Cefepime for Injection

For Intravenous Use Only

Cefepime for Injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION

Cefepime hydrochloride is a semi-synthetic, broad spectrum, cephalosporin antibiotic for parenteral administration. The chemical name is 1-[[6R,7R]-7-[2-(2-amino-4-thiazolyl)glyoxylamido]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-1-methlypyrrolidinium chloride, 72-(Z)-(O-methyloxime), monohydrochloride, monohydrate, which corresponds to the following structural formula:

![Structural formula of Cefepime hydrochloride]

Cefepime hydrochloride is a white to pale yellow powder. Cefepime hydrochloride contains the equivalent of not less that 825 mcg and not more than 911 mcg of cefepime (C19H24N6O5S2) per mg, calculated on an anhydrous basis. It is highly soluble in water.
Cefepime for Injection in the Duplex dual chamber container is supplied for intravenous administration in strengths equivalent to 1 g and 2 g of cefepime (See DOSAGE AND ADMINISTRATION.) Cefepime for Injection is supplied as a sterile, nonpyrogenic, single use packaged combination of cefepime hydrochloride with L-arginine (drug chamber) and Dextrose Injection (diluent chamber).

Cefepime for Injection contains the equivalent of not less than 90 percent and not more than 115 percent of the labeled amount of cefepime (\(\text{C}_{19}\text{H}_{24}\text{N}_{6}\text{O}_{5}\text{S}_{2}\)). The L-arginine, at an approximate concentration of 725 mg/g of cefepime, is added to control the pH of the reconstituted solution at 4.0 to 6.0.

After removing the peelable foil strip, activating the seals, and thoroughly mixing, the reconstituted drug product is intended for single intravenous use. Each 50 mL contains cefepime hydrochloride equivalent to either 1 gram or 2 grams of cefepime. Reconstituted solutions of Cefepime for Injection range in color from colorless to amber.

The DUPEX Container is Latex-free, PVC-free, and DEHP-free.

The DUPEX dual chamber container is made from a specially formulated material. The product (diluent and drug) contact layer is a mixture of thermoplastic rubber and a polypropylene ethylene copolymer that contains no plasticizers. The safety of the container system is supported by USP biological evaluation procedures.

**CLINICAL PHARMACOLOGY**

**Pharmacokinetics**

The average plasma concentrations of cefepime observed in healthy adult male volunteers (n=9) at various times following single 30-minute infusions (IV) of cefepime 500 mg, 1 g, and 2 g are summarized in Table 1. Elimination of cefepime is principally via renal excretion with an average (±SD) half-life of 2 (±0.3) hours and total body clearance of 120 (±8) mL/min in healthy volunteers. Cefepime pharmacokinetics are
linear over the range 250 mg to 2 g. There is no evidence of accumulation in healthy adult male volunteers (n=7) receiving clinically relevant doses for a period of 9 days.

Absorption

The average plasma concentrations of cefepime and its derived pharmacokinetic parameters after intravenous administration are portrayed in Table 1.

Table 1: Average Plasma Concentrations in mcg/mL of Cefepime and Derived Pharmacokinetic Parameters (±SD), Intravenous Administration

<table>
<thead>
<tr>
<th>Parameter</th>
<th>500 mg IV</th>
<th>1 g IV</th>
<th>2 g IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 h</td>
<td>38.2</td>
<td>78.7</td>
<td>163.1</td>
</tr>
<tr>
<td>1.0 h</td>
<td>21.6</td>
<td>44.5</td>
<td>85.8</td>
</tr>
<tr>
<td>2.0 h</td>
<td>11.6</td>
<td>24.3</td>
<td>44.8</td>
</tr>
<tr>
<td>4.0 h</td>
<td>5.0</td>
<td>10.5</td>
<td>19.2</td>
</tr>
<tr>
<td>8.0 h</td>
<td>1.4</td>
<td>2.4</td>
<td>3.9</td>
</tr>
<tr>
<td>12.0 h</td>
<td>0.2</td>
<td>0.6</td>
<td>1.1</td>
</tr>
</tbody>
</table>

C_{max}, mcg/mL | 39.1 (3.5) | 81.7 (5.1) | 163.9 (25.3) |
AUC, h • mcg/mL | 70.8 (6.7) | 148.5 (15.1) | 284.8 (30.6) |

Number of subjects (male) | 9 | 9 | 9

Distribution

The average steady-state volume of distribution of cefepime is 18 (±2) L. The serum protein binding of cefepime is approximately 20% and is independent of its concentration in serum.

Cefepime is excreted in human milk. A nursing infant consuming approximately 1000 mL of human milk per day would receive approximately 0.5 mg of cefepime per day. (See PRECAUTIONS: Nursing Mothers.)
Concentrations of cefepime achieved in specific tissues and body fluids are listed in Table 2.

### Table 2: Average Concentrations of Cefepime in Specific Body Fluids (mcg/mL) or Tissues (mcg/g)

<table>
<thead>
<tr>
<th>Tissue or Fluid</th>
<th>Dose/Route</th>
<th># of Patients</th>
<th>Average Time of Sample Post-Dose (h)</th>
<th>Average Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blister Fluid</td>
<td>2 g IV</td>
<td>6</td>
<td>1.5</td>
<td>81.4 mcg/mL</td>
</tr>
<tr>
<td>Bronchial Mucosa</td>
<td>2 g IV</td>
<td>20</td>
<td>4.8</td>
<td>24.1 mcg/g</td>
</tr>
<tr>
<td>Sputum</td>
<td>2 g IV</td>
<td>5</td>
<td>4.0</td>
<td>7.4 mcg/mL</td>
</tr>
<tr>
<td>Urine</td>
<td>500 mg IV</td>
<td>8</td>
<td>0-4</td>
<td>292 mcg/mL</td>
</tr>
<tr>
<td></td>
<td>1 g IV</td>
<td>12</td>
<td>0-4</td>
<td>926 mcg/mL</td>
</tr>
<tr>
<td></td>
<td>2 g IV</td>
<td>12</td>
<td>0-4</td>
<td>3120 mcg/mL</td>
</tr>
<tr>
<td>Bile</td>
<td>2 g IV</td>
<td>26</td>
<td>9.4</td>
<td>17.8 mcg/mL</td>
</tr>
<tr>
<td>Peritoneal Fluid</td>
<td>2 g IV</td>
<td>19</td>
<td>4.4</td>
<td>18.3 mcg/mL</td>
</tr>
<tr>
<td>Appendix</td>
<td>2 g IV</td>
<td>31</td>
<td>5.7</td>
<td>5.2 mcg/g</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>2 g IV</td>
<td>38</td>
<td>8.9</td>
<td>11.9 mcg/g</td>
</tr>
<tr>
<td>Prostate</td>
<td>2 g IV</td>
<td>5</td>
<td>1.0</td>
<td>31.5 mcg/g</td>
</tr>
</tbody>
</table>

Data suggest that cefepime does cross the inflamed blood-brain barrier. The clinical relevance of these data are uncertain at this time.

### Metabolism and Excretion

Cefepime is metabolized to N-methylpyrrolidine (NMP) which is rapidly converted to the N-oxide (NMP-N-oxide). Urinary recovery of unchanged cefepime accounts for approximately 85% of the administered dose. Less than 1% of the administered dose is recovered from urine as NMP, 6.8% as NMP-N-oxide, and 2.5% as an epimer of cefepime. Because renal excretion is a significant pathway of elimination, patients with renal dysfunction and patients undergoing hemodialysis require dosage adjustment. (See DOSAGE AND ADMINISTRATION.)
Special Populations

Pediatric patients: Cefepime pharmacokinetics have been evaluated in pediatric patients from 2 months to 11 years of age following single and multiple doses on q8h (n=29) and q12h (n=13) schedules. Following a single IV dose, total body clearance and the steady-state volume of distribution averaged 3.3 (±1) mL/min/kg and 0.3 (±0.1) L/kg, respectively. The urinary recovery of unchanged cefepime was 60.4 (±30.4) percent of the administered dose, and the average renal clearance was 2 (±1.1) mL/min/kg. There were no significant effects of age or gender (25 male vs. 17 female) on total body clearance or volume of distribution, corrected for body weight. No accumulation was seen when cefepime was given at 50 mg/kg q12h (n=13), while $C_{\text{max}}$, AUC, and $t_{\frac{1}{2}}$ were increased about 15% at steady state after 50 mg/kg q8h. The exposure to cefepime following a 50 mg/kg IV dose in a pediatric patient is comparable to that in an adult treated with a 2 g IV dose.

Geriatric patients: Cefepime pharmacokinetics have been investigated in elderly (65 years of age and older) men (n=12) and women (n=12) whose mean (SD) creatinine clearance was 74 (±15) mL/min. There appeared to be a decrease in cefepime total body clearance as a function of creatinine clearance. Therefore, dosage administration of cefepime in the elderly should be adjusted as appropriate if the patient’s creatinine clearance is 60 mL/min or less. (See DOSAGE AND ADMINISTRATION).

Renal insufficiency: Cefepime pharmacokinetics have been investigated in patients with various degrees of renal insufficiency (n=30). The average half-life in patients requiring hemodialysis was 13.5 (±2.7) hours and in patients requiring continuous peritoneal dialysis was 19 (±2) hours. Cefepime total body clearance decreased proportionally with creatinine clearance in patients with abnormal renal function, which serves as the basis for dosage adjustment recommendations in this group of patients. (See DOSAGE AND ADMINISTRATION.)

Hepatic insufficiency: The pharmacokinetics of cefepime were unaltered in patients with impaired hepatic function who received a single 1 g dose (n=11).
Microbiology

Cefepime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Cefepime has a broad spectrum of in vitro activity that encompasses a wide range of gram-positive and gram-negative bacteria. Cefepime has a low affinity for chromosomally-encoded beta-lactamases. Cefepime is highly resistant to hydrolysis by most beta-lactamases and exhibits rapid penetration into gram-negative bacterial cells. Within bacterial cells, the molecular targets of cefepime are the penicillin binding proteins (PBP).

Cefepime has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections as described in the INDICATIONS AND USAGE section.

Aerobic Gram-Negative Microorganisms:

Enterobacter
Escherichia coli
Klebsiella pneumoniae
Proteus mirabilis
Pseudomonas aeruginosa

Aerobic Gram-Positive Microorganisms:

Staphylococcus aureus (methicillin-susceptible strains only)
Streptococcus pneumoniae
Streptococcus pyogenes (Lancefield’s Group A streptococci)
Viridans group streptococci

The following in vitro data are available, but their clinical significance is unknown. Cefepime has been shown to have in vitro activity against most strains of the following microorganisms; however, the safety and effectiveness of cefepime in treating clinical
infections due to the microorganisms have not been established in adequate and well-controlled trials.

Aerobic Gram-Positive Microorganisms:

- *Staphylococcus epidermidis* (methicillin-susceptible strains only)
- *Staphylococcus saprophyticus*
- *Streptococcus agalactiae* (Lancefield’s Group B streptococci)

NOTE: Most strains of enterococci, e.g., *Enterococcus faecalis*, and methicillin-resistant staphylococci are resistant to cefepime.

Aerobic Gram-Negative Microorganisms:

- *Acinetobacter calcoaceticus* subsp. *Iwofi*
- *Citrobacter diversus*
- *Citrobacter freundii*
- *Enterobacter agglomerans*
- *Haemophilus influenzae* (including beta-lactamase producing strains)
- *Hafnia alvei*
- *Klebsiella oxytoca*
- *Moraxella catarrhalis* (including beta-lactamase producing strains)
- *Morganella morganii*
- *Proteus vulgaris*
- *Providencia rettgeri*
- *Providencia stuartii*
- *Serratia marcescens*

NOTE: Cefepime is inactive against many strains of *Stenotrophomonas* (formerly *Xanthomonas maltophilia* and *Pseudomonas maltophilia*).

Anaerobic Microorganisms:

NOTE: Cefepime is inactive against most strains of *Clostridium difficile*. 
Susceptibility Tests

Dilution Techniques

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure. Standardized procedures are based on a dilution method\(^1\) (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of cefepime powder. The MIC values should be interpreted according to the following criteria:

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>MIC (mcg/mL)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Susceptible (S)</td>
<td>Intermediate (I)</td>
</tr>
<tr>
<td>Microorganisms other than Haemophilus spp.* and S. pneumoniae*</td>
<td>≤8</td>
<td>16</td>
</tr>
<tr>
<td>Haemophilus spp.*</td>
<td>≤2</td>
<td><em>-</em></td>
</tr>
<tr>
<td>Streptococcus pneumoniae*</td>
<td>≤0.5</td>
<td>1</td>
</tr>
</tbody>
</table>

*NOTE: Isolates from these species should be tested for susceptibility using specialized dilution testing methods.\(^1\) Also, strains of Haemophilus spp. with MICs greater than 2 mcg/mL should be considered equivocal and should be further evaluated.

A report of “Susceptible” indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of “Intermediate” indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A
report of “Resistant” indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Standardized susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures. Laboratory control microorganisms are specific strains of microbiological assay organisms with intrinsic biological properties relating to resistance mechanisms and their genetic expression within bacteria; the specific strains are not clinically significant in their current microbiological status. Standard cefepime powder should provide the following MIC values (Table 4) when tested against the designated quality control strains:

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>ATCC</th>
<th>MIC (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>25922</td>
<td>0.016-0.12</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>29213</td>
<td>1-4</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>27853</td>
<td>1-4</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>49247</td>
<td>0.5-2</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>49619</td>
<td>0.06-0.25</td>
</tr>
</tbody>
</table>

**Diffusion Techniques**

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 30 mcg of cefepime to test the susceptibility of microorganisms of cefepime. Interpretation is identical to that stated above for results using dilution techniques.

Reports from the laboratory providing results of the standard single-disk susceptibility test with a 30-mcg cefepime disk should be interpreted according to the following criteria:
Table 5

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Susceptible (S)</th>
<th>Intermediate (I)</th>
<th>Resistant (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microorganisms other than <em>Haemophilus</em> spp.* and <em>S. pneumoniae</em></td>
<td>&gt;18</td>
<td>15-17</td>
<td>≤14</td>
</tr>
<tr>
<td><em>Haemophilus</em> spp.*</td>
<td>≥26</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

* NOTE: Isolates from these species should be tested for susceptibility using specialized diffusion testing methods. Isolates of *Haemophilus* spp. with zones smaller than 26 mm should be considered equivocal and should be further evaluated. Isolates of *S. pneumoniae* should be tested against a 1 mcg oxacillin disk; isolates with oxacillin zone sizes larger than or equal to 20 mm may be considered susceptible to cefepime.

As with standardized dilution techniques, diffusion methods require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures. Laboratory control microorganisms are specific strains of microbiological assay organisms with intrinsic biological properties relating to resistance mechanisms and their genetic expression within bacteria; the specific strains are not clinically significant in their current microbiological status. For the diffusion technique, the 30 mcg cefepime disk should provide the following zone diameters in these laboratory test quality control strains (Table 6):

Table 6

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>ATCC</th>
<th>Zone Size Range (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>25922</td>
<td>29-35</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>25923</td>
<td>23-29</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>27853</td>
<td>24-30</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>49247</td>
<td>25-31</td>
</tr>
</tbody>
</table>
INDICATIONS AND USAGE

Cefepime for Injection is indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms (see also PRECAUTIONS: Pediatric Use and DOSAGE AND ADMINISTRATION):

**Pneumonia** (moderate to severe) caused by *Streptococcus pneumoniae*, including cases associated with concurrent bacteremia. *Pseudomonas aeruginosa, Klebsiella pneumoniae,* or *Enterobacter* species.

**Empiric Therapy for Febrile Neutropenic Patients.** Cefepime as monotherapy is indicated for empiric treatment of febrile neutropenic patients. In patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, with hypotension at presentation, with an underlying hematologic malignancy, or with severe or prolonged neutropenia), antimicrobial monotherapy may not be appropriate. Insufficient data exist to support the efficacy of cefepime monotherapy in such patients. (See CLINICAL STUDIES.)

**Uncomplicated and Complicated Urinary Tract Infections (including pyelonephritis)** caused by *Escherichia coli* or *Klebsiella pneumoniae*, when the infection is severe, or caused by *Escherichia coli, Klebsiella pneumoniae,* or *Proteus mirabilis,* when the infection is mild to moderate, including cases associated with concurrent bacteremia with these microorganisms.

**Uncomplicated Skin and Skin Structure Infections** caused by *Staphylococcus aureus* (methicillin-susceptible strains only) or *Streptococcus pyogenes*.

**Complicated Intra-abdominal Infections** (used in combination with metronidazole) caused by *Escherichia coli,* viridans group streptococci, *Pseudomonas aeruginosa, Klebsiella pneumoniae,* *Enterobacter* species, or *Bacteroides fragilis.* (See CLINICAL STUDIES.)
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cefepime for Injection and other antibacterial drugs, Cefepime for Injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

**CLINICAL STUDIES**

**Febrile Neutropenic Patients**

The safety and efficacy of empiric cefepime monotherapy of febrile neutropenic patients have been assessed in two multicenter, randomized trials, comparing cefepime monotherapy (at a dose of 2 g IV q8h) to ceftazidime monotherapy (at a dose of 2 g IV q8h). These studies comprised 317 evaluable patients. Table 7 describes the characteristics of the evaluable patient population.

<table>
<thead>
<tr>
<th>Table 7: Demographics of Evaluable Patients (First Episodes Only)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Median age (yr)</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Leukemia</td>
</tr>
<tr>
<td>Other hematologic malignancies</td>
</tr>
<tr>
<td>Solid tumor</td>
</tr>
<tr>
<td>Median ANC nadir (cells/mcL)</td>
</tr>
<tr>
<td>Median duration of neutropenia (days)</td>
</tr>
<tr>
<td>Indwelling venous catheter</td>
</tr>
<tr>
<td>Prophylactic antibiotics</td>
</tr>
<tr>
<td>Bone marrow graft</td>
</tr>
<tr>
<td>SBP &lt;90 mm Hg at entry</td>
</tr>
</tbody>
</table>

ANC = absolute neutrophil count; SBP = systolic blood pressure
Table 8 describes the clinical response rates observed. For all outcome measures, cefepime was therapeutically equivalent to ceftazidime.

**Table 8: Pooled Response Rates for Empiric Therapy of Febrile Neutropenic Patients**

<table>
<thead>
<tr>
<th>Outcome Measures</th>
<th>Cefepime (n=164)</th>
<th>Ceftazidime (n = 153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary episode resolved with no treatment modification, no new febrile episodes or infection, and oral antibiotics allowed for completion of treatment</td>
<td>51</td>
<td>55</td>
</tr>
<tr>
<td>Primary episode resolved with no treatment modification, no new febrile episodes or infection and no post-treatment oral antibiotics</td>
<td>34</td>
<td>39</td>
</tr>
<tr>
<td>Survival, any treatment modification allowed</td>
<td>93</td>
<td>97</td>
</tr>
<tr>
<td>Primary episode resolved with no treatment modification and oral antibiotics allowed for completion of treatment</td>
<td>62</td>
<td>67</td>
</tr>
<tr>
<td>Primary episode resolved with no treatment modification and no post-treatment oral antibiotics</td>
<td>46</td>
<td>51</td>
</tr>
</tbody>
</table>

Insufficient data exist to support the efficacy of cefepime monotherapy in patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, with hypotension at presentation, with an underlying hematologic malignancy, or with severe or prolonged neutropenia). No data are available in patients with septic shock.

**Complicated Intra-abdominal Infections**

Patients hospitalized with complicated intra-abdominal infections participated in a randomized, double-blind, multicenter trial comparing the combination of cefepime (2 g q12h) plus intravenous metronidazole (500 mg q6h) versus imipenem/cilastatin (500 mg q6h) for a maximum duration of 14 days of therapy. The study was designed to
demonstrate equivalence of the two therapies. The primary analyses were conducted on the protocol-valid population, which consisted of those with a surgically confirmed complicated infection, at least one pathogen isolated pretreatment, at least 5 days of treatment, and a 4-6 week follow-up assessment for cured patients. Subjects in the imipenem/cilastatin arm had higher APACHE II scores at baseline. The treatment groups were otherwise generally comparable with regard to their pretreatment characteristics. The overall clinical cure rate among the protocol-valid patients was 81% (51 cured/63 evaluable patients) in the cefepime plus metronidazole group and 66% (62/94) in the imipenem/cilastatin group. The observed differences in efficacy may have been due to a greater proportion of patients with high APACHE II scores in the imipenem/cilastatin group.

CONTRAINDICATIONS

Cefepime for Injection is contraindicated in patients who have shown immediate hypersensitivity reactions to cefepime or the cephalosporin class of antibiotics, penicillins or other beta-lactam antibiotics.

Solutions containing dextrose may be contraindicated in patients with hypersensitivity to corn products.

WARNINGS

BEFORE THERAPY WITH CEFEPIME FOR INJECTION IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS IMMEDIATE HYPERSENSITIVITY REACTIONS TO CEFEPIME, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF THIS PRODUCT IS TO BE GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS-HYPERSENSITIVITY AMONG BETA-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION TO CEFEPIME FOR INJECTION OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER EMERGENCY MEASURES INCLUDING
In patients with impaired renal function (creatinine clearance <60 mL/min), the dose of Cefepime for Injection should be adjusted to compensate for the slower rate of renal elimination. Because high and prolonged serum antibiotic concentrations can occur from usual dosages in patients with renal insufficiency or other conditions that may compromise renal function, the maintenance dosage should be reduced when cefepime is administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms. (See specific recommendations for dosing adjustment in DOSAGE AND ADMINISTRATION.) During post marketing surveillance, serious adverse events have been reported including life-threatening or fatal occurrences of the following: encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, and seizures (see ADVERSE REACTIONS: Postmarketing Experience). Most cases occurred in patients with renal impairment who received doses of cefepime that exceeded the recommended dosage schedules. However, some cases of encephalopathy occurred in patients receiving a dosage adjustment for their renal function. In the majority of cases, symptoms of neurotoxicity were reversible and resolved after discontinuation of cefepime and/or after hemodialysis.

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

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

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

**PRECAUTIONS**

**General**

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

As with other antimicrobials, prolonged use of Cefepime for Injection may result in overgrowth of nonsusceptible microorganisms. Repeated evaluation of the patient’s condition is essential. Should superinfection occur during therapy, appropriate measures should be taken.

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

Positive direct Coombs’ tests have been reported during treatment with cefepime. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs’ testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs’ test may be due to the drug.

Cefepime for Injection should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
Arginine has been shown to alter glucose metabolism and elevate serum potassium transiently when administered at 33 times the amount provided by the maximum recommended human dose of cefepime. The effect of lower doses is not presently known.

As with other dextrose-containing solutions, Cefepime for Injection should be prescribed with caution in patients with overt or known subclinical diabetes mellitus or carbohydrate intolerance for any reason.

If administration is controlled by a pumping device, care must be taken to discontinue pumping action before the container runs dry or air embolism may result.

Use only if solution is clear and container and seals are intact.

**Information for Patients**

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

**Drug Interactions**

Renal function should be monitored carefully if high doses of aminoglycosides are to be administered with Cefepime for Injection because of the increased potential of nephrotoxicity and ototoxicity of aminoglycoside antibiotics. Nephrotoxicity has been reported following concomitant administration of other cephalosporins with potent diuretics such as furosemide.
Drug/Laboratory Test Interactions

The administration of cefepime may result in a false-positive reaction for glucose in the urine when using Clinitest® tablets. It is recommended that glucose tests based on enzymatic glucose oxidase reactions (such as Clinistix®) be used.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

No long-term animal carcinogenicity studies have been conducted with cefepime. A battery of *in vivo* and *in vitro* genetic toxicity tests, including the Ames Salmonella reverse mutation assay, CHO/HGPRT mammalian cell forward gene mutation assay, chromosomal aberration and sister chromatid exchange assays in human lymphocytes, CHO fibroblast clastogenesis assay, and cytogenetic and micronucleus assays in mice were conducted. The overall conclusion of these tests indicated no definitive evidence of genotoxic potential. No untoward effects on fertility or reproduction have been observed in rats, mice, and rabbits when cefepime is administered subcutaneously at 1 to 4 times the recommended maximum human dose calculated on a mg/m² basis.

Usage in Pregnancy – Teratogenic effects – Pregnancy Category B

Cefepime was not teratogenic or embryocidal when administered during the period of organogenesis to rats at doses up to 1000 mg/kg/day (4 times the recommended maximum human dose calculated on a mg/m² basis) or to mice at doses up to 1200 mg/kg (2 times the recommended maximum human dose calculated on a mg/m² basis) or to rabbits at a dose level of 100 mg/kg (approximately equal to the recommended maximum human dose calculated on a mg/m² basis).

There are, however, no adequate and well-controlled studies of cefepime use in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.
Nursing Mothers

Cefepime is excreted in human breast milk in very low concentrations (0.5 mcg/mL). Caution should be exercised when cefepime is administered to a nursing woman.

Labor and Delivery

Cefepime has not been studied for use during labor and delivery. Treatment should only be given if clearly indicated.

Pediatric Use

The safety and effectiveness of cefepime in the treatment of uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, pneumonia, and as empiric therapy for febrile neutropenic patients have been established in the age groups 2 months up to 16 years. Use of Cefepime for Injection in these age groups is supported by evidence from adequate and well-controlled studies of cefepime in adults with additional pharmacokinetic and safety data from pediatric trials (see CLINICAL PHARMACOLOGY).

Safety and effectiveness in pediatric patients below the age of 2 months have not been established. There are insufficient clinical data to support the use of cefepime in pediatric patients under 2 months of age or for the treatment of serious infections in the pediatric population where the suspected or proven pathogen is Haemophilus influenzae type b.

IN THOSE PATIENTS IN WHOM MENINGEAL SEEDING FROM A DISTANT INFECTION SITE OR IN WHOM MENINGITIS IS SUSPECTED OR DOCUMENTED, AN ALTERNATE AGENT WITH DEMONSTRATED CLINICAL EFFICACY IN THIS SETTING SHOULD BE USED.
Geriatric Use

Of the more than 6400 adults treated with cefepime in clinical studies, 35% were 65 years or older while 16% were 75 years or older. When geriatric patients received the usual recommended adult dose, clinical efficacy and safety were comparable to clinical efficacy and safety in nongeriatric adult patients.

Serious adverse events have occurred in geriatric patients with renal insufficiency given unadjusted doses of cefepime, including life-threatening or fatal occurrences of the following: encephalopathy, myoclonus, and seizures. (See WARNINGS and ADVERSE REACTIONS.)

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater to patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and renal function should be monitored. (See CLINICAL PHARMACOLOGY: Special Populations, WARNINGS, and DOSAGE AND ADMINISTRATION.)

ADVERSE REACTIONS

Clinical Trials

In clinical trials using multiple doses of cefepime, 4137 patients were treated with the recommended dosages of cefepime (500 mg to 2 g IV q12h). There were no deaths or permanent disabilities thought related to drug toxicity. Sixty-four (1.5%) patients discontinued medication due to adverse events thought by the investigators to be possibly, probably, or almost certainly related to drug toxicity. Thirty-three (51%) of these 64 patients who discontinued therapy did so because of rash. The percentage of cefepime-treated patients who discontinued study drug because of drug-related adverse events was very similar at daily doses of 500 mg, 1 g, and 2 g q12h (0.8%, 1.1%, and 2%, respectively). However, the incidence of discontinuation due to rash increased with the higher recommended doses.
The following adverse events were thought to be probably related to cefepime during evaluation of the drug in clinical trials conducted in North America (n=3125 cefepime-treated patients).

Table 9: Adverse Clinical Reactions
Cefepime Multiple-Dose Dosing Regimens
Clinical Trials – North America

| INCIDENCE EQUAL TO OR GREATER THAN 1% | Local reactions (3%), including phlebitis (1.3%), pain and/or inflammation (0.6%)*; rash (1.1%) |
| INCIDENCE LESS THAN 1% BUT GREATER THAN 0.1% | Colitis (including pseudomembranous colitis), diarrhea, fever, headache, nausea, oral moniliasis, pruritus, urticaria, vaginitis, vomiting |

* Local reactions, irrespective of relationship to cefepime in those patients who received intravenous infusion (n=3048).

At the higher dose of 2 g q8h, the incidence of probably-related adverse events was higher among the 795 patients who received this dose of cefepime. They consisted of rash (4%), diarrhea (3%), nausea (2%), vomiting (1%), pruritus (1%), fever (1%), and headache (1%).

The following adverse laboratory changes, irrespective of relationship to therapy with cefepime, were seen during clinical trials conducted in North America.
### Table 10: Adverse Laboratory Changes
Cefepime Multiple-Dose Dosing Regimens
Clinical Trials – North America

<table>
<thead>
<tr>
<th>Category</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INCIDENCE EQUAL TO OR GREATER THAN 1%</strong></td>
<td>Positive Coombs’ test (without hemolysis) (16.2%); decreased phosphorus (2.8%); increased ALT/SGPT (2.8%), AST/SGOT (2.4%), eosinophils (1.7%); abnormal PTT (1.6%), PT (1.4%)</td>
</tr>
<tr>
<td><strong>INCIDENCE LESS THAN 1% BUT GREATER THAN 0.1%</strong></td>
<td>Increased alkaline phosphatase, BUN, calcium, creatinine, phosphorus, potassium, total bilirubin; decreased calcium*, hematocrit, neutrophils, platelets, WBC</td>
</tr>
</tbody>
</table>

* Hypocalcemia was more common among elderly patients. Clinical consequences from changes in either calcium or phosphorus were not reported.

A similar safety profile was seen in clinical trials of pediatric patients (see **PRECAUTIONS: Pediatric Use**).

**Postmarketing Experience**

In addition to the events reported during North American clinical trials with cefepime, the following adverse experiences have been reported during worldwide postmarketing experience.

As with some other drugs in this class, encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, and seizures have been reported. Although most cases occurred in patients with renal impairment who received doses of cefepime that exceeded the recommended dosage schedules, some cases of encephalopathy occurred in patients receiving a dosage adjustment for their renal function. (See also **WARNINGS**.) If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated. Precautions should be taken to adjust daily dosage in patients with renal insufficiency or other conditions that may compromise renal function to reduce
antibiotic concentrations that can lead or contribute to these and other serious adverse events, including renal failure.

As with other cephalosporins, anaphylaxis including anaphylactic shock, transient leukopenia, neutropenia, agranulocytosis and thrombocytopenia have been reported.

**Cephalosporin-class Adverse Reactions**

In addition to the adverse reactions listed above that have been observed in patients treated with cefepime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Stevens-Johnson syndrome, erythematic multiforme, toxic epidermal necrolysis, renal dysfunction, toxic nephropathy, aplastic anemia, hemolytic anemia, hemorrhage, hepatic dysfunction including cholestasis, and pancytopenia.

**OVERDOSAGE**

Patients who receive an overdose should be carefully observed and given supportive treatment. In the presence of renal insufficiency, hemodialysis, not peritoneal dialysis, is recommended to aid in the removal of cefepime from the body. Accidental overdosing has occurred when large doses were given to patients with impaired renal function. Symptoms of overdose include encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, seizures, and neuromuscular excitability. (See **WARNINGS, ADVERSE REACTIONS**, and **DOSAGE AND ADMINISTRATION**.)

**DOSAGE AND ADMINISTRATION**

The recommended adult and pediatric dosages and routes of administration are outlined in the following table. Cefepime for Injection should be administered intravenously over approximately 30 minutes.
Table 11: Recommended Dosage Schedule for Cefepime for Injection in Patients with CrCL >60 mL/min

<table>
<thead>
<tr>
<th>Site and Type of Infection</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderate to Severe</strong></td>
<td>Pneumonia due to <em>S. pneumoniae</em>, <em>P. aeruginosa</em>, <em>K. pneumoniae</em>, or <em>Enterobacter</em> species</td>
<td>1-2 g IV q12h</td>
<td>10</td>
</tr>
<tr>
<td><strong>Empiric therapy for febrile neutropenic patients</strong> (See INDICATIONS AND USAGE and CLINICAL STUDIES.)</td>
<td>2 g IV q8h</td>
<td>7**</td>
<td></td>
</tr>
<tr>
<td><strong>Mild to Moderate</strong> Uncomplicated or Complicated Urinary Tract Infections, including pyelonephritis, due to <em>E. coli</em>, <em>K. pneumoniae</em>, or <em>P. mirabilis</em></td>
<td>0.5-1 g IV q12h</td>
<td>7-10</td>
<td></td>
</tr>
<tr>
<td><strong>Severe</strong> Uncomplicated or Complicated Urinary Tract Infections, including pyelonephritis, due to <em>E. coli</em> or <em>K. pneumoniae</em></td>
<td>2 g IV q12h</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>Moderate to Severe</strong> Uncomplicated Skin and Skin Structure Infections due to <em>S. aureus</em> or <em>S. pyogenes</em></td>
<td>2 g IV q12h</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>Complicated Intra-abdominal Infections</strong> (used in combination with metronidazole) caused by <em>E. coli</em>, viridans group streptococci, <em>P. aeruginosa</em>, <em>K. pneumoniae</em>, <em>Enterobacter</em> species, or <em>B. fragilis</em> (See CLINICAL STUDIES.)</td>
<td>2 g IV q12h</td>
<td>7-10</td>
<td></td>
</tr>
<tr>
<td>Pediatric Patients (2 months up to 16 years) The maximum dose for pediatric patients should not exceed the recommended adult dose. The usual recommended dosage in pediatric patients up to 40 kg in weight for uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, and pneumonia is 50 mg/kg/dose, administered q12h (50 mg/kg/dose, q8h for febrile neutropenic patients), for durations as given above.</td>
<td>50 mg/kg/dose, administered q12h (50 mg/kg/dose, q8h for febrile neutropenic patients)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* including cases associated with concurrent bacteremia

** or until resolution of neutropenia. In patients whose fever resolves but who remain neutropenic for more than 7 days, the need for continued antimicrobial therapy should be re-evaluated frequently.

Impaired Hepatic Function

No adjustment is necessary for patients with impaired hepatic function.
Impaired Renal Function

In patients with impaired renal function (creatinine clearance \(<60\) mL/min), the dose of Cefepime for Injection should be adjusted to compensate for the slower rate of renal elimination. The recommended initial dose of Cefepime for Injection should be the same as in patients with normal renal function except in patients undergoing hemodialysis. The recommended doses of Cefepime for Injection in patients with renal insufficiency are presented in Table 12.

When only serum creatinine is available, the following formula (Cockcroft and Gault equation)\(^3\) may be used to estimate creatinine clearance. The serum creatinine should represent a steady state of renal function:

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

\[
\text{Females: } 0.85 \times \text{above value}
\]

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Recommended Maintenance Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60 Normal recommended dosing schedule</td>
<td>500 mg q12h</td>
</tr>
<tr>
<td>30-60</td>
<td>500 mg q24h</td>
</tr>
<tr>
<td>11-29</td>
<td>500 mg q24h</td>
</tr>
<tr>
<td>&lt;11</td>
<td>250 mg q24h</td>
</tr>
<tr>
<td>CAPD</td>
<td>500 mg q48h</td>
</tr>
<tr>
<td>Hemodialysis*</td>
<td>1 g on day 1, then 500 mg q24h thereafter</td>
</tr>
</tbody>
</table>

* On hemodialysis days, cefepime should be administered following hemodialysis. Whenever possible, cefepime should be administered at the same time each day.
In patients undergoing continuous ambulatory peritoneal dialysis, Cefepime for Injection may be administered at normally recommended doses at a dosage interval of every 48 hours (see Table 12).

In patients undergoing hemodialysis, approximately 68% of the total amount of cefepime present in the body at the start of dialysis will be removed during a 3-hour dialysis period. The dosage of Cefepime for Injection for hemodialysis patients is 1 g on Day 1 followed by 500 mg q24h for the treatment of all infections except febrile neutropenia, which is 1 g q24h. Cefepime for Injection should be administered at the same time each day and following the completion of hemodialysis on hemodialysis days (see Table 12).

Data in pediatric patients with impaired renal function are not available; however, since cefepime pharmacokinetics are similar in adults and pediatric patients (see CLINICAL PHARMACOLOGY), changes in the dosing regimen proportional to those in adults (see Tables 11 and 12) are recommended for pediatric patients.

Administration:

This reconstituted solution is for intravenous use only.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

CAUTION: Do not use plastic containers in series connections. Such use would result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is complete.

Cefepime for Injection may be administered through the tubing system by which the patient may be receiving other intravenous solutions. However, during infusion of the solution containing Cefepime for Injection, it is advisable to temporarily discontinue administration of any other solutions at the same site.
Solutions of Cefepime for Injection, like those of most beta-lactam antibiotics, should not be added to solutions of ampicillin at concentration greater than 40 mg/mL, and should not be added to metronidazole, vancomycin, gentamicin, tobramycin, netilmicin sulfate or aminophylline because of potential interaction. However, if concurrent therapy with Cefepime for Injection is indicated, each of these antibiotics can be administered separately.

As with other cephalosporins, the color of Cefepime for Injection powder, as well as its solutions, tend to darken depending on storage conditions; however, when stored as recommended, the product potency is not adversely affected.

**Directions for Use of the DUPLEX® Drug Delivery System**

- To avoid inadvertent activation, the DUPLEX Container should remain in the folded position until activation is intended.

**Patient Labeling and Drug Powder/Diluent Inspection**

- Apply patient-specific label on foil side of container. USE CARE to avoid activation. Do not cover any portion of foil strip with patient label.
- Unlatch side tab and unfold DUPLEX Container. (See Diagram 1.)
- Visually inspect diluent chamber for particulate matter.
- Use only if container and seals are intact.
- To inspect the drug powder for foreign matter or discoloration, peel foil strip from drug chamber. (See Diagram 2.)
- Protect from light after removal of foil strip.
Note: If foil strip is removed, product must be used within 7 days, but not beyond the labeled expiration date.

- The product should be re-folded and the side tab latched until ready to activate.

Reconstitution (Activation)

- Do not use directly after storage by refrigeration, allow the product to equilibrate to room temperature before patient use.
- Unfold the DUPLEX container and point the set port in a downward direction. Starting at the hanger tab end, fold the DUPLEX Container just below the diluent meniscus trapping all air above the fold. To activate, squeeze the folded diluent chamber until the seal between the diluent and powder opens, releasing diluent into the drug powder chamber. (See Diagram 3.)
- Agitate the liquid-powder mixture until the drug powder is completely dissolved.

Note: Following reconstitution (activation), product must be used within 24 hours if stored at room temperature or within 7 days if stored under refrigeration.

Administration

- Visually inspect the reconstituted solution for particulate matter.
- Point the set port in a downwards direction. Starting at the hanger tab end, fold the DUPLEX Container just below the solution meniscus trapping all air above the fold. Squeeze the folded DUPLEX Container until the seal between reconstituted drug solution and set port opens, releasing liquid to set port. (See Diagram 4.)
• Prior to attaching the IV set, check for minute leaks by squeezing container firmly. If leaks are found, discard container and solution as sterility may be impaired.
• Using aseptic technique, remove the set port cover from the set port and attach sterile administration set.
• Refer to Directions for Use accompanying the administration set.

Precautions
• As with other cephalosporins, reconstituted Cefepime for Injection tends to darken depending on storage conditions, within the stated recommendations. However, product potency is not adversely affected.
• Use only if prepared solution is clear and free from particulate matter.
• Do not use in series connection.
• Do not introduce additives into the DUPLEX Container.
• Do not freeze.

HOW SUPPLIED

Cefepime for Injection in the DUPLEX® Drug Delivery System is a flexible dual chamber container supplied in two concentrations. After reconstitution, the concentrations are equivalent to 1 g and 2 g cefepime. The diluent chamber contains approximately 50 mL of Dextrose Injection. Dextrose Injection has been adjusted to 3.74% and 2.22% for the 1 g and 2 g doses, respectively, such that the reconstituted solution is iso-osmotic.

Cefepime for Injection is supplied sterile and nonpyrogenic in the DUPLEX Drug Delivery System Containers packaged 24 units per case.

<table>
<thead>
<tr>
<th>NDC</th>
<th>Cat. No.</th>
<th>Dose</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefepime for Injection 0264-3193-11</td>
<td>3193-11</td>
<td>1 g</td>
<td>50 mL</td>
</tr>
<tr>
<td>Cefepime for Injection 0264-3195-11</td>
<td>3195-11</td>
<td>2 g</td>
<td>50 mL</td>
</tr>
</tbody>
</table>
Storage


REFERENCES


Clinitest® and Clinistix® are registered trademarks of Bayer HealthCare LLC.
DUPLEX is a registered trademark of B. Braun Medical Inc.
Made in USA
Issued: xxxx