DESCRIPTION:
Cefotetan for Injection, as cefotetan disodium, is a sterile, semisynthetic, broad-spectrum, beta-lactamase resistant, cephalosporin (cephamycin) antibiotic for parenteral administration. It is the disodium salt of [6R-(R*,S*)]-7-[[4(2-amino-1-carboxy-2-oxoethylidene)-1,3-dithietan-2-yl]carbonyl][amino]-7-methoxy-3-[1-[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo(4.2.0)oct-2-ene-2-carboxylic acid. Structural formula:

\[
\text{C}_{17}\text{H}_{15}\text{N}_7\text{Na}_2\text{O}_8\text{S}_4 \quad \text{M.W. 619.57}
\]

Cefotetan for injection is supplied in a Pharmacy Bulk Package containing 80 mg (3.5 mEq) of sodium per gram of cefotetan activity. It is a white to pale yellow powder which is very soluble in water. Reconstituted solutions of cefotetan for injection are intended for intravenous administration. The solution varies from colorless to yellow depending on the concentration. The pH of freshly reconstituted solutions is usually between 4.5 to 6.5.

Each Pharmacy Bulk Package is supplied as a dry powder containing sterile cefotetan disodium equivalent to 10 grams cefotetan and is intended for intravenous use only. Cefotetan for injection contains 80 mg (3.5 mEq) of sodium per gram of cefotetan activity.

CLINICAL PHARMACOLOGY:
High plasma levels of cefotetan are attained after intravenous administration of single doses to normal volunteers.

PLASMA CONCENTRATIONS AFTER 1 GRAM IV or IM DOSE

<table>
<thead>
<tr>
<th>Time After Injection</th>
<th>Route</th>
<th>Mean Plasma Concentration (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 min</td>
<td>IV</td>
<td>92</td>
</tr>
<tr>
<td>30 min</td>
<td>IV</td>
<td>158</td>
</tr>
<tr>
<td>1 h</td>
<td>IV</td>
<td>103</td>
</tr>
<tr>
<td>2 h</td>
<td>IV</td>
<td>72</td>
</tr>
<tr>
<td>4 h</td>
<td>IV</td>
<td>42</td>
</tr>
<tr>
<td>8 h</td>
<td>IV</td>
<td>12</td>
</tr>
<tr>
<td>IM</td>
<td>54</td>
<td>76</td>
</tr>
<tr>
<td>67</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

30-minute infusion

PLASMA CONCENTRATIONS AFTER 2 GRAM IV or IM DOSE

<table>
<thead>
<tr>
<th>Time After Injection</th>
<th>Route</th>
<th>Mean Plasma Concentration (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 min</td>
<td>IV</td>
<td>237</td>
</tr>
<tr>
<td>10 min</td>
<td>IV</td>
<td>223</td>
</tr>
<tr>
<td>1 h</td>
<td>IV</td>
<td>135</td>
</tr>
<tr>
<td>3 h</td>
<td>IV</td>
<td>74</td>
</tr>
<tr>
<td>5 h</td>
<td>IV</td>
<td>48</td>
</tr>
<tr>
<td>9 h</td>
<td>IV</td>
<td>22</td>
</tr>
<tr>
<td>12 h</td>
<td>IV</td>
<td>12</td>
</tr>
<tr>
<td>IM</td>
<td>20</td>
<td>75</td>
</tr>
<tr>
<td>91</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

NOTE: Concentrations estimated from regression line

The plasma elimination half-life of cefotetan is 3 to 4.6 hours after intravenous administration. Repeated administration of cefotetan does not result in accumulation of the drug in normal subjects.

Cefotetan is 88% plasma protein bound. No active metabolites of cefotetan have been detected; however, small amounts (less than 7%) of cefotetan in plasma and urine may be converted to its tautomers, which has antimicrobial activity similar to the parent drug.

In normal patients, from 51% to 81% of an administered dose of cefotetan is excreted unchanged by the kidneys over a 24 hour period, which results in high and prolonged urinary concentrations. Following intravenous doses of 1 gram and 2 grams, urinary concentrations are highest during the first hour and reach concentrations of approximately 1700 and 3500 mcg/mL, respectively.

In volunteers with reduced renal function, the plasma half-life of cefotetan is prolonged. The mean terminal half-life increases with declining renal function, from approximately 4 hours in volunteers with normal renal function to about 10 hours in those with moderate renal impairment. There is a linear correlation between the systemic clearance of cefotetan and creatinine clearance. When renal function is impaired, a reduced dosing schedule based on creatinine clearance must be used (see DOSAGE AND ADMINISTRATION).

In pharmacokinetic studies of eight elderly patients (greater than 65 years) with normal renal function and seven elderly volunteers (aged 25 to 28 years), mean (± 1 sd) Total Body Clearance (1.5 (0.1) L/h vs. 1.8 (0.3) L/h) and mean Volume of Distribution (10.4 (1.2) L vs. 10.3 (1.6) L) were similar following administration of a one gram intravenous bolus dose.

Microbiology
The bactericidal action of cefotetan results from inhibition of cell wall synthesis. Cefotetan has in vitro activity against a wide range of aerobic and anaerobic gram-positive and gram-negative organisms. The methoxy group in the 7-alpha position provides cefotetan with a high degree of stability in the presence of beta-lactamases including both penicillinases and cephalosporinase of gram-negative bacteria.

Cefotetan has been shown to be active against most strains of the following organisms both in vitro and in clinical infections (see INDICATIONS AND USAGE).

Gram-Negative Aerobes
*Escherichia coli*
*Haemophilus influenzae* (including ampicillin-resistant strains)
*Klebsiella species* (including K. pneumoniae)
*Morganella morganii*
*Neisseria gonorrhoeae* (nonpenicillinase-producing strains)
*Proteus mirabilis*
*Proteus vulgaris*
*Providencia rettgeri*
*Serratia marcescens*

NOTE: Approximately one-half of the usually clinically significant strains of *Enterobacter* species (e.g., *E. aerogenes* and *E. cloacae*) are resistant to cefotetan. Most strains of *Pseudomonas aeruginosa* and *Acinetobacter* species are resistant to cefotetan.

Gram-Positive Aerobes
*Staphylococcus aureus* (including penicillinase- and nonpenicillinase-producing strains)
*Staphylococcus epidermidis*
*Streptococcus agalactiae* (group B beta-hemolytic streptococcus)
*Streptococcus pneumoniae*
*Streptococcus pyogenes*

NOTE: Most strains of *Staphylococcus* and *Streptococcus* are resistant to cefotetan. Some strains of *Streptococcus* and *Staphylococcus* are also resistant to cefotetan. Most strains of *Pseudomonas* and *Acinetobacter* species are resistant to cefotetan.

Anaerobes
*Prevotella bivia* (formerly *Bacteroides bivia*)
*Prevotella disiens* (formerly *Bacteroides disiens*)
*Bacteroides fragilis*
*Prevotella melaninigenica* (formerly *Bacteroides melaninigenicus*)
*Acidaminococcus rettgeri* (formerly *Pertinax pertinax*)
*Acinetobacter baumannii* (formerly *Pertinax pertinax*)
*Streptococcus pneumoniae*
*Streptococcus pyogenes* (formerly *S. agalactiae*)

NOTE: Most strains of *B. distasonis, B. ozaenus*, and *B. theta hominis* are resistant to cefotetan against these organisms cannot be accurately predicted on the basis of in vitro susceptibility tests alone.

The following in vitro data are available but their clinical significance is unknown. Cefotetan has been shown to be active in vitro against most strains of the following organisms:

Gram-Negative Aerobes
*Citrobacter species* (including *C. diversus* and *C. freundii*)
*Klebsiella oxytoca*
*Moraxella (Brannhamella) catarrhalis*
*Neisseria gonorrhoeae* (penicillinase-producing strains)
*Salmonella species*
*Escherichia coli*

For Intrauterine Use Only

Ceferon for injection does not contain any preservatives and should be used within 48 hours of reconstitution.
Anaerobes
Porphyromonas asaccharolytica (formerly Bacteroides asaccharolyticus)
Prevotella oralis (formerly Bacteroides oralis)
Bacteroides spiniachnichus
Clostridium tertium (see WARNINGS)
Propionibacterium species
Veillonella species

Susceptibility Tests
Dilution Techniques
Quantitative methods are used to determine antimicrobial minimal inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test procedure. Standardized procedures are based on a dilution method1 (broth or agar) or equivalent with standardized inoculum concentrations. This procedure provides a means of standardizing clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosages of drug are necessary. This category also provides a buffer zone which prevents small uncontrolled technical factors from causing major discrepancies in results. The MIC values should be interpreted according to the following criteria:

<table>
<thead>
<tr>
<th>MIC (mcg/mL)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 16</td>
<td>Susceptible (S)</td>
</tr>
<tr>
<td>32</td>
<td>Intermediate (I)</td>
</tr>
<tr>
<td>≥ 64</td>
<td>Resistant (R)</td>
</tr>
</tbody>
</table>

A report of ‘Susceptible’ indicates that the pathogen is likely to be inhibited if the antimicrobial compound reaches the concentrations usually achievable. A report of ‘Intermediate’ indicates that the results are not significant in terms of predictability of success or failure if the antimicrobial compound reaches the concentrations usually achievable. The pathogen is likely to be resistant if the results are reported as ‘Resistant’. The clinician should determine whether or not these results are susceptible to practical therapy for treatment of infections in individual patients.

MICs of Cefotetan

<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>0.06-0.25</td>
</tr>
<tr>
<td>S. aureus ATCC 29213</td>
<td>4-16</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 procedure2 requires the use of standardized dilution techniques, agar dilution methods, or disk methods. These procedures provide estimates of the susceptibility of bacteria to antimicrobial compounds. An isolated colony of the test organism is suspended in a standardized solution, and standardized dilutions of the bacterial suspension are inoculated into a nutrient medium in the presence of standardized concentrations of cefotetan powder. The MIC values obtained from agar dilution methods provide estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized dilution technique is the disk method. This category also provides a buffer zone which prevents small uncontrolled technical factors from causing major discrepancies in results. The MIC values should be interpreted according to the following criteria:

<table>
<thead>
<tr>
<th>Zone Diameter (mm)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 16</td>
<td>Susceptible (S)</td>
</tr>
<tr>
<td>13-15</td>
<td>Intermediate (I)</td>
</tr>
<tr>
<td>≤ 12</td>
<td>Resistant (R)</td>
</tr>
</tbody>
</table>

Interpretation should be as stated above for results using dilution techniques. Interpretation involves correlation of the diameter obtained in the disk test with the MIC for cefotetan.

Prophylaxis
The preoperative administration of cefotetan may reduce the incidence of certain post-operative infections in patients undergoing surgical procedures that are classified as clean contaminated or potentially contaminated (e.g., cesarean section, abdominal or vaginal hysterectomy, transurethral surgery, biliary tract surgery, and gastrointestinal surgery). If there are signs and symptoms of infection, specimens for culture should be obtained for identification of the causative organism so that appropriate therapeutic measures may be initiated.

CONTRAINdications:
Cefotetan is contraindicated in patients with a known allergy to the cephalosporin class of antibiotics and in those individuals who have experienced a cephalosporin associated hemolytic anemia.

WARNINGS:
BEFORE THERAPY WITH CEFOTETAN IS INSTI-
TUATED, THE FOLLOWING INFORMATION SHOULD BE TAKEN INTO ACCOUNT TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REA-
CtIONS TO CEFOTETAN OR TO OTHER MEMBERS OF THE CEPHALOSPORIN CLASS. THERE IS CROSS-SENSITIVITY AMONG THE MEMBERS OF THE CEPHALOSPORIN CLASS. THE HYPOTENSIVE SHOCK RESPONSE TO AN INJECTION OF AN ALKALOID, SUCH AS ATROPINE, MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION OCCURS, DISCONTINUE THE DRUG. SE-
RIous ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE THE IMMEDIATE ADMINISTRATION OF ARTIFICIAL RESPIRATION, INTRAVENOUS ANTIDOTES (HY-
DROCORTISONE, PRESSOR AMINES, AND AIR-
WAY MANAGEMENT, AS CLINICALLY INDICATED).

AN IMMUNE MEDIATED HEMOLYTIC ANEMIA HAS OCCURRED IN PATIENTS RECEIVING CEFOTETAN THERAPY DUE TO THE USE OF CEPHALOSPORIN CLASS ANTIBIOTICS. SEVERE CASES OF HEMOLYTIC ANEMIA, INCLUDING FATALITIES, HAVE BEEN REPORTED IN ASSOCIATION WITH THE ADMINISTRATION OF CEFOTETAN. SUCH REPORTS ARE UNCOMMON. THERE APPEARS TO BE AN INCREASED RISK OF DEVELOPING HEMOLYTIC ANEMIA ON CEFOTETAN RELA-
TIVE TO OTHER MEMBERS OF THE CEPHALOSPORIN CLAS-
SS. HEPATOTOXICITY HAS BEEN REPORTED IN ASSOCIATION WITH THE ADMINISTRATION OF CEFOTETAN. SUCH REPORTS ARE UNCOMMON. THERE APPEARS TO BE AN INCREASED RISK OF DEVELOPING HEMOLYTIC ANEMIA ON CEFOTETAN RELA-
TIVE TO OTHER MEMBERS OF THE CEPHALOSPORIN CLAS-
S.

C. difficile produces toxins A and B which con-
tribute to the development of CDAD. Hypertoxin produ-
cing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in any patient who develops diarrhea following antibiotic use. Careful medical history is neces-
sary since CDAD has been reported to occur over two months after the administration of antibac-
terial agents.

In CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, as well as supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clini-
cally indicated.

In common with many other broad-spectrum
antibiotics, cefotetan may be associated with a fall in prothrombin activity and, possibly, subsequent bleeding. Those at increased risk include patients with renal or hepatobiliary impairment or poor nutritional state, the elderly, and patients with cancer. Prothrombin time should be monitored and exogenous vitamin K administered as indicated.

PRECAUTIONS:
General
Prescribing cefotetan 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 broad-spectrum antibiotics, prolonged use of cefotetan may result in overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection does occur during therapy, appropriate measures should be taken.

Cefotetan should be used with caution in individuals with a history of gastrointestinal disease, particularly colitis.

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

Patients should be counseled that antibacterial drugs alone do not treat viral infections; that patients should continue to take any other medications as directed; that administration of antacids may reduce the absorption of cefotetan; that antibiotics can kill the helpful bacteria in the gut; that if a second infection occurs during treatment with cefotetan, the antibiotic may be ineffective; that patients should report any new allergies; that patients should report any new allergies; that patients should be advised to wash hands before and after use of the medication; and that 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 cefotetan or other antibacterial drugs in the future.

As with some other cephalosporins, a disulfiram-like reaction characterized by flushing, sweating, headache, and tachycardia may occur when alcohol (beer, wine, etc.) is ingested within 72 hours after cefotetan administration. Patients should be cautioned about the ingestion of alcoholic beverages following the administration of cefotetan.

Drug Interactions
Increases in serum creatinine have occurred when cefotetan was given alone. If cefotetan and an aminoglycoside are used concomitantly, a renal function should be carefully monitored, because nephrotoxicity may be potentiated.

Drug/Laboratory Test Interactions
The administration of cefotetan may result in a false positive reaction for glucose in the urine using Clinistix®; Benedict’s solution, or Fehling’s solution. It is recommended that glucose tests based on enzymatic glucose oxidase be used. As with other cephalosporins, high concentrations of cefotetan may interfere with measurement of serum and urine creatinine levels by Jaffé reaction and produce false increases in the levels of creatinine reported.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Although long-term studies in animals have not been performed to evaluate carcinogenic potential, no mutagenic potential of cefotetan was found in standard laboratory tests. Cefotetan has adverse effects on the testes of pubertal rats. Subcutaneous administration of 500 mg/kg/day (approximately 8-16 times the usual adult human dose) on days 6 to 35 of life (thought to be developmentally analogous to late childhood and puberty in humans) resulted in reduced testicular weight and seminiferous tubule degeneration in 10 of 10 animals. Affected cells included spermatagonia and spermatocytes; Sertoli and Leydig cells were unaffected. Incidence and severity of lesions were dose-dependent; at 120 mg/kg/day (approximately 2 to 4 times the usual human dose) only 1 of 10 treated animals was affected, and the degree of degeneration was mild.

Similar lesions have been observed in experiments of comparable design with other methyloxime-containing antibiotics and impaired fertility has been reported, particularly at high dose levels. No testicular effects were observed in 7-week-old rats treated with up to 1000 mg/kg/day SC for 5 weeks, or in infant dogs (3 weeks old) that received up to 300 mg/kg/day IV for 5 weeks. The relevance of these findings to humans is unknown.

Pregnancy
Teratogenic Effects. Pregnancy
Category B
Reproductive studies have been performed in rats and monkeys at doses up to 20 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to cefotetan. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers
Cefotetan is excreted in human milk in very low concentrations. Caution should be exercised when cefotetan is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
Of the 925 subjects who received cefotetan in clinical studies, 482 (53%) were 60 years and older, while 78 (8%) were 80 years and older. No overall differences in safety or effectiveness were observed between these and younger subjects, and the other reported clinical experience has not identified differences in responses between elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, since dosing may be very useful to monitor renal function (see DOSAGE AND ADMINISTRATION, Impaired Renal Function).

ADVERSE REACTIONS:
In clinical studies, the following adverse effects were considered related to cefotetan therapy. Those appearing in italics have been reported during postmarketing experience.

Gastrointestinal: symptoms occurred in 1.5% of patients, the most frequent were diarrhea (1 in 80) and nausea (1 in 700); pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment or surgical prophylaxis (see WARNINGS).

Hematologic: laboratory abnormalities occurred in 1.4% of patients and included eosinophilia (1 in 200), positive direct Coombs’ test (1 in 250), and thrombocytosis (1 in 300); agranulocytosis, hemolytic anemia, leukopenia, thrombocytopenia, and prolonged prothrombin time with or without bleeding.

Hepatic: enzyme elevations occurred in 1.2% of patients and included a rise in ALT (SGPT) (1 in 150), AST (SGOT) (1 in 300), alkaline phosphatase (1 in 700), and LDH (1 in 700).

Hypersensitivity: reactions were reported in 1.2% of patients and included rash (1 in 150) and itching (1 in 700); anaphylactic reactions and urticaria.

Local: effects were reported in less than 1% of patients and included phlebitis at the site of injection (1 in 300), and discomfort (1 in 500).

Renal: Elevations in BUN and serum creatinine have been reported.

Urogenital: Nephrotoxicity has rarely been reported.

Miscellaneous: Fever
In addition to the adverse reactions listed above which have been observed in patients treated with cefotetan, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics: puritus, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, vomiting, abdominal pain, colitis, superinfection, vaginitis, including vaginal candidiasis, renal dysfunction, toxic nephropathy, hepatic dysfunction independent of cholestasis, aplastic anemia, hemorrhage, elevated bilirubin, pancytopenia, and neutropenia.

Several cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment, when the dosage was not reduced (see DOSAGE AND ADMINISTRATION AND OVERDOSAGE). If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated.
OVERDOSE:
Information on overdose with cefotetan in humans is not available. If overdosage should occur, it should be treated symptomatically and hemodialysis considered, particularly if renal function is compromised.

DOSAGE AND ADMINISTRATION:

TREATMENT

The usual adult dosage is 1 or 2 grams of Cefotetan for Injection administered intravenously. Proper dosage and route of administration should be determined by the condition of the patient, severity of the infection, and susceptibility of the causative organism.

General Guidelines For Dosage of Cefotetan for Injection

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Daily Dose</th>
<th>Frequency and Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary Tract</td>
<td>1 to 4 grams</td>
<td>Every 12 hours IV</td>
</tr>
<tr>
<td>Skin &amp; Soft Structure</td>
<td>2 grams</td>
<td>Every 24 hours IV</td>
</tr>
<tr>
<td>Mild: Moderatea</td>
<td>2 grams</td>
<td>Every 24 hours IV</td>
</tr>
<tr>
<td>Severe</td>
<td>4 grams</td>
<td>Every 12 hours IV</td>
</tr>
<tr>
<td>Other Sites</td>
<td>2 to 4 grams</td>
<td>Every 12 hours IV</td>
</tr>
<tr>
<td>Life-Threatening</td>
<td>6 grams</td>
<td>Every 12 hours IV</td>
</tr>
</tbody>
</table>

*Dose determined by the type and severity of infection, and susceptibility of the causative organism.

Alternatively, the dosing interval may remain constant at 12 hour intervals, but the dose reduced to one-half the usual recommended dose for patients with a creatinine clearance of 10 to 30 mL/min, and one-quarter the usual recommended dose for patients with a creatinine clearance of less than 10 mL/min.

When only serum creatinine levels are available, creatinine clearance may be calculated from the following formula. The serum creatinine level

Creatinine Clearance

\[ \text{Creatinine Clearance} \text{ mL/min} = \frac{140 \times \text{Weight} (\text{kg})}{(72 \times \text{serum creatinine} \text{ mg/100 mL})} \]

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Usual Recommended Dose*</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 30</td>
<td>Every 12 hours IV</td>
<td></td>
</tr>
<tr>
<td>10 to 30</td>
<td>Every 24 hours IV</td>
<td></td>
</tr>
<tr>
<td>&lt; 10</td>
<td>Every 48 hours IV</td>
<td></td>
</tr>
</tbody>
</table>

*Dosage determined by the type and severity of infection, and susceptibility of the causative organism.

Im paired Renal Function

When renal function is impaired, a reduced dosage schedule must be employed. The following dosage guidelines may be used.

DOSAGE GUIDELINES FOR PATIENTS WITH IMPAIRED RENAL FUNCTION

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 30</td>
<td>Usual Recommended Dose*</td>
<td>Every 12 hours</td>
</tr>
<tr>
<td>10 to 30</td>
<td>Usual Recommended Dose*</td>
<td>Every 24 hours</td>
</tr>
<tr>
<td>&lt; 10</td>
<td>Usual Recommended Dose*</td>
<td>Every 48 hours</td>
</tr>
</tbody>
</table>

*Dosage determined by the type and severity of infection, and susceptibility of the causative organism.

Compatibility and Stability

Frozen samples should be thawed at room temperature before use. After the periods mentioned below, any unused solutions or frozen material should be discarded. DO NOT REFREEZE.

NOTE: Solutions of cefotetan for injection must not be admixed with solutions containing amino-glycosides. If cefotetan for injection and aminoglycosides are to be administered to the same patient, they must be administered separately and not as a mixed injection. DO NOT ADD SUPPLEMENTARY MEDICATION.

DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE

Transfer individual doses to appropriate intravenous solutions as soon as possible following reconstitution of the pharmacy bulk package. Reconstituted solution should be used within 4 hours from initial closure entry is permitted to complete fluid transfer operations. This time limit should begin with the introduction of solvent or diluents into the Pharmacy Bulk Package. Unused portions of solutions held longer than the recommended time periods should be discarded.

OVERDOSAGE:

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

HOW SUPPLIED:

Cefotetan for Injection, in the Pharmacy Bulk Package, is a dry, white to pale yellow powder supplied in a Pharmacy Bulk Package containing cefotetan disodium equivalent to 10 g of cefotetan activity for intravenous administration as follows:

<table>
<thead>
<tr>
<th>Product No.</th>
<th>NDC No.</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>309661</td>
<td>63323-396-61</td>
<td>10 grams</td>
</tr>
</tbody>
</table>

Solutions should be protected from light. Vial stoppers do not contain natural rubber latex.

REFERENCES:


<Ref. 1 Clinistest® is a registered trademark of Ames Division, Miles Laboratories, Inc.>

APP Pharmaceuticals, LLC
Schaumberg, IL 60173

451077E

Revised: January 2009