

PRESCRIBING INFORMATION

FORTAZ[®] **(ceftazidime for injection)**

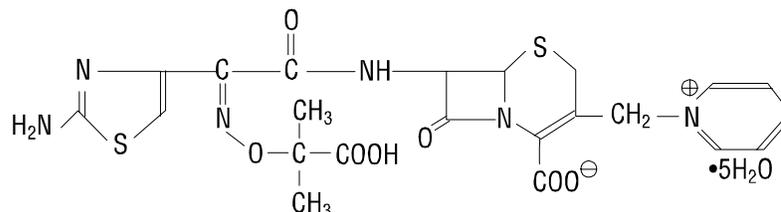
FORTAZ[®] **(ceftazidime injection)**

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 α ,7 β (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[®] 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 Hydrus, 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

36 room temperature. The osmolality of the solution is approximately 300 mOsmol/kg, and the pH of
37 thawed solutions ranges from 5 to 7.5.

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

43 **CLINICAL PHARMACOLOGY**

44 After IV administration of 500-mg and 1-g doses of ceftazidime over 5 minutes to normal adult
45 male volunteers, mean peak serum concentrations of 45 and 90 mcg/mL, respectively, were
46 achieved. After IV infusion of 500-mg, 1-g, and 2-g doses of ceftazidime over 20 to 30 minutes to
47 normal adult male volunteers, mean peak serum concentrations of 42, 69, and 170 mcg/mL,
48 respectively, were achieved. The average serum concentrations following IV infusion of 500-mg,
49 1-g, and 2-g doses to these volunteers over an 8-hour interval are given in Table 1.

50

51 **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

52

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

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

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

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

70 excreted between 2 and 4 hours after dosing, and approximately another 12% of the dose appeared
71 in the urine between 4 and 8 hours later. The elimination of ceftazidime by the kidneys resulted in
72 high therapeutic concentrations in the urine.

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

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

81 Therapeutic concentrations of ceftazidime are achieved in the following body tissues and fluids.
82

83 **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 (inflamed meninges)	2 g q8hr IV	5	120 min	9.8
	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

84

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

90 by both gram-negative and gram-positive organisms and, consequently, is active against many
91 strains resistant to ampicillin and other cephalosporins.

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

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

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

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

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

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

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

115 **Susceptibility Tests: Diffusion Techniques:** Quantitative methods that require
116 measurement of zone diameters give an estimate of antibiotic susceptibility. One such procedure¹⁻³
117 has been recommended for use with disks to test susceptibility to ceftazidime.

118 Reports from the laboratory giving results of the standard single-disk susceptibility test with a
119 30-mcg ceftazidime disk should be interpreted according to the following criteria:

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

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

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

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

129 Standardized procedures require the use of laboratory control organisms. The 30-mcg
130 ceftazidime disk should give zone diameters between 25 and 32 mm for *Escherichia coli*
131 ATCC 25922. For *Pseudomonas aeruginosa* ATCC 27853, the zone diameters should be between
132 22 and 29 mm. For *Staphylococcus aureus* ATCC 25923, the zone diameters should be between
133 16 and 20 mm.

134 **Dilution Techniques:** In other susceptibility testing procedures, e.g., ICS agar dilution or the
135 equivalent, a bacterial isolate may be considered susceptible if the minimum inhibitory
136 concentration (MIC) value for ceftazidime is not more than 16 mcg/mL. Organisms are considered
137 resistant to ceftazidime if the MIC is ≥ 64 mcg/mL. Organisms having an MIC value of
138 < 64 mcg/mL but > 16 mcg/mL are expected to be susceptible if high dosage is used or if the
139 infection is confined to tissues and fluids (e.g., urine) in which high antibiotic levels are attained.

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

145 INDICATIONS AND USAGE

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

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

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

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

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

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

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

188 **CONTRAINDICATIONS**

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

191 **WARNINGS**

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

205 **Pseudomembranous colitis has been reported with nearly all antibacterial agents,**
206 **including ceftazidime, and may range in severity from mild to life threatening. Therefore, it**
207 **is important to consider this diagnosis in patients who present with diarrhea subsequent to**
208 **the administration of antibacterial agents.**

209 Treatment with antibacterial agents alters the normal flora of the colon and may permit
210 overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one
211 primary cause of "antibiotic-associated colitis."

212 After the diagnosis of pseudomembranous colitis has been established, appropriate therapeutic
213 measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug
214 discontinuation alone. In moderate to severe cases, consideration should be given to management
215 with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug
216 clinically effective against *Clostridium difficile* colitis.

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

220 **PRECAUTIONS**

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

280 **Geriatric Use:** Of the 2,221 subjects who received ceftazidime in 11 clinical studies, 824
281 (37%) were 65 and over while 391 (18%) were 75 and over. No overall differences in safety or
282 effectiveness were observed between these subjects and younger subjects, and other reported
283 clinical experience has not identified differences in responses between the elderly and younger

284 patients, but greater susceptibility of some older individuals to drug effects cannot be ruled out.
285 This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to
286 this drug may be greater in patients with impaired renal function. Because elderly patients are
287 more likely to have decreased renal function, care should be taken in dose selection, and it may
288 be useful to monitor renal function (see DOSAGE AND ADMINISTRATION).

289 **ADVERSE REACTIONS**

290 Ceftazidime is generally well tolerated. The incidence of adverse reactions associated with the
291 administration of ceftazidime was low in clinical trials. The most common were local reactions
292 following IV injection and allergic and gastrointestinal reactions. Other adverse reactions were
293 encountered infrequently. No disulfiramlike reactions were reported.

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

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

298 **Hypersensitivity Reactions**, reported in 2% of patients, were pruritus, rash, and fever.

299 Immediate reactions, generally manifested by rash and/or pruritus, occurred in 1 in 285 patients.

300 Toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme have also been
301 reported with cephalosporin antibiotics, including ceftazidime. Angioedema and anaphylaxis
302 (bronchospasm and/or hypotension) have been reported very rarely.

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

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

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

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

314 **Laboratory Test Changes** noted during clinical trials with FORTAZ were transient and
315 included: eosinophilia (1 in 13), positive Coombs test without hemolysis (1 in 23), thrombocytosis
316 (1 in 45), and slight elevations in one or more of the hepatic enzymes, aspartate aminotransferase
317 (AST, SGOT) (1 in 16), alanine aminotransferase (ALT, SGPT) (1 in 15), LDH (1 in 18), GGT (1
318 in 19), and alkaline phosphatase (1 in 23). As with some other cephalosporins, transient elevations
319 of blood urea, blood urea nitrogen, and/or serum creatinine were observed occasionally. Transient
320 leukopenia, neutropenia, agranulocytosis, thrombocytopenia, and lymphocytosis were seen very
321 rarely.

322 **POSTMARKETING EXPERIENCE WITH FORTAZ PRODUCTS**

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

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

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

330 **Renal and Genitourinary:** Renal impairment.

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

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

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

338 **OVERDOSAGE**

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

344 **DOSAGE AND ADMINISTRATION**

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

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

350

351 **Table 3. Recommended Dosage Schedule**

	Dose	Frequency
Adults		
Usual recommended dosage	1 gram IV or IM	q8-12hr
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
Neonates (0-4 weeks)	30 mg/kg IV	q12hr
Infants and children (1 month-12 years)	30-50 mg/kg IV to a maximum of 6 grams per day [†]	q8hr

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

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

356

357 **Impaired Hepatic Function:** No adjustment in dosage is required for patients with hepatic
358 dysfunction.

359 **Impaired Renal Function:** Ceftazidime is excreted by the kidneys, almost exclusively by
360 glomerular filtration. Therefore, in patients with impaired renal function (glomerular filtration rate
361 [GFR] <50 mL/min), it is recommended that the dosage of ceftazidime be reduced to compensate
362 for its slower excretion. In patients with suspected renal insufficiency, an initial loading dose of
363 1 gram of FORTAZ may be given. An estimate of GFR should be made to determine the
364 appropriate maintenance dosage. The recommended dosage is presented in Table 4.

365

366 **Table 4. Recommended Maintenance Dosages of FORTAZ in Renal Insufficiency**
367 **NOTE: IF THE DOSE RECOMMENDED IN TABLE 3 ABOVE IS LOWER THAN**
368 **THAT RECOMMENDED FOR PATIENTS WITH RENAL INSUFFICIENCY AS**
369 **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

370

371 When only serum creatinine is available, the following formula (Cockcroft's equation)⁴ may be
372 used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal
373 function:

374

375 Males: Creatinine clearance (mL/min) = $\frac{\text{Weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine (mg/dL)}}$
376

377 Females: 0.85 x male value

378

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

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

386 In patients undergoing hemodialysis, a loading dose of 1 gram is recommended, followed by
387 1 gram after each hemodialysis period.

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

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

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

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

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

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

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

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

417 ADD-Vantage vials are to be constituted only with 50 or 100 mL of 5% Dextrose Injection,
418 0.9% Sodium Chloride Injection, or 0.45% Sodium Chloride Injection in Abbott ADD-Vantage
419 flexible diluent containers (see Instructions for Constitution). ADD-Vantage vials that have been
420 joined to Abbott ADD-Vantage diluent containers and activated to dissolve the drug are stable for
421 24 hours at room temperature or for 7 days under refrigeration. Joined vials that have not been
422 activated may be used within a 14-day period; this period corresponds to that for use of Abbott
423 ADD-Vantage containers following removal of the outer packaging (overwrap).

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

425

426 **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	5.0	5.3	100
1-gram vial	10.0	10.6	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

427 ***Note:** Addition should be in 2 stages (see Instructions for Constitution).
428

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

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

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

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

442 Thaw container at room temperature (25°C) or under refrigeration (5°C). Do not force thaw
443 by immersion in water baths or by microwave irradiation. Components of the solution may
444 precipitate in the frozen state and will dissolve upon reaching room temperature with little or no
445 agitation. Potency is not affected. Mix after solution has reached room temperature. Check for
446 minute leaks by squeezing bag firmly. Discard bag if leaks are found as sterility may be
447 impaired. Do not add supplementary medication. Do not use unless solution is clear and seal is
448 intact.

449 Use sterile equipment.

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

453 **Preparation for Administration:**

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

457 **COMPATIBILITY AND STABILITY**

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

465 **Intravenous:** FORTAZ, when constituted as directed with Sterile Water for Injection, maintains
466 satisfactory potency for 24 hours at room temperature or for 7 days under refrigeration. Solutions
467 in Sterile Water for Injection in the infusion vial or in 0.9% Sodium Chloride Injection in
468 VIAFLEX® small-volume containers that are frozen immediately after constitution are stable for
469 6 months when stored at -20°C. Do not force thaw by immersion in water baths or by microwave
470 irradiation. Once thawed, solutions should not be refrozen. Thawed solutions may be stored for up
471 to 24 hours at room temperature or for 7 days in a refrigerator. More concentrated solutions in
472 Sterile Water for Injection in the original container that are frozen immediately after constitution
473 are stable for 3 months when stored at -20°C. Once thawed, solutions should not be refrozen.
474 Thawed solutions may be stored for up to 8 hours at room temperature or for 4 days in a
475 refrigerator.

476 FORTAZ is compatible with the more commonly used IV infusion fluids. Solutions at
477 concentrations between 1 and 40 mg/mL in 0.9% Sodium Chloride Injection; 1/6 M Sodium
478 Lactate Injection; 5% Dextrose Injection; 5% Dextrose and 0.225% Sodium Chloride Injection;
479 5% Dextrose and 0.45% Sodium Chloride Injection; 5% Dextrose and 0.9% Sodium Chloride
480 Injection; 10% Dextrose Injection; Ringer's Injection, USP; Lactated Ringer's Injection, USP; 10%
481 Invert Sugar in Water for Injection; and NORMOSOL®-M in 5% Dextrose Injection may be
482 stored for up to 24 hours at room temperature or for 7 days if refrigerated.

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

486 FORTAZ is less stable in Sodium Bicarbonate Injection than in other IV fluids. It is not
487 recommended as a diluent. Solutions of FORTAZ in 5% Dextrose Injection and 0.9% Sodium

488 Chloride Injection are stable for at least 6 hours at room temperature in plastic tubing, drip
489 chambers, and volume control devices of common IV infusion sets.

490 Ceftazidime at a concentration of 4 mg/mL has been found compatible for 24 hours at room
491 temperature or for 7 days under refrigeration in 0.9% Sodium Chloride Injection or 5% Dextrose
492 Injection when admixed with: cefuroxime sodium (ZINACEF[®]) 3 mg/mL; heparin 10 or 50 U/mL;
493 or potassium chloride 10 or 40 mEq/L.

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

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

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

504 **HOW SUPPLIED**

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

508 NDC 0173-0377-31 500-mg* Vial (Tray of 25)

509 NDC 0173-0378-35 1-g* Vial (Tray of 25)

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

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

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

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

514 NDC 0173-0434-00 1-g ADD-Vantage[®] Vial (Tray of 25)

515 NDC 0173-0435-00 2-g ADD-Vantage[®] Vial (Tray of 10)

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

518 FORTAZ frozen as a premixed solution of ceftazidime sodium should not be stored above
519 -20°C. FORTAZ is supplied frozen in 50-mL, single-dose, plastic containers as follows:

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

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

522 *Equivalent to anhydrous ceftazidime.

523 **REFERENCES**

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525 standardized single disk method. *Am J Clin Pathol.* 1966;45:493-496.

- 526 2. National Committee for Clinical Laboratory Standards. *Approved Standard: Performance*
527 *Standards for Antimicrobial Disc Susceptibility Tests*. (M2-A3). December 1984.
528 3. Certification procedure for antibiotic sensitivity discs (21 CFR 460.1). *Federal Register*. May
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530 4. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*.
531 1976;16:31-41.
532
533



534
535 GlaxoSmithKline
536 FORTAZ[®] (ceftazidime for injection):
537 GlaxoSmithKline
538 Research Triangle Park, NC 27709
539
540 FORTAZ[®] (ceftazidime injection):
541 Manufactured for GlaxoSmithKline
542 Research Triangle Park, NC 27709
543 by Baxter Healthcare Corporation,
544 Deerfield, IL 60015

545
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547 ADD-Vantage is a registered trademark of Abbott Laboratories.
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549 Inc.

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552
553 October 2003

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556 TEAR AWAY

557
558 **FORTAZ[®]**
559 **(ceftazidime for injection)**

560
561 **Instructions for Constitution**
562

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

564

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

572

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

575

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

577

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

584

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

587

588 **ADD-Vantage[®] Vials:** 1 g, 2 g

589

590 ***To Open Diluent Container:***

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

595

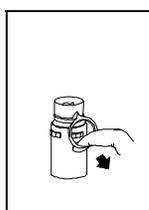
596 **To Assemble Vial and Flexible Diluent Container (Use Aseptic Technique):**

597 1. Remove the protective covers from the top of the vial and the vial port on the diluent container
598 as follows:

599 a. To remove the breakaway vial cap, swing the pull ring over the top of the vial and pull
600 down far enough to start the opening (see Figure 1), then pull straight up to remove the cap
601 (see Figure 2).

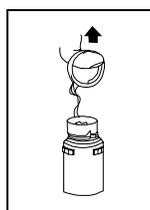
602 **Note:** Once the breakaway cap has been removed, do not access vial with syringe.

603



604

605 Figure 1



606 Figure 2

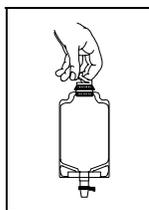
606

607 b. To remove the vial port cover, grasp the tab on the pull ring, pull up to break the three tie
608 strings, then pull back to remove the cover (see Figure 3).

609 2. Screw the vial into the vial port until it will go no further. **THE VIAL MUST BE SCREWED**
610 **IN TIGHTLY TO ASSURE A SEAL.** This occurs approximately one-half turn (180°) after
611 the first audible click (see Figure 4). The clicking sound does not assure a seal; the vial must
612 be turned as far as it will go.

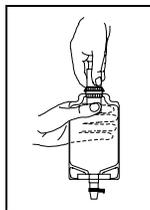
613 **Note:** Once vial is seated, do not attempt to remove (see Figure 4).

614



615

616 Figure 3



617 Figure 4

618 3. Recheck the vial to assure that it is tight by trying to turn it further in the direction of
619 assembly.

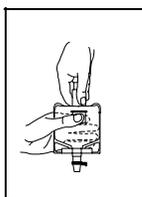
620 4. Label appropriately.

621

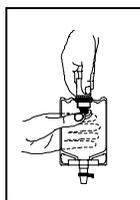
622 ***To Prepare Admixture:***

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

629



630
631 Figure 5



632
633 Figure 6

634

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

634

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

- 636 1. Confirm the activation and admixture of vial contents.
- 637 2. Check for leaks by squeezing container firmly. If leaks are found, discard unit as sterility may
638 be impaired.
- 639 3. Close flow control clamp of administration set.
- 640 4. Remove cover from outlet port at bottom of container.
- 641 5. Insert piercing pin of administration set into port with a twisting motion until the pin is firmly
642 seated.

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

- 644 6. Lift the free end of the hanger loop on the bottom of the vial, breaking the two tie strings.
645 Bend the loop outward to lock it in the upright position, then suspend container from hanger.
- 646 7. Squeeze and release drip chamber to establish proper fluid level in chamber.
- 647 8. Open flow control clamp and clear air from set. Close clamp.
- 648 9. Attach set to venipuncture device. If device is not indwelling, prime and make venipuncture.

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

650

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

652

653 **Pharmacy Bulk Package: 6 g**

654

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

657 2. Shake to dissolve; a clear solution containing approximately 1 g of ceftazidime activity per
658 5 mL will be obtained in 1 to 2 minutes.

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

661

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

664

665



666

667 GlaxoSmithKline

668 Research Triangle Park, NC 27709

669

670 October 2003

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