SUMMARY OF PRODUCT CHARACTERISTICS

C-Zid 1.0 g

[Ceftazidime for Injection USP]

Table of Contents

1 NAME OF THE MEDICAL PRODUCT

C-Zid 1.0 g (Ceftazidime for Injection USP)
I.M./I.V. use

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

C-Zid 1.0 g:
Each vial contains
Ceftazidime USP….. 1.0 g
(As Ceftazidime Pentahydrate)
A blend of Sterile Ceftazidime Pentahydrate and Sterile Sodium Carbonate.

3 PHARMACEUTICAL FORM

Injection

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ceftazidime is indicated for the treatment of patients with infections caused by susceptible strains of the designated organisms in the following diseases:

Lower Respiratory Tract Infections, including pneumonia, caused by *Pseudomonas aeruginosa* and other *Pseudomonas* spp.; *Haemophilus influenzae*, including ampicillin resistant strains; *Klebsiella* spp.; *Enterobacter* spp.; *Proteus mirabilis*; *Escherichia coli*; *Serratia* spp.; *Citrobacter* spp.; *Streptococcus pneumoniae*; and *Staphylococcus aureus* (methicillin-susceptible strains).

Skin and Skin-Structure Infections caused by *Pseudomonas aeruginosa*; *Klebsiella* spp.; *Escherichia coli*; *Proteus* spp., including *Proteus mirabilis* and indole-positive *Proteus*; *Enterobacter* spp.; *Serratia* spp.; *Staphylococcus aureus* (methicillin susceptible strains); and *Streptococcus pyogenes* (group A beta-hemolytic streptococci).

Urinary Tract Infections, both complicated and uncomplicated, caused by *Pseudomonas aeruginosa*; *Enterobacter* spp.; *Proteus* spp., including *Proteus mirabilis* and indole-positive *Proteus*; *Klebsiella* spp.; and *Escherichia coli*.

Bacterial Septicemia caused by *Pseudomonas aeruginosa*, *Klebsiella* spp., *Haemophilus influenzae, Escherichia coli*, *Serratia* spp., *Streptococcus pneumoniae,* and *Staphylococcus aureus* (methicillin-susceptible strains).

Bone and Joint Infections caused by *Pseudomonas aeruginosa, Klebsiella* spp., *Enterobacter* spp., and *Staphylococcus aureus* (methicillin-susceptible strains).

Gynecologic Infections, including endometritis, pelvic cellulitis, and other infections of the female genital tract caused by *Escherichia coli*.

Intra-abdominal Infections, including peritonitis caused by *Escherichia coli*, *Klebsiella* spp., and *Staphylococcus aureus* (methicillin-susceptible strains) and polymicrobial infections caused by aerobic and anaerobic organisms and *Bacteroides* spp. (many strains of *Bacteroides fragilis* are resistant).

Central Nervous System Infections, including meningitis, caused by *Haemophilus influenzae* and *Neisseria meningitidis*. Ceftazidime had also been used successfully in a limited number of cases of meningitis due to *Pseudomonas aeruginosa* and *Streptococcus pneumoniae.*

C-Zid 1.0 g might be used alone in cases of confirmed or suspected sepsis. Ceftazidime injection had been used successfully as an empiric therapy in cases where various concomitant therapies with other antibacterial drugs had been used.

C-Zid 1.0 g might also be used concomitantly with other antibacterial drugs, such as aminoglycosides, vancomycin, and clindamycin; in severe and life-threatening infections; and in the immuno-compromised patient. When such concomitant treatment is appropriate, prescribing information in the

labeling for the other antibacterial drugs should be followed. The dose depends on the severity of the infection and the patient's condition.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of **C-Zid 1.0 g** and other antibacterial drugs, **C-Zid 1.0 g** should be used only to treat infections that were proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns might contribute to the empiric selection of therapy.

4.2 Posology and Method of administration

Posology

The usual adult dosage is 1 gram administered intravenously or intramuscularly every 8 to 12 hours. The dosage and route should be determined by the susceptibility of the causative organisms, the severity of infection, and the condition and renal function of the patient.

The guidelines for dosage of **C-Zid 1.0 g** were listed in table 1 below**Table *1***. The following dosage schedule is recommended.

Table 1. Recommended Dosage Schedule

	Dose	**Frequency**
Adult		
Usual recommended dosage	1 gram intravenous or intramuscular	every 8 to 12 hours
Uncomplicated urinary tract infection	250 mg intravenous or intramuscular	every 12 hours
Bone and joint infections	2 grams intravenous	every 12 hours
Complicated urinary tract infections	500 mg intravenous or intramuscular	every 8 to 12 hours
Uncomplicated pneumonia; mild skin and skin-structure infections	500 mg to 1 gram intravenous or intramuscular	every 8 hours
Serious gynecological and intra-abdominal infections	2 grams intravenous	every 8 hours
Meningitis	2 grams intravenous	every 8 hours
Very severe life-threatening infections, especially in immunocompromised patients	2 grams intravenous	every 8 hours
Lung infections caused by *Pseudomonas* spp. in patients with cystic fibrosis with normal renal function *	30 to 50 mg/kg intravenous to a maximum of 6 grams per day	every 8 hours
Neonates (0-4 weeks)	30 mg/kg intravenous	every 12 hours
Infants and children (1 month – 12 years)	30 to 50 mg/kg intravenous to a maximum of 6 grams per day †	every 8 hours

* Although clinical improvement had been shown, bacteriologic cures could not be expected in patients with chronic respiratory disease and cystic fibrosis.

† The higher dose should be reserved for immunocompromised pediatric patients or pediatric patients with cystic fibrosis or meningitis.

Impaired Hepatic Function
No adjustment in dosage is required for patients with hepatic dysfunction.

Impaired Renal Function
Ceftazidime is excreted by the kidneys, almost exclusively by glomerular filtration. Therefore, in patients with impaired renal function (glomerular filtration rate [GFR] <50 mL/min), it is recommended that the dosage of ceftazidime be reduced to compensate for its slower excretion.
In patients with suspected renal insufficiency, an initial loading dose of 1 gram of **C-Zid 1.0 g** might be given. An estimate of GFR should be made to determine the appropriate maintenance dosage.
The recommended dosage is presented in table 2 below.

Table 2. Recommended Maintenance Dosages of C-Zid 1.0 g in Renal Insufficiency

NOTE: if the dose recommended in *Table 1* above is lower than that recommended for patients with renal insufficiency as outlined in *Table 2,* the lower dose should be used.		
Creatinine Clearance (mL/min)	**Recommended Unit Dose of C-Zid 1.0 g**	**Frequency of Dosing**
50-31	1 gram	every 12 hours
30-16	1 gram	every 24 hours
15-6	500 mg	every 24 hours
Less than 5	500 mg	every 48 hours

When only serum creatinine is available, the following formula (Cockcroft's equation)1 might be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function:

Males: Creatinine clearance (mL/min) = Weight (kg) x (140 – age)/72 x serum creatinine (mg/dL)
Females: 0.85 x male value

In patients with severe infections who would normally receive 6 grams of Ceftazidime Injection daily were it not for renal insufficiency, the unit dose given in the table above might be increased by 50% or the dosing frequency might be increased appropriately. Further dosing should be determined by therapeutic monitoring, severity of the infection, and susceptibility of the causative organism.

In pediatric patients as for adults, the creatinine clearance should be adjusted for body surface area or lean body mass, and the dosing frequency should be reduced in cases of renal insufficiency.
In patients undergoing hemodialysis, a loading dose of 1 gram is recommended, followed by 1 gram after each hemodialysis period.

C-Zid 1.0 g could also be used in patients undergoing intraperitoneal dialysis and continuous ambulatory peritoneal dialysis. In such patients, a loading dose of 1 gram of **C-Zid 1.0 g** might be given, followed by 500 mg every 24 hours. In addition to IV use, **C-Zid 1.0 g** could be incorporated in the dialysis fluid at a concentration of 250 mg for 2 L of dialysis fluid.
Note: Generally, **C-Zid 1.0 g** should be continued for 2 days after the signs and symptoms of infection have disappeared, but in complicated infections longer therapy might be required.

Method of Administration

C-Zid might be given intravenously or by deep IM injection into a large muscle mass such as the upper

outer quadrant of the gluteus maximus or lateral part of the thigh. Intra-arterial administration should be avoided.

Intramuscular administration: For IM administration, **C-Zid** should be constituted with one of the following diluents: Sterile Water for Injection, Bacteriostatic Water for Injection, or 0.5% of 1% Lidocaine Hydrochloride Injection. Refer to table 3 below.

Intravenous administration: The IV route is preferable for patients with bacterial septicemia, bacterial meningitis, peritonitis, or other severe or life-threatening infections, or for patients who might be poor risks because of lowered resistance resulting from such debilitating conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or pending.

For Direct intermittent IV administration, constitute **C-Zid** as directed in table 3 below with Sterile Water for Injection. Slowly inject directly into vein over a period of 3 to 5 minutes or give through the tubing of an administration set while the patient is also receiving one of the compatible fluids.

Intermittent IV infusion with a Y-type administration set could be accomplished with compatible solutions. However, during infusion of a solution containing ceftazidime, it is desirable to discontinue the other resolution.

Table 3 . Preparation of solutions of C-Zid

Size of Vial	Route	Amount of Diluent to be added (mL)	Approximate Ceftazidime Concentration (mg/mL)
1 g	Intramuscular	3 mL	333.3
1 g	Intravenous bolus	10 mL	100
1 g	Intravenous infusion	50 mL	20

Solutions of **C-Zid**, like those of most beta-lactam antibiotics, should not be added to solutions of aminoglycoside antibiotics because of potential interaction. However, if concurrent therapy with C-Zid and an aminoglycoside is indicated, each of these antibiotics could be administered separately to the same patient.

4.3 Contraindications

C-Zid 1.0 g is contraindicated in patients who have shown hypersensitivity to ceftazidime or the cephalosporin group of antibacterial drugs.

4.4 Special warnings and precautions for use

Before therapy with **C-Zid 1.0 g** is instituted, careful inquiry should be made to determine whether the patient had previous hypersensitivity reactions to ceftazidime, cephalosporins, penicillins, or other drugs. If this product is to be given to penicillin-sensitive patients, caution should be exercised because cross-hypersensitivity among beta-lactam antibacterial drugs had been clearly documented and might occur in up to 10% of patients with a history of penicillin allergy. If an allergic reaction to **C-Zid 1.0 g** occurs, discontinue the drug. Serious acute hypersensitivity reactions might require treatment with epinephrine and other emergency measures, including oxygen, i.v. fluids, i.v. antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.

Clostridium difficile associated diarrhea (CDAD) had been reported with use of nearly all antibacterial agents, including Ceftazidime Injection, and might range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile.*

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections could be refractory to antimicrobial therapy and might require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial drug use. Careful medical history is necessary since CDAD had been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against *C. difficile* might need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial drug treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

Elevated levels of ceftazidime in patients with renal insufficiency could lead to seizures, nonconvulsive status epilepticus (NCSE), encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia.

General

High and prolonged serum ceftazidime concentrations could occur from usual dosages in patients with transient or persistent reduction of urinary output because of renal insufficiency. The total daily dosage should be reduced when ceftazidime is administered to patients with renal insufficiency. Elevated levels of ceftazidime in these patients could lead to seizures, nonconvulsive status epilepticus, encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms.

As with other antibacterial drugs, prolonged use of Ceftazidime Injection might result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Inducible type I beta-lactamase resistance had been noted with some organisms (e.g., *Enterobacter* spp., *Pseudomonas* spp., and *Serratia* spp.). As with other extended-spectrum beta-lactam antibacterial drugs, resistance could develop during therapy, leading to clinical failure in some cases. When treating infections caused by these organisms, periodic susceptibility testing should be performed when clinically appropriate. If patients fail to respond to monotherapy, an aminoglycoside or similar agent should be considered.

Cephalosporins might be associated with a fall in prothrombin activity. Those at risk include patients with renal and hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

C-Zid 1.0 g should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Distal necrosis could occur after inadvertent intra-arterial administration of ceftazidime.

Prescribing Ceftazidime Injection in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

4.5 Interaction with other medicinal products and other forms of Interaction

Nephrotoxicity had been reported following concomitant administration of cephalosporins with aminoglycoside antibacterial drugs or potent diuretics such as furosemide. Renal function should be

carefully monitored, especially if higher dosages of the aminoglycosides are to be administered or if therapy is prolonged, because of the potential nephrotoxicity and ototoxicity of aminoglycoside antibacterial drugs. Nephrotoxicity and ototoxicity were not noted when ceftazidime was given alone.

Chloramphenicol had been shown to be antagonistic to beta-lactam antibacterial drugs, including ceftazidime, based on *in vitro* studies and time kill curves with enteric gram-negative bacilli. Due to the possibility of antagonism *in vivo*, particularly when bactericidal activity is desired, this drug combination should be avoided.

In common with other antibacterial drugs, ceftazidime might affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral estrogen/progesterone contraceptives.

Drug/Laboratory Test Interactions

The administration of ceftazidime might result in a false-positive reaction for glucose in the urine when using Clinitest® tablets, Benedict's solution, or Fehling's solution. It is recommended that glucose tests based on enzymatic glucose oxidase reactions be used.

4.6 Fertility, pregnancy and Lactation

Pregnancy:

Teratogenic Effects

Pregnancy Category B. Reproduction studies had been performed in mice and rats at doses up to 40 times the human dose and revealed no evidence of impaired fertility or harm to the fetus due to Ceftazidime Injection. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Breast-feeding

Ceftazidime is excreted in human milk in low concentrations. Caution should be exercised when Ceftazidime Injection is administered to a nursing woman.

Fertility

No data are available.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects might occur (e.g. dizziness), which might influence the ability to drive and use machines.

4.8 Undesirable Effects

The most common adverse reactions are eosinphilia, thrombocytosis, phlebitis or thrombophlebitis with intravenous administration, diarrhoea, transient increases in hepatic enzymes, maculopapular or uticarcial rash, pain and/or inflammation following intramuscular injection and positive Coomb's test.

Data from sponsored and unsponsored clinical trials have been used to determine the frequency of common and uncommon undesirable effects. The frequencies assigned to all other undesirable effects were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. The following convention had been used for the classification of frequency:

Very common ≥1/10; Common ≥1/100 and <1/10; Uncommon ≥1/1,000 and <1/100; Rare ≥1/10,000 and <1/1000; Very rare <1/10,000; and Unknown (could not be estimated from the available data)

System Organ Class	Common	Uncommon	Very rare	Unknown
Infections and infestations		Candidiasis (including vaginitis and oral thrush)		
Blood and lymphatic system disorders	Eosinophilia Thrombocytosis	Neutropenia Leucopenia Thrombocytopenia		Agranulocytosis Haemolytic anaemia Lymphocytosis
Immune system disorders				Anaphylaxis (including bronchospasm and/or hypotension)
Nervous system disorders		Headache Dizziness		Neurological sequelae[1] Paraesthesia
Vascular disorders	Phlebitis or thrombophlebitis with intravenous administration			
Gastrointestinal disorders	Diarrhoea	Antibacterial agent-associated diarrhoea and colitis[2] Abdominal pain Nausea Vomiting		Bad taste
Heptobiliary disorders	Transient elevations in one or more hepatic enzymes[3]			Jaundice
Skin and subcutaneous tissue disorders	Maculopapular or urticarial rash	Pruritus		Toxic epidermal necrolysis Stevens-Johnson syndrome Erythema multiforme Angioedema Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)[4]
Renal and urinary disorders		Transient elevations of blood urea, blood urea nitrogen and/or serum creatinine	Interstitial nephritis Acute renal failure	
General disorders and administration site conditions	Pain and/or inflammation after intramuscular injection	Fever		
Investigations	Positive Coombs' test[5]			

[1]There had been reports of neurological sequelae including tremor, myoclonia, convulsions, encephalopathy and coma in patients with renal impairment in whom the dose of Ceftazidime Injection had not been appropriately reduced.
[2]Diarrhoea and colitis might be associated with *Clostridium difficile* and might present as pseudomembranous colitis.
[3]ALT (SGPT), AST (SOGT), LHD, GGT, alkaline phosphatase.
[4]There have been rare reports where DRESS had been associated with ceftazidime.
[5]A positive Coombs test develops in about 5% of patients and might interfere with blood cross matching.

The below adverse were observed with Ceftazidime with frequency not known:

- No disulfiram-like reactions were reported.
- Seizures have been reported with several cephalosporins, including ceftazidime. In addition, asterixis, and neuromuscular excitability had been reported in renally impaired patients treated with unadjusted dosing regimens of ceftazidime.
- General allergic reactions, which, in rare instances, were severe (e.g., cardiopulmonary arrest).

- Hyperbilirubinemia, renal impairment, toxic nephropathy, hepatic dysfunction including cholestasis, aplastic anemia, and hemorrhage.
- Altered laboratory tests: prolonged prothrombin time, false-positive test for urinary glucose, pancytopenia.

4.9 Overdose

Ceftazidime overdosage occurred in patients with renal failure. Reactions included seizure activity, encephalopathy, asterixis, neuromuscular excitability, and coma. Patients who received an acute overdosage should be carefully observed and given supportive treatment. In the presence of renal insufficiency, hemodialysis or peritoneal dialysis might aid in the removal of ceftazidime from the body.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

Mechanism of Action

Ceftazidime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis.

Ceftazidime had activity in the presence of some beta-lactamases, both penicillinases and cephalosporinases, of Gram-negative and Gram-positive bacteria.

Mechanism of Resistance

Resistance to ceftazidime is primarily through hydrolysis by beta-lactamase, alteration of penicillin-binding proteins (PBPs), and decreased permeability.

Interaction with Other Antimicrobials

In an *in vitro* study, antagonistic effects have been observed with the combination of chloramphenicol and ceftazidime.

Ceftazidime had been shown to be active against most isolates of the following bacteria, both *in vitro* and in clinical infections:

Gram-negative bacteria

- *Citrobacter* species
- *Enterobacter* species
- *Escherichia coli*
- *Klebsiella* species
- *Haemophilus influenzae*
- *Neisseria meningitidis*
- *Proteus mirabilis*
- *Proteus vulgaris*
- *Pseudomonas aeruginosa*
- *Serratia* species

Gram-positive bacteria

- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- *Streptococcus agalactiae*

Anaerobic bacteria

- *Bacteroides* species (Note: many isolates of *Bacteroides* species are resistant)

The following *in vitro* data were available, but their clinical significance is unknown. At least 90 percent of the following microorganisms exhibit an *in vitro* minimum inhibitory concentration (MIC) less than

or equal to the susceptible breakpoint for ceftazidime. However, the efficacy of ceftazidime in treating clinical infections due to these microorganisms had not been established in adequate and well-controlled clinical trials.

Gram-negative bacteria

- *Acinetobacter* species
- *Citrobacter diversus*
- *Citrobacter freundii*
- *Providencia* species (including *Providencia rettgeri*)
- *Salmonella* species
- *Shigella* species
- *Haemophilus parainfluenzae*
- *Morganella morganii*
- *Neisseria gonorrhoeae*
- *Yersinia enterocolitica*

Gram-positive bacteria

- *Staphylococcus epidermidis*

Anaerobic bacteria

- *Clostridium* species (Not including *Clostridium difficile*)
- *Peptostreptococcus* species

5.2 Pharmacokinetic properties:

IV administration of 500-mg and 1-g doses of ceftazidime over 5 minutes to normal adult male volunteers, mean peak serum concentrations of 45 and 90 mcg/mL, respectively, were achieved. After IV infusion of 500-mg, 1-g, and 2-g doses of ceftazidime over 20 to 30 minutes to normal adult male volunteers, mean peak serum concentrations of 42, 69, and 170 mcg/mL, respectively, were achieved. The average serum concentrations following IV infusion of 500-mg, 1-g, and 2-g doses to these volunteers over an 8-hour interval are given in table 4 given below**Table 4**.

Table 4. Average Serum Concentrations of Ceftazidime

Ceftazidime IV Dose	Serum Concentrations (mcg/mL)				
	0.5 hr	1 hr	2 hr	4 hr	8 hr
500 mg	42	25	12	6	2
1 g	60	39	23	11	3
2 g	129	75	42	13	5

The absorption and elimination of ceftazidime were directly proportional to the size of the dose. The half-life following IV administration was approximately 1.9 hours. Less than 10% of ceftazidime was protein bound. The degree of protein binding was independent of concentration.

There was no evidence of accumulation of ceftazidime in the serum in individuals with normal renal function following multiple IV doses of 1 and 2 g every 8 hours for 10 days.

Following intramuscular (IM) administration of 500-mg and 1-g doses of ceftazidime to normal adult volunteers, the mean peak serum concentrations were 17 and 39 mcg/mL, respectively, at approximately 1 hour. Serum concentrations remained above 4 mcg/mL for 6 and 8 hours after the IM

administration of 500-mg and 1-g doses, respectively. The half-life of ceftazidime in these volunteers was approximately 2 hours.
The presence of hepatic dysfunction had no effect on the pharmacokinetics of ceftazidime in individuals administered 2 g intravenously every 8 hours for 5 days. Therefore, a dosage adjustment from the normal recommended dosage is not required for patients with hepatic dysfunction, provided renal function is not impaired.

Approximately 80% to 90% of an IM or IV dose of ceftazidime is excreted unchanged by the kidneys over a 24-hour period. After the IV administration of single 500-mg or 1-g doses, approximately 50% of the dose appeared in the urine in the first 2 hours. An additional 20% was excreted between 2 and 4 hours after dosing, and approximately another 12% of the dose appeared in the urine between 4 and 8 hours later. The elimination of ceftazidime by the kidneys resulted in high therapeutic concentrations in the urine. The mean renal clearance of ceftazidime was approximately 100 mL/min. The calculated plasma clearance of approximately 115 mL/min indicated nearly complete elimination of ceftazidime by the renal route. Administration of probenecid before dosing had no effect on the elimination kinetics of ceftazidime. This suggested that ceftazidime is eliminated by glomerular filtration and is not actively secreted by renal tubular mechanisms.

Since ceftazidime is eliminated almost solely by the kidneys, its serum half-life is significantly prolonged in patients with impaired renal function. Consequently, dosage adjustments in such patients has been discussed in other section of this document section are suggested.
Therapeutic concentrations of ceftazidime are achieved in the following body tissues and fluids, described in table 5.

Table 5. Ceftazidime Concentrations in Body Tissues and Fluids

Tissue or Fluid	Dose/Route	No. of Patients	Time of Sample Post Dose	Average Tissue or Fluid Level (mcg/mL or mcg/g)
Urine	500 mg IM	6	0-2 hr	2,100.0
	2 g IV	6	0-2 hr	12,000.0
Bile	2 g IV	3	90 min	36.4
Synovial fluid	2 g IV	13	2 hr	25.6
Peritoneal fluid	2 g IV	8	2 hr	48.6
Sputum	1 g IV	8	1 hr	9.0
Cerebrospinal fluid	2 g q8hr IV	5	120 min	9.8
(inflamed meninges)	2 g q8hr IV	6	180 min	9.4
Aqueous humor	2 g IV	13	1-3 hr	11.0
Blister fluid	1 g IV	7	2-3 hr	19.7
Lymphatic fluid	1 g IV	7	2-3 hr	23.4
Bone	2 g IV	8	0.67 hr	31.1
Heart muscle		35	30-280 min	12.7
Skin		22	30-180 min	6.6
Skeletal muscle		35	30-280 min	9.4
Myometrium		31	1-2 hr	18.7

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeat dose toxicity, genotoxicity, toxicity to reproduction. Carcinogenicity studies had not been performed with ceftazidime.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipient(s)

NA

6.2 Incompatibilities-

No incompatibilities

6.3 Shelf-life

24 Months

6.4 Special precautions for storage

Store in a cool, dry place, below 25°C. Protect from light

6.5 Nature and contents of container

Sterile C-Zid 1.0 g is filled in Sterilized and siliconized flint glass vial. The vial is sealed using Rubber Stopper and Aluminium seal. The filled and properly sealed vial is packed in a carton along with leaflet.

6.6 Instructions for use and handling

C-Zid might be given intravenously or by deep IM injection into a large muscle mass such as the upper outer quadrant of the gluteus maximus or lateral part of the thigh. Intra-arterial administration should be avoided.

Intramuscular administration: For IM administration, **C-Zid** should be constituted with one of the following diluents: Sterile Water for Injection, Bacteriostatic Water for Injection, or 0.5% of 1% Lidocaine Hydrochloride Injection. Refer to table 6 below.

Intravenous administration: The IV route is preferable for patients with bacterial septicemia, bacterial meningitis, peritonitis, or other severe or life-threatening infections, or for patients who might be poor risks because of lowered resistance resulting from such debilitating conditions such as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or pending.

For Direct intermittent IV administration, constitute **C-Zid** as directed in table 6 below with Sterile Water for Injection. Slowly inject directly into vein over a period of 3 to 5 minutes or give through the tubing of an administration set while the patient is also receiving one of the compatible fluids.

Intermittent IV infusion with a Y-type administration set could be accomplished with compatible solutions. However, during infusion of a solution containing ceftazidime, it is desirable to discontinue the other resolution.

Table 6. Preparation of solutions of C-Zid

Size of Vial	Route	Amount of Diluent to be added (mL)	Approximate Ceftazidime Concentration (mg/mL)
1 g	Intramuscular	3 mL	333.3
1 g	Intravenous bolus	10 mL	100
1 g	Intravenous infusion	50 mL	20

Solutions of **C-Zid**, like those of most beta-lactam antibiotics, should not be added to solutions of aminoglycoside antibiotics because of potential interaction. However, if concurrent therapy with C-Zid and an aminoglycoside is indicated, each of these antibiotics could be administered separately to the same patient.

7 MARKETING AUTHORISATION HOLDER
Emcure Pharmaceuticals Limited

8 MARKETING AUTHORISATION NUMBER(S)
We shall provide when available

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Not available

10 DATE OF REVISION OF THE TEXT
29.11.2020