

## PRESCRIBING INFORMATION

### **FORTAZ<sup>®</sup>** **(ceftazidime for injection)**

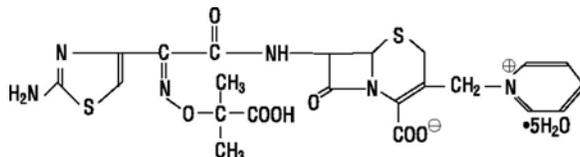
### **FORTAZ<sup>®</sup>** **(ceftazidime injection)**

#### **For Intravenous or Intramuscular Use**

To reduce the development of drug-resistant bacteria and maintain the effectiveness of FORTAZ and other antibacterial drugs, FORTAZ should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

#### **DESCRIPTION**

Ceftazidime is a semisynthetic, broad-spectrum, beta-lactam antibiotic for parenteral administration. It is the pentahydrate of pyridinium, 1-[[7-[[[(2-amino-4-thiazolyl)](1-carboxy-1-methylethoxy)imino]acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-, hydroxide, inner salt, [6R-[6 $\alpha$ ,7 $\beta$ (Z)]]]. It has the following structure:



The empirical formula is  $C_{22}H_{32}N_6O_{12}S_2$ , representing a molecular weight of 636.6.

FORTAZ is a sterile, dry-powdered mixture of ceftazidime pentahydrate and sodium carbonate. The sodium carbonate at a concentration of 118 mg/g of ceftazidime activity has been admixed to facilitate dissolution. The total sodium content of the mixture is approximately 54 mg (2.3 mEq)/g of ceftazidime activity.

FORTAZ in sterile crystalline form is supplied in vials equivalent to 500 mg, 1 g, 2 g, or 6 g of anhydrous ceftazidime and in ADD-Vantage<sup>®</sup> vials equivalent to 1 or 2 g of anhydrous ceftazidime. Solutions of FORTAZ range in color from light yellow to amber, depending on the diluent and volume used. The pH of freshly constituted solutions usually ranges from 5 to 8.

FORTAZ is available as a frozen, iso-osmotic, sterile, nonpyrogenic solution with 1 or 2 g of ceftazidime as ceftazidime sodium premixed with approximately 2.2 or 1.6 g, respectively, of Dextrose Hydrous, USP. Dextrose has been added to adjust the osmolality. Sodium hydroxide is used to adjust pH and neutralize ceftazidime pentahydrate free acid to the sodium salt. The pH may have been adjusted with hydrochloric acid. Solutions of premixed FORTAZ range in color from light yellow to amber. The solution is intended for intravenous (IV) use after thawing to room temperature. The osmolality of the solution is approximately 300 mOsmol/kg, and the pH of thawed solutions ranges from 5 to 7.5.

36 The plastic container for the frozen solution is fabricated from a specially designed multilayer  
37 plastic, PL 2040. Solutions are in contact with the polyethylene layer of this container and can  
38 leach out certain chemical components of the plastic in very small amounts within the expiration  
39 period. The suitability of the plastic has been confirmed in tests in animals according to USP  
40 biological tests for plastic containers as well as by tissue culture toxicity studies.

#### 41 **CLINICAL PHARMACOLOGY**

42 After IV administration of 500-mg and 1-g doses of ceftazidime over 5 minutes to normal adult  
43 male volunteers, mean peak serum concentrations of 45 and 90 mcg/mL, respectively, were  
44 achieved. After IV infusion of 500-mg, 1-g, and 2-g doses of ceftazidime over 20 to 30 minutes to  
45 normal adult male volunteers, mean peak serum concentrations of 42, 69, and 170 mcg/mL,  
46 respectively, were achieved. The average serum concentrations following IV infusion of 500-mg,  
47 1-g, and 2-g doses to these volunteers over an 8-hour interval are given in Table 1.  
48

49 **Table 1. 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

50  
51 The absorption and elimination of ceftazidime were directly proportional to the size of the dose.  
52 The half-life following IV administration was approximately 1.9 hours. Less than 10% of  
53 ceftazidime was protein bound. The degree of protein binding was independent of concentration.  
54 There was no evidence of accumulation of ceftazidime in the serum in individuals with normal  
55 renal function following multiple IV doses of 1 and 2 g every 8 hours for 10 days.

56 Following intramuscular (IM) administration of 500-mg and 1-g doses of ceftazidime to normal  
57 adult volunteers, the mean peak serum concentrations were 17 and 39 mcg/mL, respectively, at  
58 approximately 1 hour. Serum concentrations remained above 4 mcg/mL for 6 and 8 hours after the  
59 IM administration of 500-mg and 1-g doses, respectively. The half-life of ceftazidime in these  
60 volunteers was approximately 2 hours.

61 The presence of hepatic dysfunction had no effect on the pharmacokinetics of ceftazidime in  
62 individuals administered 2 g intravenously every 8 hours for 5 days. Therefore, a dosage  
63 adjustment from the normal recommended dosage is not required for patients with hepatic  
64 dysfunction, provided renal function is not impaired.

65 Approximately 80% to 90% of an IM or IV dose of ceftazidime is excreted unchanged by the  
66 kidneys over a 24-hour period. After the IV administration of single 500-mg or 1-g doses,  
67 approximately 50% of the dose appeared in the urine in the first 2 hours. An additional 20% was  
68 excreted between 2 and 4 hours after dosing, and approximately another 12% of the dose appeared

69 in the urine between 4 and 8 hours later. The elimination of ceftazidime by the kidneys resulted in  
70 high therapeutic concentrations in the urine.

71 The mean renal clearance of ceftazidime was approximately 100 mL/min. The calculated  
72 plasma clearance of approximately 115 mL/min indicated nearly complete elimination of  
73 ceftazidime by the renal route. Administration of probenecid before dosing had no effect on the  
74 elimination kinetics of ceftazidime. This suggested that ceftazidime is eliminated by glomerular  
75 filtration and is not actively secreted by renal tubular mechanisms.

76 Since ceftazidime is eliminated almost solely by the kidneys, its serum half-life is significantly  
77 prolonged in patients with impaired renal function. Consequently, dosage adjustments in such  
78 patients as described in the DOSAGE AND ADMINISTRATION section are suggested.

79 Therapeutic concentrations of ceftazidime are achieved in the following body tissues and fluids.  
80

81 **Table 2. Ceftazidime Concentrations in Body Tissues and Fluids**

Tissue or Fluid	Dose/Route	No. of Patients	Time of Sample Postdose	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	2 g IV	35	30-280 min	12.7
Skin	2 g IV	22	30-180 min	6.6
Skeletal muscle	2 g IV	35	30-280 min	9.4
Myometrium	2 g IV	31	1-2 hr	18.7

82  
83 **Microbiology:** Ceftazidime is bactericidal in action, exerting its effect by inhibition of enzymes  
84 responsible for cell-wall synthesis. A wide range of gram-negative organisms is susceptible to  
85 ceftazidime in vitro, including strains resistant to gentamicin and other aminoglycosides. In  
86 addition, ceftazidime has been shown to be active against gram-positive organisms. It is highly  
87 stable to most clinically important beta-lactamases, plasmid or chromosomal, which are produced  
88 by both gram-negative and gram-positive organisms and, consequently, is active against many  
89 strains resistant to ampicillin and other cephalosporins.

90 Ceftazidime has been shown to be active against the following organisms both in vitro and in  
91 clinical infections (see INDICATIONS AND USAGE).

92 **Aerobes, Gram-negative:** *Citrobacter* spp., including *Citrobacter freundii* and *Citrobacter*  
93 *diversus*; *Enterobacter* spp., including *Enterobacter cloacae* and *Enterobacter aerogenes*;  
94 *Escherichia coli*; *Haemophilus influenzae*, including ampicillin-resistant strains; *Klebsiella* spp.  
95 (including *Klebsiella pneumoniae*); *Neisseria meningitidis*; *Proteus mirabilis*; *Proteus vulgaris*;  
96 *Pseudomonas* spp. (including *Pseudomonas aeruginosa*); and *Serratia* spp.

97 **Aerobes, Gram-positive:** *Staphylococcus aureus*, including penicillinase- and  
98 non-penicillinase-producing strains; *Streptococcus agalactiae* (group B streptococci);  
99 *Streptococcus pneumoniae*; and *Streptococcus pyogenes* (group A beta-hemolytic streptococci).

100 **Anaerobes:** *Bacteroides* spp. (NOTE: many strains of *Bacteroides fragilis* are resistant).

101 Ceftazidime has been shown to be active in vitro against most strains of the following  
102 organisms; however, the clinical significance of these data is unknown: *Acinetobacter* spp.,  
103 *Clostridium* spp. (not including *Clostridium difficile*), *Haemophilus parainfluenzae*, *Morganella*  
104 *morganii* (formerly *Proteus morganii*), *Neisseria gonorrhoeae*, *Peptococcus* spp.,  
105 *Peptostreptococcus* spp., *Providencia* spp. (including *Providencia rettgeri*, formerly *Proteus*  
106 *rettgeri*), *Salmonella* spp., *Shigella* spp., *Staphylococcus epidermidis*, and *Yersinia enterocolitica*.

107 Ceftazidime and the aminoglycosides have been shown to be synergistic in vitro against  
108 *Pseudomonas aeruginosa* and the enterobacteriaceae. Ceftazidime and carbenicillin have also  
109 been shown to be synergistic in vitro against *Pseudomonas aeruginosa*.

110 Ceftazidime is not active in vitro against methicillin-resistant staphylococci, *Streptococcus*  
111 *faecalis* and many other enterococci, *Listeria monocytogenes*, *Campylobacter* spp., or *Clostridium*  
112 *difficile*.

113 **Susceptibility Tests: Diffusion Techniques:** Quantitative methods that require  
114 measurement of zone diameters give an estimate of antibiotic susceptibility. One such procedure<sup>1-3</sup>  
115 has been recommended for use with disks to test susceptibility to ceftazidime.

116 Reports from the laboratory giving results of the standard single-disk susceptibility test with a  
117 30-mcg ceftazidime disk should be interpreted according to the following criteria:

118 Susceptible organisms produce zones of 18 mm or greater, indicating that the test organism  
119 is likely to respond to therapy.

120 Organisms that produce zones of 15 to 17 mm are expected to be susceptible if high dosage  
121 is used or if the infection is confined to tissues and fluids (e.g., urine) in which high antibiotic  
122 levels are attained.

123 Resistant organisms produce zones of 14 mm or less, indicating that other therapy should be  
124 selected.

125 Organisms should be tested with the ceftazidime disk since ceftazidime has been shown by in  
126 vitro tests to be active against certain strains found resistant when other beta-lactam disks are used.

127 Standardized procedures require the use of laboratory control organisms. The 30-mcg  
128 ceftazidime disk should give zone diameters between 25 and 32 mm for *Escherichia coli*  
129 ATCC 25922. For *Pseudomonas aeruginosa* ATCC 27853, the zone diameters should be between

130 22 and 29 mm. For *Staphylococcus aureus* ATCC 25923, the zone diameters should be between  
131 16 and 20 mm.

132 **Dilution Techniques:** In other susceptibility testing procedures, e.g., ICS agar dilution or the  
133 equivalent, a bacterial isolate may be considered susceptible if the minimum inhibitory  
134 concentration (MIC) value for ceftazidime is not more than 16 mcg/mL. Organisms are considered  
135 resistant to ceftazidime if the MIC is  $\geq 64$  mcg/mL. Organisms having an MIC value of  
136  $< 64$  mcg/mL but  $> 16$  mcg/mL are expected to be susceptible if high dosage is used or if the  
137 infection is confined to tissues and fluids (e.g., urine) in which high antibiotic levels are attained.

138 As with standard diffusion methods, dilution procedures require the use of laboratory control  
139 organisms. Standard ceftazidime powder should give MIC values in the range of 4 to 16 mcg/mL  
140 for *Staphylococcus aureus* ATCC 25923. For *Escherichia coli* ATCC 25922, the MIC range  
141 should be between 0.125 and 0.5 mcg/mL. For *Pseudomonas aeruginosa* ATCC 27853, the MIC  
142 range should be between 0.5 and 2 mcg/mL.

### 143 **INDICATIONS AND USAGE**

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

- 146 1. **Lower Respiratory Tract Infections**, including pneumonia, caused by *Pseudomonas*  
147 *aeruginosa* and other *Pseudomonas* spp.; *Haemophilus influenzae*, including  
148 ampicillin-resistant strains; *Klebsiella* spp.; *Enterobacter* spp.; *Proteus mirabilis*;  
149 *Escherichia coli*; *Serratia* spp.; *Citrobacter* spp.; *Streptococcus pneumoniae*; and  
150 *Staphylococcus aureus* (methicillin-susceptible strains).
- 151 2. **Skin and Skin-Structure Infections** caused by *Pseudomonas aeruginosa*; *Klebsiella* spp.;  
152 *Escherichia coli*; *Proteus* spp., including *Proteus mirabilis* and indole-positive *Proteus*;  
153 *Enterobacter* spp.; *Serratia* spp.; *Staphylococcus aureus* (methicillin-susceptible strains); and  
154 *Streptococcus pyogenes* (group A beta-hemolytic streptococci).
- 155 3. **Urinary Tract Infections**, both complicated and uncomplicated, caused by *Pseudomonas*  
156 *aeruginosa*; *Enterobacter* spp.; *Proteus* spp., including *Proteus mirabilis* and indole-positive  
157 *Proteus*; *Klebsiella* spp.; and *Escherichia coli*.
- 158 4. **Bacterial Septicemia** caused by *Pseudomonas aeruginosa*, *Klebsiella* spp., *Haemophilus*  
159 *influenzae*, *Escherichia coli*, *Serratia* spp., *Streptococcus pneumoniae*, and *Staphylococcus*  
160 *aureus* (methicillin-susceptible strains).
- 161 5. **Bone and Joint Infections** caused by *Pseudomonas aeruginosa*, *Klebsiella* spp.,  
162 *Enterobacter* spp., and *Staphylococcus aureus* (methicillin-susceptible strains).
- 163 6. **Gynecologic Infections**, including endometritis, pelvic cellulitis, and other infections of the  
164 female genital tract caused by *Escherichia coli*.
- 165 7. **Intra-abdominal Infections**, including peritonitis caused by *Escherichia coli*, *Klebsiella*  
166 spp., and *Staphylococcus aureus* (methicillin-susceptible strains) and polymicrobial  
167 infections caused by aerobic and anaerobic organisms and *Bacteroides* spp. (many strains of  
168 *Bacteroides fragilis* are resistant).

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

173 FORTAZ may be used alone in cases of confirmed or suspected sepsis. Ceftazidime has been  
174 used successfully in clinical trials as empiric therapy in cases where various concomitant therapies  
175 with other antibiotics have been used.

176 FORTAZ may also be used concomitantly with other antibiotics, such as aminoglycosides,  
177 vancomycin, and clindamycin; in severe and life-threatening infections; and in the  
178 immunocompromised patient. When such concomitant treatment is appropriate, prescribing  
179 information in the labeling for the other antibiotics should be followed. The dose depends on the  
180 severity of the infection and the patient's condition.

181 To reduce the development of drug-resistant bacteria and maintain the effectiveness of  
182 FORTAZ and other antibacterial drugs, FORTAZ should be used only to treat or prevent  
183 infections that are proven or strongly suspected to be caused by susceptible bacteria. When  
184 culture and susceptibility information are available, they should be considered in selecting or  
185 modifying antibacterial therapy. In the absence of such data, local epidemiology and  
186 susceptibility patterns may contribute to the empiric selection of therapy.

## 187 **CONTRAINDICATIONS**

188 FORTAZ is contraindicated in patients who have shown hypersensitivity to ceftazidime or the  
189 cephalosporin group of antibiotics.

## 190 **WARNINGS**

191 BEFORE THERAPY WITH FORTAZ IS INSTITUTED, CAREFUL INQUIRY SHOULD BE  
192 MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS  
193 HYPERSENSITIVITY REACTIONS TO CEFTAZIDIME, CEPHALOSPORINS,  
194 PENICILLINS, OR OTHER DRUGS. IF THIS PRODUCT IS TO BE GIVEN TO  
195 PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE  
196 CROSS-HYPERSENSITIVITY AMONG BETA-LACTAM ANTIBIOTICS HAS BEEN  
197 CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A  
198 HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION TO FORTAZ  
199 OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY  
200 REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER  
201 EMERGENCY MEASURES, INCLUDING OXYGEN, IV FLUIDS, IV ANTIHISTAMINES,  
202 CORTICOSTEROIDS, PRESSOR AMINES, AND AIRWAY MANAGEMENT, AS  
203 CLINICALLY INDICATED.

204 *Clostridium difficile* associated diarrhea (CDAD) has been reported with use of nearly all  
205 antibacterial agents, including FORTAZ, and may range in severity from mild diarrhea to fatal  
206 colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to  
207 overgrowth of *C. difficile*.

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

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

218 Elevated levels of ceftazidime in patients with renal insufficiency can lead to seizures,  
219 encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia (see  
220 PRECAUTIONS).

## 221 **PRECAUTIONS**

222 **General:** High and prolonged serum ceftazidime concentrations can occur from usual dosages in  
223 patients with transient or persistent reduction of urinary output because of renal insufficiency. The  
224 total daily dosage should be reduced when ceftazidime is administered to patients with renal  
225 insufficiency (see DOSAGE AND ADMINISTRATION). Elevated levels of ceftazidime in these  
226 patients can lead to seizures, encephalopathy, coma, asterixis, neuromuscular excitability, and  
227 myoclonia. Continued dosage should be determined by degree of renal impairment, severity of  
228 infection, and susceptibility of the causative organisms.

229 As with other antibiotics, prolonged use of FORTAZ may result in overgrowth of  
230 nonsusceptible organisms. Repeated evaluation of the patient's condition is essential. If  
231 superinfection occurs during therapy, appropriate measures should be taken.

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

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

242 FORTAZ should be prescribed with caution in individuals with a history of gastrointestinal  
243 disease, particularly colitis.

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

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

248 **Information for Patients:** Patients should be counseled that antibacterial drugs, including  
249 FORTAZ, should only be used to treat bacterial infections. They do not treat viral infections  
250 (e.g., the common cold). When FORTAZ is prescribed to treat a bacterial infection, patients  
251 should be told that although it is common to feel better early in the course of therapy, the  
252 medication should be taken exactly as directed. Skipping doses or not completing the full course  
253 of therapy may: (1) decrease the effectiveness of the immediate treatment, and (2) increase the  
254 likelihood that bacteria will develop resistance and will not be treatable by FORTAZ or other  
255 antibacterial drugs in the future.

256 Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is  
257 discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery  
258 and bloody stools (with or without stomach cramps and fever) even as late as 2 or more months  
259 after having taken the last dose of the antibiotic. If this occurs, patients should contact their  
260 physician as soon as possible.

261 **Drug Interactions:** Nephrotoxicity has been reported following concomitant administration of  
262 cephalosporins with aminoglycoside antibiotics or potent diuretics such as furosemide. Renal  
263 function should be carefully monitored, especially if higher dosages of the aminoglycosides are to  
264 be administered or if therapy is prolonged, because of the potential nephrotoxicity and ototoxicity  
265 of aminoglycosidic antibiotics. Nephrotoxicity and ototoxicity were not noted when ceftazidime  
266 was given alone in clinical trials.

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

271 In common with other antibiotics, ceftazidime may affect the gut flora, leading to lower  
272 estrogen reabsorption and reduced efficacy of combined oral estrogen/progesterone  
273 contraceptives.

274 **Drug/Laboratory Test Interactions:** The administration of ceftazidime may result in a  
275 false-positive reaction for glucose in the urine when using CLINITEST<sup>®</sup> tablets, Benedict's  
276 solution, or Fehling's solution. It is recommended that glucose tests based on enzymatic glucose  
277 oxidase reactions (such as CLINISTIX<sup>®</sup>) be used.

278 **Carcinogenesis, Mutagenesis, Impairment of Fertility:** Long-term studies in animals have  
279 not been performed to evaluate carcinogenic potential. However, a mouse Micronucleus test and  
280 an Ames test were both negative for mutagenic effects.

281 **Pregnancy: Teratogenic Effects:** Pregnancy Category B. Reproduction studies have been  
282 performed in mice and rats at doses up to 40 times the human dose and have revealed no evidence  
283 of impaired fertility or harm to the fetus due to FORTAZ. There are, however, no adequate and

284 well-controlled studies in pregnant women. Because animal reproduction studies are not always  
285 predictive of human response, this drug should be used during pregnancy only if clearly needed.

286 **Nursing Mothers:** Ceftazidime is excreted in human milk in low concentrations. Caution should  
287 be exercised when FORTAZ is administered to a nursing woman.

288 **Pediatric Use:** (see DOSAGE AND ADMINISTRATION).

289 **Geriatric Use:** Of the 2,221 subjects who received ceftazidime in 11 clinical studies, 824  
290 (37%) were 65 and over while 391 (18%) were 75 and over. No overall differences in safety or  
291 effectiveness were observed between these subjects and younger subjects, and other reported  
292 clinical experience has not identified differences in responses between the elderly and younger  
293 patients, but greater susceptibility of some older individuals to drug effects cannot be ruled out.  
294 This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to  
295 this drug may be greater in patients with impaired renal function. Because elderly patients are  
296 more likely to have decreased renal function, care should be taken in dose selection, and it may  
297 be useful to monitor renal function (see DOSAGE AND ADMINISTRATION).

## 298 **ADVERSE REACTIONS**

299 Ceftazidime is generally well tolerated. The incidence of adverse reactions associated with the  
300 administration of ceftazidime was low in clinical trials. The most common were local reactions  
301 following IV injection and allergic and gastrointestinal reactions. Other adverse reactions were  
302 encountered infrequently. No disulfiram-like reactions were reported.

303 The following adverse effects from clinical trials were considered to be either related to  
304 ceftazidime therapy or were of uncertain etiology:

305 **Local Effects,** reported in fewer than 2% of patients, were phlebitis and inflammation at the site  
306 of injection (1 in 69 patients).

307 **Hypersensitivity Reactions,** reported in 2% of patients, were pruritus, rash, and fever.  
308 Immediate reactions, generally manifested by rash and/or pruritus, occurred in 1 in 285 patients.  
309 Toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme have also been  
310 reported with cephalosporin antibiotics, including ceftazidime. Angioedema and anaphylaxis  
311 (bronchospasm and/or hypotension) have been reported very rarely.

312 **Gastrointestinal Symptoms,** reported in fewer than 2% of patients, were diarrhea (1 in 78),  
313 nausea (1 in 156), vomiting (1 in 500), and abdominal pain (1 in 416). The onset of  
314 pseudomembranous colitis symptoms may occur during or after treatment (see WARNINGS).

315 **Central Nervous System Reactions** (fewer than 1%) included headache, dizziness, and  
316 paresthesia. Seizures have been reported with several cephalosporins, including ceftazidime. In  
317 addition, encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia have been  
318 reported in renally impaired patients treated with unadjusted dosing regimens of ceftazidime (see  
319 PRECAUTIONS: General).

320 **Less Frequent Adverse Events** (fewer than 1%) were candidiasis (including oral thrush) and  
321 vaginitis.

322 **Hematologic:** Rare cases of hemolytic anemia have been reported.

323 **Laboratory Test Changes** noted during clinical trials with FORTAZ were transient and  
324 included: eosinophilia (1 in 13), positive Coombs test without hemolysis (1 in 23), thrombocytosis  
325 (1 in 45), and slight elevations in one or more of the hepatic enzymes, aspartate aminotransferase  
326 (AST, SGOT) (1 in 16), alanine aminotransferase (ALT, SGPT) (1 in 15), LDH (1 in 18), GGT (1  
327 in 19), and alkaline phosphatase (1 in 23). As with some other cephalosporins, transient elevations  
328 of blood urea, blood urea nitrogen, and/or serum creatinine were observed occasionally. Transient  
329 leukopenia, neutropenia, agranulocytosis, thrombocytopenia, and lymphocytosis were seen very  
330 rarely.

### 331 **POSTMARKETING EXPERIENCE WITH FORTAZ PRODUCTS**

332 In addition to the adverse events reported during clinical trials, the following events have been  
333 observed during clinical practice in patients treated with FORTAZ and were reported  
334 spontaneously. For some of these events, data are insufficient to allow an estimate of incidence or  
335 to establish causation.

336 **General:** Anaphylaxis; allergic reactions, which, in rare instances, were severe (e.g.,  
337 cardiopulmonary arrest); urticaria; pain at injection site.

338 **Hepatobiliary Tract:** Hyperbilirubinemia, jaundice.

339 **Renal and Genitourinary:** Renal impairment.

340 **Cephalosporin-Class Adverse Reactions:** In addition to the adverse reactions listed above  
341 that have been observed in patients treated with ceftazidime, the following adverse reactions and  
342 altered laboratory tests have been reported for cephalosporin-class antibiotics:

343 **Adverse Reactions:** Colitis, toxic nephropathy, hepatic dysfunction including cholestasis,  
344 aplastic anemia, hemorrhage.

345 **Altered Laboratory Tests:** Prolonged prothrombin time, false-positive test for urinary  
346 glucose, pancytopenia.

### 347 **OVERDOSAGE**

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

### 353 **DOSAGE AND ADMINISTRATION**

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

357 The guidelines for dosage of FORTAZ are listed in Table 3. The following dosage schedule is  
358 recommended.

359

360 **Table 3. Recommended Dosage Schedule**

	Dose	Frequency
<b>Adults</b>		
<b>Usual recommended dosage</b>	<b>1 gram IV or IM</b>	<b>q8-12hr</b>
Uncomplicated urinary tract infections	250 mg IV or IM	q12hr
Bone and joint infections	2 grams IV	q12hr
Complicated urinary tract infections	500 mg IV or IM	q8-12hr
Uncomplicated pneumonia; mild skin and skin-structure infections	500 mg-1 gram IV or IM	q8hr
Serious gynecologic and intra-abdominal infections	2 grams IV	q8hr
Meningitis	2 grams IV	q8hr
Very severe life-threatening infections, especially in immunocompromised patients	2 grams IV	q8hr
Lung infections caused by <i>Pseudomonas</i> spp. in patients with cystic fibrosis with normal renal function*	30-50 mg/kg IV to a maximum of 6 grams per day	q8hr
<b>Neonates (0-4 weeks)</b>	30 mg/kg IV	q12hr
<b>Infants and children (1 month-12 years)</b>	30-50 mg/kg IV to a maximum of 6 grams per day <sup>†</sup>	q8hr

361 \* Although clinical improvement has been shown, bacteriologic cures cannot be expected in  
 362 patients with chronic respiratory disease and cystic fibrosis.

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

365  
 366 **Impaired Hepatic Function:** No adjustment in dosage is required for patients with hepatic  
 367 dysfunction.

368 **Impaired Renal Function:** Ceftazidime is excreted by the kidneys, almost exclusively by  
 369 glomerular filtration. Therefore, in patients with impaired renal function (glomerular filtration rate  
 370 [GFR] <50 mL/min), it is recommended that the dosage of ceftazidime be reduced to compensate  
 371 for its slower excretion. In patients with suspected renal insufficiency, an initial loading dose of  
 372 1 gram of FORTAZ may be given. An estimate of GFR should be made to determine the  
 373 appropriate maintenance dosage. The recommended dosage is presented in Table 4.

374

375 **Table 4. Recommended Maintenance Dosages of FORTAZ in Renal Insufficiency**  
 376 **NOTE: IF THE DOSE RECOMMENDED IN TABLE 3 ABOVE IS LOWER THAN**  
 377 **THAT RECOMMENDED FOR PATIENTS WITH RENAL INSUFFICIENCY AS**  
 378 **OUTLINED IN TABLE 4, THE LOWER DOSE SHOULD BE USED.**

Creatinine Clearance (mL/min)	Recommended Unit Dose of FORTAZ	Frequency of Dosing
50-31	1 gram	q12hr
30-16	1 gram	q24hr
15-6	500 mg	q24hr
<5	500 mg	q48hr

379  
 380 When only serum creatinine is available, the following formula (Cockcroft's equation)<sup>4</sup> may be  
 381 used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal  
 382 function:

383 Males: Creatinine clearance (mL/min) = 
$$\frac{\text{Weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine (mg/dL)}}$$

384 Females: 0.85 x male value

385  
 386 In patients with severe infections who would normally receive 6 grams of FORTAZ daily were  
 387 it not for renal insufficiency, the unit dose given in the table above may be increased by 50% or  
 388 the dosing frequency may be increased appropriately. Further dosing should be determined by  
 389 therapeutic monitoring, severity of the infection, and susceptibility of the causative organism.

390 In pediatric patients as for adults, the creatinine clearance should be adjusted for body surface  
 391 area or lean body mass, and the dosing frequency should be reduced in cases of renal  
 392 insufficiency.

393 In patients undergoing hemodialysis, a loading dose of 1 gram is recommended, followed by  
 394 1 gram after each hemodialysis period.

395 FORTAZ can also be used in patients undergoing intraperitoneal dialysis and continuous  
 396 ambulatory peritoneal dialysis. In such patients, a loading dose of 1 gram of FORTAZ may be  
 397 given, followed by 500 mg every 24 hours. In addition to IV use, FORTAZ can be incorporated in  
 398 the dialysis fluid at a concentration of 250 mg for 2 L of dialysis fluid.

399 **Note:** Generally FORTAZ should be continued for 2 days after the signs and symptoms of  
 400 infection have disappeared, but in complicated infections longer therapy may be required.

401 **Administration:** FORTAZ may be given intravenously or by deep IM injection into a large  
 402 muscle mass such as the upper outer quadrant of the gluteus maximus or lateral part of the thigh.  
 403 Intra-arterial administration should be avoided (see PRECAUTIONS).

404 **Intramuscular Administration:** For IM administration, FORTAZ should be constituted  
 405 with one of the following diluents: Sterile Water for Injection, Bacteriostatic Water for Injection,  
 406 or 0.5% or 1% Lidocaine Hydrochloride Injection. Refer to Table 5.

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

412 **For direct intermittent IV administration,** constitute FORTAZ as directed in Table 5 with  
413 Sterile Water for Injection. Slowly inject directly into the vein over a period of 3 to 5 minutes or  
414 give through the tubing of an administration set while the patient is also receiving one of the  
415 compatible IV fluids (see COMPATIBILITY AND STABILITY).

416 **For IV infusion,** constitute the 1- or 2-gram infusion pack with 100 mL of Sterile Water for  
417 Injection or one of the compatible IV fluids listed under the COMPATIBILITY AND  
418 STABILITY section. Alternatively, constitute the 500-mg, 1-gram, or 2-gram vial and add an  
419 appropriate quantity of the resulting solution to an IV container with one of the compatible IV  
420 fluids.

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

424 ADD-Vantage vials are to be constituted only with 50 or 100 mL of 5% Dextrose Injection,  
425 0.9% Sodium Chloride Injection, or 0.45% Sodium Chloride Injection in Abbott ADD-Vantage  
426 flexible diluent containers (see Instructions for Constitution). ADD-Vantage vials that have been  
427 joined to Abbott ADD-Vantage diluent containers and activated to dissolve the drug are stable for  
428 24 hours at room temperature or for 7 days under refrigeration. Joined vials that have not been  
429 activated may be used within a 14-day period; this period corresponds to that for use of Abbott  
430 ADD-Vantage containers following removal of the outer packaging (overwrap).

431 Freezing solutions of FORTAZ in the ADD-Vantage system is not recommended.

432

433 **Table 5. Preparation of Solutions of FORTAZ**

Size	Amount of Diluent to be Added (mL)	Approximate Available Volume (mL)	Approximate Ceftazidime Concentration (mg/mL)
Intramuscular			
500-mg vial	1.5	1.8	280
1-gram vial	3.0	3.6	280
Intravenous			
500-mg vial	5.3	5.7*	100
1-gram vial	10.0	10.8†	100
2-gram vial	10.0	11.5‡	170
Infusion pack			
1-gram vial	100§	100	10
2-gram vial	100§	100	20
Pharmacy bulk package			
6-gram vial	26	30	200

434 \* To obtain a dose of 500 mg, withdraw 5.0 mL from the vial following reconstitution.

435 † To obtain a dose of 1 g, withdraw 10.0 mL from the vial following reconstitution.

436 ‡ To obtain a dose of 2 g, withdraw 11.5 mL from the vial following reconstitution.

437 § **Note:** Addition should be in 2 stages (see Instructions for Constitution).

438

439 All vials of FORTAZ as supplied are under reduced pressure. When FORTAZ is dissolved,  
 440 carbon dioxide is released and a positive pressure develops. For ease of use please follow the  
 441 recommended techniques of constitution described on the detachable Instructions for  
 442 Constitution section of this insert.

443 Solutions of FORTAZ, like those of most beta-lactam antibiotics, should not be added to  
 444 solutions of aminoglycoside antibiotics because of potential interaction.

445 However, if concurrent therapy with FORTAZ and an aminoglycoside is indicated, each of  
 446 these antibiotics can be administered separately to the same patient.

447 **Directions for Use of FORTAZ Frozen in Galaxy® Plastic Containers:** FORTAZ  
 448 supplied as a frozen, sterile, iso-osmotic, nonpyrogenic solution in plastic containers is to be  
 449 administered after thawing either as a continuous or intermittent IV infusion. The thawed solution  
 450 is stable for 24 hours at room temperature or for 7 days if stored under refrigeration. **Do not**  
 451 **refreeze.**

452 Thaw container at room temperature (25°C) or under refrigeration (5°C). Do not force thaw  
 453 by immersion in water baths or by microwave irradiation. Components of the solution may  
 454 precipitate in the frozen state and will dissolve upon reaching room temperature with little or no  
 455 agitation. Potency is not affected. Mix after solution has reached room temperature. Check for  
 456 minute leaks by squeezing bag firmly. Discard bag if leaks are found as sterility may be

457 impaired. Do not add supplementary medication. Do not use unless solution is clear and seal is  
458 intact.

459 Use sterile equipment.

460 **Caution:** Do not use plastic containers in series connections. Such use could result in air  
461 embolism due to residual air being drawn from the primary container before administration of the  
462 fluid from the secondary container is complete.

463 **Preparation for Administration:**

- 464 1. Suspend container from eyelet support.  
465 2. Remove protector from outlet port at bottom of container.  
466 3. Attach administration set. Refer to complete directions accompanying set.

467 **COMPATIBILITY AND STABILITY**

468 **Intramuscular:** FORTAZ, when constituted as directed with Sterile Water for Injection,  
469 Bacteriostatic Water for Injection, or 0.5% or 1% Lidocaine Hydrochloride Injection, maintains  
470 satisfactory potency for 24 hours at room temperature or for 7 days under refrigeration. Solutions  
471 in Sterile Water for Injection that are frozen immediately after constitution in the original  
472 container are stable for 3 months when stored at -20°C. Once thawed, solutions should not be  
473 refrozen. Thawed solutions may be stored for up to 8 hours at room temperature or for 4 days in a  
474 refrigerator.

475 **Intravenous:** FORTAZ, when constituted as directed with Sterile Water for Injection, maintains  
476 satisfactory potency for 24 hours at room temperature or for 7 days under refrigeration. Solutions  
477 in Sterile Water for Injection in the infusion vial or in 0.9% Sodium Chloride Injection in  
478 VIAFLEX<sup>®</sup> small-volume containers that are frozen immediately after constitution are stable for  
479 6 months when stored at -20°C. Do not force thaw by immersion in water baths or by microwave  
480 irradiation. Once thawed, solutions should not be refrozen. Thawed solutions may be stored for up  
481 to 24 hours at room temperature or for 7 days in a refrigerator. More concentrated solutions in  
482 Sterile Water for Injection in the original container that are frozen immediately after constitution  
483 are stable for 3 months when stored at -20°C. Once thawed, solutions should not be refrozen.  
484 Thawed solutions may be stored for up to 8 hours at room temperature or for 4 days in a  
485 refrigerator.

486 FORTAZ is compatible with the more commonly used IV infusion fluids. Solutions at  
487 concentrations between 1 and 40 mg/mL in 0.9% Sodium Chloride Injection; 1/6 M Sodium  
488 Lactate Injection; 5% Dextrose Injection; 5% Dextrose and 0.225% Sodium Chloride Injection;  
489 5% Dextrose and 0.45% Sodium Chloride Injection; 5% Dextrose and 0.9% Sodium Chloride  
490 Injection; 10% Dextrose Injection; Ringer's Injection, USP; Lactated Ringer's Injection, USP; 10%  
491 Invert Sugar in Water for Injection; and NORMOSOL<sup>®</sup>-M in 5% Dextrose Injection may be  
492 stored for up to 24 hours at room temperature or for 7 days if refrigerated.

493 The 1- and 2-g FORTAZ ADD-Vantage vials, when diluted in 50 or 100 mL of 5% Dextrose  
494 Injection, 0.9% Sodium Chloride Injection, or 0.45% Sodium Chloride Injection, may be stored  
495 for up to 24 hours at room temperature or for 7 days under refrigeration.

496 FORTAZ is less stable in Sodium Bicarbonate Injection than in other IV fluids. It is not  
497 recommended as a diluent. Solutions of FORTAZ in 5% Dextrose Injection and 0.9% Sodium  
498 Chloride Injection are stable for at least 6 hours at room temperature in plastic tubing, drip  
499 chambers, and volume control devices of common IV infusion sets.

500 Ceftazidime at a concentration of 4 mg/mL has been found compatible for 24 hours at room  
501 temperature or for 7 days under refrigeration in 0.9% Sodium Chloride Injection or 5% Dextrose  
502 Injection when admixed with: cefuroxime sodium (ZINACEF<sup>®</sup>) 3 mg/mL, heparin 10 or 50 U/mL,  
503 or potassium chloride 10 or 40 mEq/L.

504 Vancomycin solution exhibits a physical incompatibility when mixed with a number of drugs,  
505 including ceftazidime. The likelihood of precipitation with ceftazidime is dependent on the  
506 concentrations of vancomycin and ceftazidime present. It is therefore recommended, when both  
507 drugs are to be administered by intermittent IV infusion, that they be given separately, flushing the  
508 IV lines (with 1 of the compatible IV fluids) between the administration of these 2 agents.

509 **Note:** Parenteral drug products should be inspected visually for particulate matter before  
510 administration whenever solution and container permit.

511 As with other cephalosporins, FORTAZ powder, as well as solutions, tend to darken depending  
512 on storage conditions; within the stated recommendations, however, product potency is not  
513 adversely affected.

#### 514 **HOW SUPPLIED**

515 FORTAZ in the dry state should be stored between 15° and 30°C (59° and 86°F) and protected  
516 from light. FORTAZ is a dry, white to off-white powder supplied in vials and infusion packs as  
517 follows:

518 NDC 0173-0377-10 500-mg\* Vial (Tray of 10)

519 NDC 0173-0378-10 1-g\* Vial (Tray of 10)

520 NDC 0173-0379-34 2-g\* Vial (Tray of 10)

521 NDC 0173-0380-32 1-g\* Infusion Pack (Tray of 10)

522 NDC 0173-0381-32 2-g\* Infusion Pack (Tray of 10)

523 NDC 0173-0382-37 6-g\* Pharmacy Bulk Package (Tray of 6)

524 NDC 0173-0434-00 1-g ADD-Vantage<sup>®</sup> Vial (Tray of 25)

525 NDC 0173-0435-00 2-g ADD-Vantage<sup>®</sup> Vial (Tray of 10)

526 (The above ADD-Vantage vials are to be used only with Abbott ADD-Vantage diluent  
527 containers.)

528 FORTAZ frozen as a premixed solution of ceftazidime sodium should not be stored above  
529 -20°C. FORTAZ is supplied frozen in 50-mL, single-dose, plastic containers as follows:

530 NDC 0173-0412-00 1-g\* Plastic Container (Carton of 24)

531 NDC 0173-0413-00 2-g\* Plastic Container (Carton of 24)

532 \*Equivalent to anhydrous ceftazidime.

533 **REFERENCES**

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535 standardized single disk method. *Am J Clin Pathol.* 1966;45:493-496.  
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540 4. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine.  
541 *Nephron.* 1976;16:31-41.

542  
543



544  
545 GlaxoSmithKline  
546 FORTAZ<sup>®</sup> (ceftazidime for injection):  
547 GlaxoSmithKline  
548 Research Triangle Park, NC 27709

549  
550 FORTAZ<sup>®</sup> (ceftazidime injection):  
551 Manufactured for GlaxoSmithKline  
552 Research Triangle Park, NC 27709  
553 by Baxter Healthcare Corporation  
554 Deerfield, IL 60015

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557 ADD-Vantage is a registered trademark of Abbott Laboratories.  
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559 Inc.  
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562 January 2007 RL-2352

563 -----  
564 **TEAR AWAY**

565  
566 **FORTAZ<sup>®</sup>**  
567 **(ceftazidime for injection)**

568  
569 **Instructions for Constitution**

570  
571 **Vials:** 500 mg IM/IV, 1 g IM/IV, 2 g IV

572

- 573 1. Insert the syringe needle through the vial closure and inject the recommended volume of  
574 diluent. The vacuum may assist entry of the diluent. Remove the syringe needle.
- 575 2. Shake to dissolve; a clear solution will be obtained in 1 to 2 minutes.
- 576 3. Invert the vial. Ensuring that the syringe plunger is fully depressed, insert the needle through  
577 the vial closure and withdraw the total volume of solution into the syringe (the pressure in the  
578 vial may aid withdrawal). Ensure that the needle remains within the solution and does not  
579 enter the headspace. The withdrawn solution may contain some bubbles of carbon dioxide.

580

581 **Note:** As with the administration of all parenteral products, accumulated gases should be  
582 expressed from the syringe immediately before injection of FORTAZ.

583

584 **Infusion Pack:** 1 g, 2 g

585

- 586 1. Insert the syringe needle through the vial closure and inject 10 mL of diluent. The vacuum  
587 may assist entry of the diluent. Remove the syringe needle.
- 588 2. Shake to dissolve; a clear solution will be obtained in 1 to 2 minutes.
- 589 3. Insert a gas-relief needle through the vial closure to relieve the internal pressure. With the  
590 gas-relief needle in position, add the remaining 90 mL of diluent. Remove the gas-relief  
591 needle and syringe needle; shake the vial and set up for infusion in the normal way.

592

593 **Note:** To preserve product sterility, it is important that a gas-relief needle is *not* inserted through  
594 the vial closure before the product has dissolved.

595

596 **ADD-Vantage<sup>®</sup> Vials:** 1 g, 2 g

597

598 ***To Open Diluent Container:***

599 Peel the corner of the ADD-Vantage diluent overwrap and remove flexible diluent container.  
600 Some opacity of the plastic flexible container due to moisture absorption during the sterilization  
601 process may be observed. This is normal and does not affect the solution quality or safety. The  
602 opacity will diminish gradually.

603

604 ***To Assemble Vial and Flexible Diluent Container (Use Aseptic Technique):***

- 605 1. Remove the protective covers from the top of the vial and the vial port on the diluent  
606 container as follows:
  - 607 a. To remove the breakaway vial cap, swing the pull ring over the top of the vial and pull  
608 down far enough to start the opening (see Figure 1), then pull straight up to remove the cap  
609 (see Figure 2).

610 **Note:** Once the breakaway cap has been removed, do not access vial with syringe.

611



Figure 1

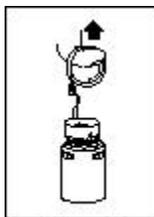


Figure 2

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- b. To remove the vial port cover, grasp the tab on the pull ring, pull up to break the three tie strings, then pull back to remove the cover (see Figure 3).
- 2. Screw the vial into the vial port until it will go no further. **THE VIAL MUST BE SCREWED IN TIGHTLY TO ASSURE A SEAL.** This occurs approximately one-half turn (180°) after the first audible click (see Figure 4). The clicking sound does not assure a seal; the vial must be turned as far as it will go.

**Note:** Once vial is seated, do not attempt to remove (see Figure 4).

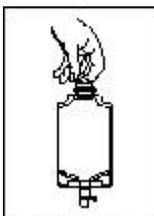


Figure 3

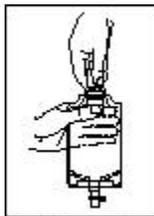


Figure 4

622  
623  
624  
625  
626

- 3. Recheck the vial to assure that it is tight by trying to turn it further in the direction of assembly.
- 4. Label appropriately.

**To Prepare Admixture:**

627  
628  
629  
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631  
632  
633  
634  
635

- 1. Squeeze the bottom of the diluent container gently to inflate the portion of the container surrounding the end of the drug vial.
- 2. With the other hand, push the drug vial down into the container, telescoping the walls of the container. Grasp the inner cap of the vial through the walls of the container (see Figure 5).
- 3. Pull the inner cap from the drug vial (see Figure 6). Verify that the rubber stopper has been pulled out, allowing the drug and diluent to mix.

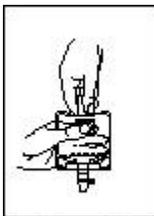


Figure 5

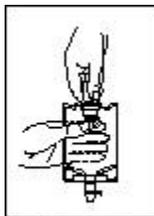


Figure 6

636  
637

638 4. Mix container contents thoroughly and use within the specified time.

639

640 ***Preparation for Administration (Use Aseptic Technique):***

641 1. Confirm the activation and admixture of vial contents.

642 2. Check for leaks by squeezing container firmly. If leaks are found, discard unit as sterility  
643 may be impaired.

644 3. Close flow control clamp of administration set.

645 4. Remove cover from outlet port at bottom of container.

646 5. Insert piercing pin of administration set into port with a twisting motion until the pin is firmly  
647 seated.

648 **Note:** See full directions on administration set carton.

649 6. Lift the free end of the hanger loop on the bottom of the vial, breaking the two tie strings.

650 Bend the loop outward to lock it in the upright position, then suspend container from hanger.

651 7. Squeeze and release drip chamber to establish proper fluid level in chamber.

652 8. Open flow control clamp and clear air from set. Close clamp.

653 9. Attach set to venipuncture device. If device is not indwelling, prime and make venipuncture.

654 10. Regulate rate of administration with flow control clamp.

655

656 **WARNING: Do not use flexible container in series connections.**

657

658 **Pharmacy Bulk Package: 6 g**

659

660 1. Insert the syringe needle through the vial closure and inject 26 mL of diluent. The vacuum  
661 may assist entry of the diluent. Remove the syringe needle.

662 2. Shake to dissolve; a clear solution containing approximately 1 g of ceftazidime activity per  
663 5 mL will be obtained in 1 to 2 minutes.

664 3. Insert a gas-relief needle through the vial closure to relieve the internal pressure. Remove the  
665 gas-relief needle before extracting any solution.

666

667 **Note:** To preserve product sterility, it is important that a gas-relief needle is *not* inserted through  
668 the vial closure before the product has dissolved.

669

670



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672 GlaxoSmithKline

673 Research Triangle Park, NC 27709

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675 January 2007

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