment must be discontinued immediately and adequate emergency measures must be initiated. Before initiating the treatment, it should be established whether the patient has a history of severe hypersensitivity reactions to zidime, to other cephalosporins or to any other type of beta-lactam agent. Ceftazidime has a limited spectrum of antibacterial activity. It is not suitable for use as a single agent for the treatment of some types of infections unless the pathogen

is known to be susceptible or there is a very high suspicion that the most likely pathogen(s) would be suitable for treatment with ceftazidime. In addition, ceftazidime is susceptible to hydrolysis by several of the extended spectrum beta lactamases (ESBLs). Therefore, information on the prevalence of ESBL producing organisms should be taken into account when selecting ceftazidime for treatment. Antibacterial agent-associated colitis and pseudo-membranous colitis have been reported with nearly all anti-bacterial agents, including ceftazidime, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of ceftazidime. Discontinuation of therapy with ceftazidime and the administration of specific treatment for Clostridium difficile should be considered. Medicinal products that inhibit peristalsis should not be given.

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.

Ceftazidime is eliminated via the kidneys, therefore the dose should be reduced according to the degree of renal impairment. Patients with renal impairment should be closely monitored for both safety and efficacy. Neurological sequelae have occasionally been reported when the dose has not been reduced in patients with renal impairment. Prolonged use of ceftazidime 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. Ceftazidime does not interfere with enzyme-based tests for glycosuria, but slight interference (false positive) may occur with copper reduction methods (Benedict's, Fehling's, Clinitest).

Pregnancy: There are limited amounts of data from the use of ceftazidime in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development. Ceftazidime should be prescribed to pregnant women only if the benefit outweighs the risk.

Lactation: Ceftazidime is excreted in human milk in small quantities but at therapeutic doses of ceftazidime no effects on the breast-fed infant are anticipated. Ceftazidime can be used during breast-feeding.

OVERDOSAGE:

Overdosage 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.

STORAGE CONDITIONS

Store below 30°C in dry form.

Protect from heat, light and moisture.

PRESENTATION

Injex Injection 250mg: Pack of 1 vial with 5ml Sterile Water for Injection.

Injex Injection 500mg: Pack of 1 vial with 5ml Sterile Water for Injection.

Injex Injection 1g: Pack of 1 vial with 10ml Sterile Water for Injection.

To be sold on the prescription of a registered medical practitioner only.

Keep all medicines out of the reach of children.



Manufactured by :

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