

Drug/Laboratory Test Interactions

The administration of cefotetan may result in a false positive reaction for glucose in the urine using Clinitest®‡, 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 affects on the testes of prepubertal rats. Subcutaneous administration of 500 mg/kg/day (approximately 0.8 times the maximum adult human dose on a body surface area basis) on days 6 to 35 of life (thought to be developmentally analogous to late childhood and prepuberty in humans) resulted in reduced testicular weight and seminiferous tubule degeneration in 10 of 10 animals. Affected cells included spermatogonia and spermatocytes; Sertoli and Leydig cells were unaffected. Incidence and severity of lesions were dose-dependant; at 120 mg/kg/day (0.2 times the maximum human dose on a body surface area basis) 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 methylthiotetrazole-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 (both 1.6 times the maximum recommended human dose on a body surface area basis). The relevance of these findings to humans is unknown.

Pregnancy

Teratogenic Effects.

Pregnancy Category B

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.

Reproduction studies have been performed in rats and monkeys at doses of up to 2000 and 600 mg/kg/day, or 3 and 2 times the maximum recommended human dose on a body surface area basis, and have revealed no evidence of impaired fertility or harm to the fetus due to cefotetan.

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, 492 (53%) were 60 years and older, while 76 (8%) were 80 years and older. No overall differences in safety or effectiveness were observed between these subjects 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, and it may be 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: pruritus, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, vomiting, abdominal pain, colitis, superinfection, vaginitis including vaginal candidiasis,

renal dysfunction, toxic nephropathy, hepatic dysfunction including 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.

To report **SUSPECTED ADVERSE REACTIONS**, contact Fresenius Kabi, USA LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**.

OVERDOSAGE:

Information on overdosage 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 gram (g) or 2 grams of Cefotetan for Injection, USP administered intravenously or intramuscularly. 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, USP		
Type of Infection	Daily Dose	Frequency and Route
Urinary Tract	1 g to 4 g	500 mg every 12 hours intravenous or intramuscular 1 or 2 g every 24 hours intravenous or intramuscular 1 or 2 g every 12 hours intravenous or intramuscular
Skin & Skin Structure Mild - Moderate ^a	2 g	2 g every 24 hours intravenous 1 g every 12 hours intravenous or intramuscular
Severe	4 g	2 g every 12 hours intravenous
Other Sites	2 to 4 g	1 or 2 g every 12 hours intravenous or intramuscular
Severe	4 grams	2 g every 12 hours intravenous
Life-Threatening	6 grams ^b	3 g every 12 hours intravenous
^a <i>Klebsiella pneumoniae</i> skin and skin structure infections should be treated with 1 or 2 grams every 12 hours intravenous or intramuscular.		
^b Maximum daily dosage should not exceed 6 grams.		

If *Chlamydia trachomatis* is a suspected pathogen in gynecologic infections, appropriate antichlamydia coverage should be added, since cefotetan has no activity against this organism.

Prophylaxis

To prevent postoperative infection in clean contaminated or potentially contaminated surgery in adults, the recommended dosage is 1 or 2 g of Cefotetan for Injection, USP administered once, intravenously, 30 to 60 minutes prior to surgery. In patients undergoing cesarean section, the dose should be administered as soon as the umbilical cord is clamped.

Impaired 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		
Creatinine Clearance mL/min	Dose	Frequency
Greater than 30	Usual Recommended Dosage*	Every 12 hours
10 to 30	Usual Recommended Dosage*	Every 24 hours
Less than 10	Usual Recommended Dosage*	Every 48 hours
* 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 should represent a steady state of renal function.

Males:

Weight
(
kg
)
×
(
140
−
age
)

72
×
serum
creatinine
(
mg
/
100
mL
)

Females: 0.85 x value for males

Cefotetan is dialyzable and it is recommended that for patients undergoing intermittent hemodialysis, one-quarter of the usual recommended dose be given every 24 hours on days between dialysis and one-half the usual recommended dose on the day of dialysis.

Preparation of Solution

For Intravenous Use

Reconstitute with Sterile Water for Injection. Shake to dissolve and let stand until clear.

	Amount of Diluent Added (mL)	Approximate Withdrawable Volume (mL)	Approximate Average Concentration (mg/mL)
1 gram	10	10.5	95
2 gram	10 to 20	11 to 21	182 to 95

For Intramuscular Use

Reconstitute with Sterile Water for Injection; Bacteriostatic Water for Injection; Sodium Chloride Injection 0.9%, USP; 0.5% Lidocaine HCl; or 1% Lidocaine HCl. Shake to dissolve and let stand until clear.

	Amount of Diluent Added (mL)	Approximate Withdrawable Volume (mL)	Approximate Average Concentration (mg/mL)
1 gram	2	2.5	400
2 gram	3	4	500

Intravenous Administration

The intravenous route is preferable for patients with bacteremia, bacterial septicemia, or other severe or life-threatening infections, or for patients who may be poor risks because of lowered resistance resulting from such debilitating conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or impending.

For intermittent intravenous administration, a solution containing 1 gram or 2 grams of Cefotetan for Injection, USP in Sterile Water for Injection can be injected over a period of three to five minutes. Using an infusion system, the solution may also be given over a longer period of time through the tubing system by which the patient may be receiving other intravenous solutions. Butterfly® or scalp vein-type needles are preferred for this type of infusion. However, during infusion of the solution containing Cefotetan for Injection, USP, it is advisable to discontinue temporarily the administration of other solutions at the same site.

NOTE: Solutions of cefotetan must not be admixed with solutions containing aminoglycosides. If cefotetan and aminoglycosides are to be administered to the same patient, they must be administered separately and not as a mixed injection.

Intramuscular Administration

As with all intramuscular preparations, Cefotetan for Injection, USP should be injected well within the body of a relatively large muscle such as the upper outer quadrant of the buttock (i.e., gluteus maximus); aspiration is necessary to avoid inadvertent injection into a blood vessel.

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, USP must not be admixed with solutions containing aminoglycosides. If Cefotetan for Injection, USP 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.**

Cefotetan for Injection, USP reconstituted as described above (see **DOSAGE AND ADMINISTRATION, *Preparation of Solution***) maintains satisfactory potency for 24 hours at room temperature (25°C/77°F), for 96 hours under refrigeration (5°C/41°F), and for at least 1 week in the frozen state (-20°C/-4°F). After reconstitution and subsequent storage in disposable glass or plastic syringes, Cefotetan for Injection, USP is stable for 24 hours at room temperature and 96 hours under refrigeration.

NOTE: 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, USP is a dry, white to pale yellow powder supplied in vials containing cefotetan disodium equivalent to 1 g and 2 g cefotetan activity for intravenous and intramuscular administration. The vials should be stored at 20° to 25°C (68° to 77° F) [see USP Controlled Room Temperature]. **PROTECT FROM LIGHT.**

The container closure is not made with natural rubber latex.

The following packages are available:

Product Code	Unit of Sale	Strength	Each
308510	NDC 63323-385-10 Unit of 10	1 gram per vial	NDC 63323-385-01 10 mL single dose vial
308620	NDC 63323-386-20 Unit of 10	2 grams per vial	NDC 63323-386-01 20 mL single dose vial

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Manufactured for:



Lake Zurich, IL 60047

Made in Italy

www.fresenius-kabi.com/us

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