# FORTECARE 1GM

## CEFTAZIDIME FOR INJECTION USP 1 gm

**COMPOSITION :**
Each Vial contains :
Ceftazidime USP.....1 gm
(As Ceftazidime Pentahydrate)
(A blend of sterile Ceftazidime pentahydrate and Sterile Sodium Carbonate)

**PHARMACOLOGICAL PROPERTIES :**
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.

**INDICATIONS :**
Single infections
Mixed infections caused by two or more susceptible organisms
Severe infections in general
Respiratory tract infections
Ear, nose and throat infections
Urinary tract infections
Skin and soft tissue infections
Gastrointestinal, biliary and abdominal infections
Bone and joint infections
**Dialysis:** infections associated with haemo - and peritoneal dialysis and with continuous peritoneal dialysis (CAPD)
In meningitis it is recommended that the results of a sensitivity test are known before treatment with ceftazidime as a single agent. It may be used for infections caused by organisms resistant to other antibiotics including aminoglycosides and many cephalosporins. When appropriate, however, it may be used in combination with an aminoglycoside or other beta-lactam antibiotic for example, in the presence of severe neutropenia, or with an antibiotic active against anaerobes when the presence of bacteroides fragilis is suspected. In addition, ceftazidime is indicated in the perioperative prophylaxis of transurethral prostatectomy.
**Bacteriology :** Ceftazidime is bactericidal in action, exerting its effect on target cell wall proteins and causing inhibition of cell wall synthesis. A wide range of pathogenic strains and isolates associated with hospital-acquired infections are susceptible to ceftazidime in vitro, including strains resistant to gentamicin and other aminoglycosides. It is highly stable to most clinically important beta-lactamases produced by both gram-positive and gram-negative organisms and consequently is active against many ampicillin- and cephalothin-resistant strains. Ceftazidime has high intrinsic activity in vitro and acts within a narrow mic range for most genera with minimal changes in mic at varied inoculum levels. Ceftazidime has been shown to have in vitro activity against the following organisms:
**Gram-negative:** pseudomonas aeruginosa, pseudomonas spp (other), klebsiella pneumoniae, klebsiella spp (other), proteus mirabilis, proteus vulgaris, morganella morganii (formerly proteus morganii), proteus rettgeri, providencia spp, escherichia coli, enterobacter spp, citrobacter spp, serratia spp, salmonella spp, shigella spp, yersinia enterocolitica, pasteurella multocida, acinetobacter spp, neisseria gonorrhoeae, neisseria meningitidis, haemophilus influenzae (including ampicillin-resistant strains), haemophilus parainfluenzae (including ampicillin-resistant strains).
**Gram-positive:** staphylococcus aureus (methicillin-sensitive strains), staphylococcus epidermidis (methicillin-sensitive strains), micrococcus spp, streptococcus pyogenes, streptococcus group b, streptococcus pneumoniae, streptococcus mitis, streptococcus spp (excluding enterococcus (streptococcus) faecalis).
**Anaerobic strains:** peptococcus spp, peptostreptococcus spp, streptococcus spp, propionibacterium spp, clostridium perfringens, fusobacterium spp, bacteroides spp (many strains of bact fragilis are resistant).
Ceftazidime is not active in vitro against methicillin-resistant staphylococci, enterococcus (streptococcus) faecalis and many other enterococci, listeria monocytogenes, campylobacter spp or clostridium difficile.
In vitro the activities of ceftazidime and aminoglycoside antibiotics in combination have been shown to be at least additive; there is evidence of synergy in some strains tested. This property may be important in the treatment of febrile neutropenic patients.

**POSOLOGY AND METHOD OF ADMINISTRATION :**

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

**Adults:** The adult dosage range for ceftazidime is 1 to 6g per day 8 or 12 hourly (im or iv). In the majority of infections, 1g 8-hourly or 2g 12-hourly should be given. In urinary tract infections and in many less serious infections, 500mg or 1g 12-hourly is usually adequate. In very severe infections, especially immunocompromised patients, including those with neutropenia, 2g, 8 or 12-hourly or 3g, 12-hourly should be administered.

When used as a prophylactic agent in prostatic surgery 1g (from the 1g vial) should be given at the induction of anaesthesia. A second dose should be considered at the time of catheter removal.

**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.

**Cystic fibrosis:** In fibrocystic adults with normal renal function who have pseudomonal lung infections, high doses of 100 to 150mg/kg/day as three divided doses should be used. In adults with normal renal function 9g/day has been used.

**Infants and children:** The usual dosage range for children aged over two months is 30 to 100mg/kg/day, given as two or three divided doses.

Doses up to 150mg/kg/day (maximum 6g daily) in three divided doses may be given to infected immunocompromised or fibrocystic children or children with meningitis.

**Neonates and children up to 2 months of age:** Whilst clinical experience is limited, a dose of 25 to 60mg/kg/day given as two divided doses has proved to be effective. In the neonate the serum half-life of ceftazidime can be three to four times that in adults.

**Dosage in impaired renal function:** Ceftazidime is excreted by the kidneys almost exclusively by glomerular filtration. Therefore, in patients with impaired renal function it is recommended that the dosage of ceftazidime should be reduced to compensate for its slower excretion, except in mild impairment, i.e. glomerular filtration rate (GFR) greater than 50ml/min. In patients with suspected renal insufficiency, an initial loading dose of 1g of ceftazidime may be given. An estimate of GFR should be made to determine the appropriate maintenance dose.

**Renal impairment:** For patients in renal failure on continuous arteriovenous haemodialysis or high-flux haemofiltration in intensive therapy units, it is recommended that the dosage should be 1g daily in divided doses. For low-flux haemofiltration it is recommended that the dosage should be that suggested under impaired renal function.

Recommended maintenance doses are shown below:

RECOMMENDED MAINTENANCE DOSES OF CEFTAZIDIME IN RENAL insufficiency

| Creatinine clearance (ml/min) | Approx. Serum creatinine* µmol/l(mg/dl) | Recommended unit dose of ceftazidime (g) | Frequency of dosing (hourly) |
|---|---|---|---|
| 50-31 | 150-200 (1.7-2.3) | 1 | 12 |
| 30-16 | 200-350 (2.3-4.0) | 1 | 24 |
| 15-6 | 350-500 (4.0-5.6) | 0.5 | 24 |
| <5 | >500 >5.6) | 0.5 | 48 |

* These values are guidelines and may not accurately predict renal function in all patients especially in the elderly in whom the serum creatinine concentration may overestimate renal function.

In patients with severe infections, especially in neutropenics, who would normally receive 6g of ceftazidime daily were it not for renal insufficiency, the unit dose given in the table above may be increased by 50% or the dosing frequency increased appropriately. In such patients it is recommended that ceftazidime serum levels should be monitored and trough levels should not exceed 40mg/litre.

When only serum creatinine is available, the following formula (Cockcroft's equation) may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function:

**Males:** Creatinine clearance = $\frac{\text{Weight (kg)} \times (140 - \text{age in years})}{(\text{ml/min}) \; 72 \times \text{serum creatinine (mg/dl)}}$

**Females:** 0.85 x above value.

To convert serum creatinine in ml/litre into mg/dl divide by 88.4.

In children the creatinine clearance should be adjusted for body surface area or lean body mass and the dosing frequency reduced in cases of renal insufficiency as for adults.

The serum half-life of ceftazidime during haemodialysis ranges from 3 to 5 hours. The appropriate maintenance dose of ceftazidime should be repeated following each

haemodialysis period.
Dosage in peritoneal dialysis: Ceftazidime may also be used in peritoneal dialysis and continuous ambulatory peritoneal dialysis (CAPD). As well as using ceftazidime intravenously, it can be incorporated into the dialysis fluid (usually 125 to 250mg for 2L of dialysis fluid).
Administration: Ceftazidime may be given intravenously or by deep intramuscular injection into a large muscle mass such as the upper outer quadrant of the gluteus maximus or lateral part of the thigh.

**CONTRAINDICATIONS:**
Ceftazidime is contraindicated in patients with known hypersensitivity to cephalosporin antibiotics.

**OVERDOSE:**
Overdosage can lead to neurological sequelae including encephalopathy, convulsions and coma. Serum levels of ceftazidime can be reduced by dialysis.

**SPECIAL WARNINGS AND PRECAUTIONS FOR USE:**
**Hypersensitivity reactions:** As with other beta-lactam antibiotics, before therapy with ceftazidime is instituted, careful inquiry should be made for a history of hypersensitivity reactions to ceftazidime, cephalosporins, penicillins or other drugs. Special care is indicated in patients who have experienced an allergic reaction to penicillins or beta-lactams. Ceftazidime should be given only with special caution to patients with type I 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.
**Renal function:** Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with nephrotoxic drugs, e.g. aminoglycoside antibiotics, or potent diuretics such as frusemide, as these combinations are suspected of affecting renal function adversely. Clinical experience with ceftazidime has shown that this is not likely to be a problem at the recommended dose levels. There is no evidence that ceftazidime adversely affects renal function at normal therapeutic doses: however, as for all antibiotics eliminated via the kidneys, it is necessary to reduce the dosage according to the degree of reduction in renal function to avoid the clinical consequences of elevated antibiotic levels, e.g. neurological sequelae, which have occasionally been reported when the dose has not been reduced appropriately.
**Overgrowth of non-susceptible organisms:** As with other broad spectrum antibiotics, prolonged use of ceftazidime may result in the overgrowth of non-susceptible organisms (e.g. Candida, Enterococci and Serratia spp.) which may require interruption of treatment or adoption of appropriate measures. Repeated evaluation of the patient's condition is essential.

**INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:**
Ceftazidime does not interfere with enzyme-based tests for glycosuria. Slight interference with copper reduction methods (Benedict's, Fehling's, Clinitest) may be observed. Ceftazidime does not interfere in the alkaline picrate assay for creatinine. The development of a positive Coombs' test associated with the use of ceftazidime in about 5% of patients may interfere with the cross-matching of blood.
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.

**PREGNANCY AND LACTATION:**
There is no experimental evidence of embryopathic or teratogenic effects attributable to ceftazidime but, as with all drugs, it should be administered with caution during the early months of pregnancy and in early infancy. Use in pregnancy requires that the anticipated benefit be weighed against the possible risks.
Ceftazidime is excreted in human milk in low concentrations and consequently caution should be exercised when ceftazidime is administered to a nursing mother.

**EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:**
None reported.

**UNDESIRABLE EFFECTS:**
Clinical trial experience has shown that ceftazidime is generally well tolerated.

**HYPERSENSITIVITY:**
maculopapular or urticarial rash, fever, pruritus, and very rarely angioedema and anaphylaxis (including bronchospasm and/or hypotension).
Adverse reactions are infrequent and include:
**Nervous System Disorders**: Headache, dizziness, paraesthesiae and bad taste. There have been reports of neurological sequelae including tremor, myoclonia, convulsions, and encephalopathy in patients with renal impairment in whom the dose of ceftazidime has not been appropriately reduced.
**Gastrointestinal Disorders:** diarrhoea, nausea, vomiting, abdominal pain, and very rarely oral thrush or colitis. As with other cephalosporins, colitis may be associated with Clostridium difficile and may present as pseudomembranous colitis.
Hepato - biliary disorders: very rarely jaundice.
**Skin and subcutaneous tissue disorders:** As with other cephalosporins, there have been rare reports of erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis.
**Reproductive system disorders:**
Candidiasis, vaginitis.
**General disorders and administration site conditions:**
Phlebitis or thrombophlebitis with i.v. administration, pain and/or inflammation after i.m. injection.
**Investigations:** Laboratory test changes noted transiently during ceftazidime therapy include: eosinophilia, positive Coombs' test, 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 elevation of blood urea, blood urea nitrogen and/or serum creatinine have been observed occasionally. Very rarely, leucopenia, neutropenia, agranulocytosis, thrombocytopenia and lymphocytosis have been seen.

**Reconstitution / Direction for use:**
**For Intramuscular Use:**
• Sterile water for injection or if required Bacteriostotic water for injection 0.5 to 1.0% Lidocaine Hydrochloride injection
**Reconstitution Table:**

| Vial Size | Diluent to be added to vial | Approximate available volume | Approximate Average Concentration |
|---|---|---|---|
| 1.0 g. Vial | 3.0 ml | 3.6 ml | 280mg/ml |

**For I.V. Use:**
Sterile water for injections

| Vial Size | Diluent to be added to vial | Approximate available volume | Approximate Average Concentration |
|---|---|---|---|
| 1.0 g. Vial | 5 or 10 ml | 5.6 or 10.6 ml | 180 or 95 mg/ml |
| 2.0 g. Vial | 10 ml | 11.2 ml | 180 mg/ml |

**STORAGE:**
Store in a dark place below 25°C.
**KEEP OUT OF THE REACH OF CHILDREN.**

**PRESENTATION:**
**FORTECARE 1GM** available in a glass vial.

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