Endocrine & metabolic: Changes in LDH, increased gamma-glutamyl transferase, nutrition disorder (vitamin B complex deficiency), vitamin K deficiency
Gastrointestinal: Diarrhea (<5%), anorexia, nausea, severe colitis, stomatitis, vomiting
Genitourinary: Hematuria, oliguria, proteinuria
Hematologic & oncologic: Eosinophilia (<5%), granulocytopenia (<5%), decreased hematocrit, decreased hemoglobin, decreased red blood cells, increased leukocyte alkaline phosphatase, pancytopenia, prolonged prothrombin time, thrombocytopenia
Hepatic: Increased serum alkaline phosphatase (<5%), increased serum ALT (<5%), increased serum AST (<5%), hepatic insufficiency, increased serum bilirubin, jaundice
Infection: Candidiasis
Renal: Increased blood urea nitrogen, increased serum creatinine
Miscellaneous: Fever

Drug Interactions

Metabolism/Transport Effects None known.

Avoid Concomitant Use

Avoid concomitant use of Cefminox with any of the following: Alcohol (Ethyl); BCG (Intravesical); Cholera Vaccine

Increased Effect/Toxicity

Cefminox may increase the levels/effects of: Alcohol (Ethyl); Aminoglycosides; Vitamin K Antagonists

The levels/effects of Cefminox may be increased by: Probenecid

Decreased Effect

Cefminox may decrease the levels/effects of: BCG (Intravesical); BCG Vaccine (Immunization); Cholera Vaccine; Lactobacillus and Estriol; Sodium Picosulfate; Typhoid Vaccine

Preparation for Administration

IV injection: Reconstitute 1 g in 20 mL of water for injection, dextrose/glucose solution, or electrolyte solution
IV infusion: Reconstitute 1 g in 100 to 500 mL of dextrose/glucose or electrolyte solution

Storage/Stability Store at room temperature; reconstituted solution stable for 12 hours at room temperature or 24 hours in refrigerator

Mechanism of Action Inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in turn inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Bacteria eventually lyse due to ongoing activity of cell wall autolytic enzymes (autolysins and murein hydrolases) while cell wall assembly is arrested.

Pharmacodynamics/Kinetics

Protein binding: 61%
Metabolism: No active metabolites have been identified
Half-life elimination: Normal renal function: ~2 hours; prolonged with renal impairment
Excretion: Normal renal function: Urine (90%)

Dosing

Adult & Geriatric Susceptible infections: IV: Usual dosage: 1 g every 12 hours; may administer up to 1.5 g every 6 hours or 2 g every 8 hours for septicemia or refractory/severe infections

Pediatric Susceptible infections: Infants, Children, and Adolescents: IV: Usual dosage: 20 mg/kg every 6 to 8 hours (maximum: 1.5 g every 6 hours or 2 g every 8 hours)

Renal Impairment There are no specific dosage adjustments provided in the manufacturer's labeling; however, dosage reduction or prolonged dosing interval are recommended in severe renal impairment.

Hepatic Impairment There are no dosage adjustments provided in the manufacturer's labeling.

Administration IV: May administer as slow injection or as continuous infusion over 1 to 2 hours

Monitoring Parameters Renal function; prothrombin time/INR in select patients (nutritionally-deficient, prolonged treatment, renal or hepatic disease, elderly). Observe for signs and symptoms of anaphylaxis.

Product Availability (US) Not available in US

Dosage Forms: International Excipient information presented when available (limited, particularly for generics); consult specific product labeling. **Note:** Availability of specific dosage forms may vary by country/region.

Solution Reconstituted, Injection, as sodium [strength expressed as base]: 1 g

◆ **Cefminox Sodium Hydrate** *see* Cefminox *on page 447*

Cefoperazone

Brand Names: International Acefa (CZ); Bicafar (MY); Bifotik (ID); Bioperazone (IT); Biorazon (ID); Cebid (TW); Cefina (IN); Cefobactam (KR); Cefobid (AE, AT, CN, CZ, EG, HK, HR, HU, ID, JO, KR, MY, OM, SG, SK, TH, UY, VN); Cefolatam (KR); Cefoperazin (JP); Cefophar (ID); Cefozon (RO); Cefozone (SG, TH); Cefpar (IN); Ceperatam (KR); Ceropid (ID); Cerozon (ID); Cezone (TW); Cizon (IN); CPZ (TW); Dardum (IT, PK); Defocef (VN); Ferzobat (ID); Glorimed (VN); Logafox (ID); Magnamycin (IN); Medocef (CN, MY, RO, TR, VN); Medocefazone (JO); Medotsef (UA); Over (IN); Perasul (KR); Peratam (KR); Shilexin (CN); Stabixin (ID); Syntocef (TR); Tsefobid (UA); Xianbi (CN); Yazon (ID)

Index Terms Cefoperazone Sodium

Pharmacologic Category Antibiotic, Cephalosporin (Third Generation)

Use Note: Not approved in the US and/or Canada

Susceptible infections: Treatment of susceptible bacterial infections including respiratory tract, peritonitis, intra-abdominal, skin and skin structure, urinary tract, gynecologic, and septicemia.

Pregnancy Considerations Adverse events were not observed in animal reproduction studies. Cefoperazone crosses the placenta.

Breastfeeding Considerations Cefoperazone is present in breast milk. The manufacturer recommends that caution be exercised when administering cefoperazone to breastfeeding women.

Contraindications Hypersensitivity to cefoperazone, other cephalosporins, or any component of the formulation

Warnings/Precautions Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have occurred in patients on beta-lactam antibacterial agents. Risk is increased in patients with a history of sensitivity to multiple allergens. Use with caution in patients with a history of penicillin, cephalosporin, or carbapenem allergy. Maintain clinical supervision if given to beta-lactam allergic patients. If a serious reaction occurs, treatment should be discontinued and supportive care measures instituted immediately. Serious hemorrhage (including fatalities) has occurred with cefoperazone use. Monitor for signs of bleeding, thrombocytopenia, and coagulopathy. Discontinue therapy with persistent unexplained bleeding. Use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; increased risk of CDAD may persist up to 3 months postantibiotic treatment (Hensgens 2012). May be associated with vitamin K deficiency, especially in patients with poor nutrition, malabsorption states, alcohol dependence, or on prolonged hyperalimentation therapy. Hypoprothrombinemia with or without bleeding may occur; monitor prothrombin time.

Use with caution in patients with a history of GI disease, especially colitis. Use with caution in patients with hepatic impairment and/or biliary obstruction, half-life may be prolonged. Monitor serum concentrations with use of higher doses. Use with caution in patients with renal impairment. Monitor serum concentrations with use of higher doses; adjust dose if accumulation occurs.

Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Flushing, sweating, headache, and palpitations may occur with cefoperazone and concomitant alcohol consumption (disulfiram-like reactions); avoid alcoholic beverages or products during therapy and for at least 72 hours after therapy completion.

Adverse Reactions

1% to 10%:
Dermatologic: Allergic skin reaction (2%)
Gastrointestinal: Diarrhea (3%), loose stools (3%)
Hematologic & oncologic: Eosinophilia (10%), decreased hematocrit (5%), decreased hemoglobin (5%), neutropenia (2%)
Hepatic: Increased liver enzymes (5% to 10%)
Immunologic: Abnormal Coombs test (2%)
Renal: Increased blood urea nitrogen (6%), increased serum creatinine (2%)
Frequency not defined: Gastrointestinal: Pseudomembranous colitis
<1%, postmarketing, and/or case reports: Anaphylaxis, drug fever, hemorrhage, hepatic insufficiency, hypoprothrombinemia, injection site phlebitis, jaundice, nausea, pain, pruritus, shock, Stevens-Johnson syndrome, thrombocytopenia, toxic epidermal necrolysis, vomiting

Drug Interactions

Metabolism/Transport Effects None known.

Avoid Concomitant Use
Avoid concomitant use of Cefoperazone with any of the following: BCG (Intravesical); Cholera Vaccine
Increased Effect/Toxicity
Cefoperazone may increase the levels/effects of: Alcohol (Ethyl); Aminoglycosides; Vitamin K Antagonists

The levels/effects of Cefoperazone may be increased by: Probenecid
Decreased Effect
Cefoperazone may decrease the levels/effects of: BCG (Intravesical); BCG Vaccine (Immunization); Cholera Vaccine; Lactobacillus and Estriol; Sodium Picosulfate; Typhoid Vaccine

Preparation for Administration
IM, IV: Reconstitute powder with an appropriate compatible diluent (including D5W, NS, SWFI, bacteriostatic water; consult local product labeling); variation may occur due to route of administration or patient population being treated (neonates). More vigorous agitation of the vial may be necessary to solubilize the product with a concentration >333 mg/mL. Allow solution to settle to allow for visual inspection. Maximum solubility of cefoperazone is 475 mg/mL. Preparations containing benzyl alcohol should not be used in neonates.
IM:
When using a diluent other that lidocaine, reconstitute 1 g vial with 2.6 to 3.8 mL of appropriate diluent (including D5W, NS, SWFI, bacteriostatic water) to achieve final concentrations ranging from 333 to 250 mg/mL, respectively.
When concentrations to be administered are >250 mg/mL, a lidocaine solution should be used. An approximate 0.5% lidocaine solution should be prepared using SWFI combined with 2% lidocaine injection in the following two-step dilution process:
1 g: Reconstitute with 2 mL SWFI first, followed by 0.6 mL 2% lidocaine; final concentration 333 mg/mL.
1 g: Reconstitute with 2.8 mL SWFI first, followed by 1 mL 2% lidocaine; final concentration 250 mg/mL.
IV:
Initial: Reconstitute with 2.8 to 5 mL (preferred) of appropriate diluent (including D5W, D10W, NS) per 1 g of product.
Further dilution: Withdraw entire contents of vial for further dilution in an appropriate compatible diluent (including D5W, D10W, LR, NS). Final concentration should be between 2 and 50 mg/mL. Continuous infusions final concentrations should be between 2 and 25 mg/mL.

Storage/Stability
Intact vial: Store <25°C (77°F); protect from light.
Stability of reconstituted solutions:
2 mg/mL: Reconstituted in LR: Stable for 24 hours at room temperature of 15°C to 25°C (59°F to 77°F) or for 5 days when refrigerated at 2°C to 8°C (36°F to 46°F)
Reconstituted in D5NS or D5 1/4NS: Stable for 3 weeks when frozen at -20°C to -10°C (-4°F to 14°F)
2 to 50 mg/mL: Reconstituted in D5W, D5LR, D5NS, D5 1/4NS, D10W, Normosol M and D5W, Normosol R: Stable for 24 hours at room temperature of 15°C to 25°C (59°F to 77°F)
Reconstituted in D5W, D5NS, D5 1/4NS, Normosol M and D5W, Normosol R: Stable for 5 days when refrigerated at 2°C to 8°C (36°F to 46°F)
2 to 300 mg/mL: Reconstituted in NS: Stable for 24 hours at room temperature of 15°C to 25°C (59°F to 77°F) or for 5 days when refrigerated at 2°C to 8°C (36°F to 46°F)
50 mg/mL: Reconstituted in D5W: Stable for 3 weeks when frozen at -20°C to -10°C (-4°F to 14°F)
300 mg/mL: Reconstituted in bacteriostatic water for injection, 0.5% lidocaine, SWFI: Stable for 24 hours at room temperature of 15°C to 25°C (59°F to 77°F) or for 5 days when refrigerated at 2°C to 8°C (36°F to 46°F)
Reconstituted in NS or SWFI: Stable for 5 weeks when frozen at -20°C to -10°C (-4°F to 14°F)

Mechanism of Action Inhibits bacterial cell wall synthesis by binding to the penicillin-binding proteins (PBPs) which in turn inhibits peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis.

Pharmacodynamics/Kinetics
Protein binding: 82% to 93% (concentration dependent)
Half-life elimination: Adults: ≈2 hours; Low birth-weight neonates: 6 to 10 hours
Excretion: Bile (primarily), urine (20% to 30%)

Dosing
Adult
Susceptible infections: IM, IV:
Usual dose: 1 to 2 g every 12 hours.
Severe infections/infections caused by less sensitive organisms: 6 to 12 g daily in 2 to 4 divided doses (1.5 to 4 g/dose)
Geriatric Refer to adult doing; use caution and initiate therapy on the low end of the dosing range.
Renal Impairment No dosage adjustment necessary with use of usual doses. If higher doses are administered, it is recommended to monitor serum concentrations periodically; decrease dose with drug accumulation. **Note:** In patients with concurrent renal and hepatic impairment, maximum dose should not exceed 1 to 2 g/day unless serum levels are being monitored.
Hemodialysis: Administer dose after dialysis.
Hepatic Impairment Maximum dose should not exceed 4 g/day. If higher doses are administered, monitor serum concentrations; decrease dose with drug accumulation. In patients with concurrent hepatic and severe renal impairment, maximum dose should not exceed 1 to 2 g/day unless serum levels are being monitored.

Administration
IV: Concentrations between 2 and 50 mg/mL are recommended. Administer intermittent infusions over 15 to 30 minutes. May be administered as a continuous infusion after dilution to a final concentration between 2 and 25 mg/mL.
IM: For concentrations ≥250 mg/mL, use a lidocaine solution.

Monitoring Parameters Monitor for coagulation abnormalities, bleeding, platelets, prothrombin time; observe for signs and symptoms of anaphylaxis

Product Availability (US) Not available in the US

Dosage Forms: International Excipient information presented when available (limited, particularly for generics); consult specific product labeling. **Note:** Availability of specific dosage forms may vary by country/region.
Solution Reconstituted, Injection: 1 g

◆ **Cefoperazone Sodium** *see* Cefoperazone *on page 448*
◆ **Cefotan** *see* CefoTEtan *on page 452*

Cefotaxime

Brand Names: US Claforan in D5W [DSC]; Claforan [DSC]
Brand Names: Canada Cefotaxime Sodium For Injection; Claforan
Index Terms Cefotaxime Sodium
Pharmacologic Category Antibiotic, Cephalosporin (Third Generation)
Use
Bacteremia/Septicemia: Treatment of bacteremia/septicemia caused by *Escherichia coli*, *Klebsiella* species, and *Serratia marcescens*, *Staphylococcus aureus* and *Streptococcus* species (including *Streptococcus pneumoniae*).
Bone or joint infections: Treatment of bone or joint infections caused by *S. aureus* (penicillinase and nonpenicillinase producing strains), *Streptococcus* species (including *Streptococcus pyogenes*), *Pseudomonas* species (including *Pseudomonas aeruginosa*), and *Proteus mirabilis*.
CNS infections: Treatment of CNS infections (eg, meningitis, ventriculitis) caused by *Neisseria meningitidis*, *Haemophilus influenzae*, *S. pneumoniae*, *Klebsiella pneumoniae*, and *E. coli*.
Genitourinary infections: Treatment of genitourinary infections, including urinary tract infections (UTIs), caused by *Enterococcus* species, *Staphylococcus epidermidis*, *S. aureus* (penicillinase and nonpenicillinase producing), *Citrobacter* species, *Enterobacter* species, *E. coli*, *Klebsiella* species, *P. mirabilis*, *Proteus vulgaris*, *Providencia stuartii*, *Morganella morganii*, *Providencia rettgeri*, *S. marcescens*, and *Pseudomonas* species (including *P. aeruginosa*). Also, uncomplicated gonorrhea (cervical/urethral and rectal) caused by *Neisseria gonorrhoeae*, including penicillinase-producing strains. **Note:** CDC STD guidelines do not recommend cefotaxime as a treatment option for uncomplicated gonorrhea; ceftriaxone is the preferred cephalosporin (CDC [Workowski 2015]).
Gynecologic infections: Treatment of gynecologic infections, including pelvic inflammatory disease, endometritis, and pelvic cellulitis, caused by *S. epidermidis*, *Streptococcus* species, *Enterococcus* species, *Enterobacter* species, *Klebsiella* species, *E. coli*, *P. mirabilis*, *Bacteroides* species (including *Bacteroides fragilis*), *Clostridium* species, and anaerobic cocci (including *Peptostreptococcus* and *Peptococcus* species) and *Fusobacterium* species (including *Fusobacterium nucleatum*).