Minimize tissue inflammation by changing infusion sites when needed. Use with caution in patients with a history of penicillin allergy, especially IgE-mediated reactions (eg, anaphylaxis, urticaria). Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis. CDAD has been observed >2 months postantibiotic treatment. Use with caution in patients with renal impairment; dosage adjustment may be required. Use with caution in patients with a history of colitis. Potentially significant drug-drug interactions may exist, requiring dose of frequency adjustment, additional monitoring, and/or selection of alternative therapy.

Adverse Reactions
Dermatologic: Pruritus, skin rash
Gastrointestinal: Colitis, diarrhea, nausea, vomiting
Hematologic & oncologic: Neutropenia
Local: Induration at injection site (IM), inflammation of tissue at injection site (IM)
Miscellaneous: Fever

Rare but important or life-threatening: Acute generalized exanthematous pustulosis, acute renal failure, agranulocytosis, anaphylaxis, bone marrow failure, brain disease, candidiasis, cardiomyopathy (after rapid IV injection via central catheter), cholestasis, Clostridium difficile associated diarrhea, erythema multiforme, granulocytopenia, hemorrhagic anemia, hemolysis, increased blood urea nitrogen, increased gamma-glutamyl transferase, increased lactate dehydrogenase, increased serum alkaline phosphatase, increased serum ALT, increased serum ldh, increased serum bilirubin, increased ST segment elevation, jaundice, leukopenia, neutropenia, pancytopenia, positive direct Coombs test, pseudomembranous colitis, Stevens-Johnson syndrome, thrombocytopenia, toxic epidermal necrolysis, vaginitis

Drug Interactions
Metabolism/Transport Effects None known.
Avoid Concomitant Use
Avoid concomitant use of Cefotaxime with any of the following: BCGR (Intravesical); Cholora Vaccine
Increased Effect/Toxicity
Cefotaxime may increase the levels/effects of: Aminoglycosides; Vitamin K Antagonists

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

Decreased Effect
Cefotaxime may decrease the levels/effects of: BCGR (Intravesical); BCG Vaccine (Immunization); Cholora Vaccine; Lactobacillus and Estriol; Sodium Picosulfate; Typhoid Vaccine

Storage/ Stability
Store intact vials below 30°C (86°F).
Protect from light. Reconstituted solution is stable for 12 to 24 hours at room temperature, 7 to 10 days when refrigerated. For IV infusion in NS or D5W, solution is stable for 24 hours at room temperature, 5 days when refrigerated, or 13 weeks when frozen. For IV infusion in NS or D5W, solution is stable for 24 hours at room temperature, 5 days when refrigerated, or 13 weeks when frozen. In Vialflex plastic containers. Thawed solutions of frozen preparation may be stable for 24 hours at room temperature or 10 days when refrigerated.

Mechanism of Action Inhibits bacterial cell wall synthesis by binding to or one 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 peptidoglycan hydrolysis when cell wall assembly is arrested. Cefotaxime has activity in the presence of some beta-lactamases, both penicillins and cephalosporins, of gram-negative and gram-positive bacteria. Enterococcus species may be intrinsically resistant to cefotaxime. Most extended-spectrum beta-lactamase (ESBL)-producing and carbapenemase-producing isolates are resistant to cefotaxime.

Pharmacodynamics/Kinetics (Adult data unless noted)
Distribution: Widely to body tissues and fluids including aqueous humor, ascitic fluid, bronchoalveolar fluid, bone, pen- etrates CSF best when meningitis are inflamed
Protein binding: 31% to 50%
Metabolism: Partial hepatic to active metabolite, desa- cetylc efotaxime
Half-life elimination:
Cefotaxime: Infants ≤1500 g: 4.6 hours; Infants >1500 g: 3.4 hours; Children: 1.5 hours; Adults: 1 to 1.5 hours; prolonged with renal and/or hepatic impairment
Desacetylcefotaxime: 1.3 to 1.9 hours; prolonged with renal impairment (Lins 1982)

Time to peak, serum: IM: Within 30 minutes

Excretion: Urine (~80% as unchanged drug and metabo- lites)

Dosing
General dosing, susceptible infection: IM, IV: Gestational age-directed dosing (Red Book [AAP 2018]):

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Postnatal Age</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;32 weeks</td>
<td>&lt;14 days</td>
<td>50 mg/kg/dose every 12 hours</td>
</tr>
<tr>
<td>14 to 28 days</td>
<td>7 to 14 days</td>
<td>50 mg/kg/dose every 12 hours</td>
</tr>
<tr>
<td>≥32 weeks</td>
<td>≥7 days</td>
<td>50 mg/kg/dose every 12 hours</td>
</tr>
</tbody>
</table>

Weight-directed dosing (Bradley 2018):

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Postnatal Age</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 kg</td>
<td>&lt;14 days</td>
<td>50 mg/kg/dose every 12 hours</td>
</tr>
<tr>
<td>10 to 2 kg</td>
<td>≤2 kg</td>
<td>100 to 150 mg/kg/day divided every 8 to 12 hours</td>
</tr>
<tr>
<td>≥2 kg</td>
<td>≥7 days</td>
<td>150 to 200 mg/kg/day divided every 8 to 12 hours</td>
</tr>
</tbody>
</table>

Gonococcal infections, disseminated (including sep- sis, arthritis, and meningitis)/scab abscesses: IM: IV: 25 mg/kg/dose every 12 hours for 7 days; therapy should be extended for ≥2 weeks if meningitis is documented (CDC [Workowski 2015])
Meningitis (IDSA [Tunkel 2004]): IV: Note: Treat for a minimum of 21 days; use smaller doses and longer interval for neonates <2 kg
PNA ≤7 days and ≥2 kg: 100 to 150 mg/kg/day divided every 8 to 12 hours
PNA >7 days and ≥2 kg: 150 to 200 mg/kg/day divided every 8 to 12 hours

Pediatric

General dosing, susceptible infection: Infants, Chil- dren, and Adolescents: IM: 150 to 180 mg/kg/day divided doses every 8 hours; maximum daily dose: 8 g/day; higher doses necessary for treatment of meningi- tis (Bradley 2018; Red Book [AAP 2018])

Acute bacterial rhinosinusitis, severe infection requiring hospitalization: Children and Adolescents: IV: 100 to 200 mg/kg/day divided every 6 hours for 10 to 14 days; maximum dose: 2,000 mg (IDSA [Chow 2012])
Endocarditis, treatment: Children and Adolescents: IV: 200 mg/kg/day in divided doses every 6 hours; maximum dose: 12,000 mg/kg/day for 4 to 6 weeks; longer durations may be necessary; may use in combination with gentamicin for some organisms (AHA [Baltimore 2015])
Enterococcal infections, empirical treatment (HIV- exposed/positive): Adolescents: IV: 1,000 mg every 8 hours (HHS [Ol adult 2018])

Gonorrhea, disseminated infections (including arthritis and arthritis-dermatitis syndrome): an alternative to ceftriaxone (CDC [Workowski 2015]): Adolescents: IV: 1,000 mg every 8 hours in combina- tion with azithromycin for a total duration of at least 7 days
Intra-abdominal infection, complicated: Infants, Chil- dren, and Adolescents: IV: 150 to 200 mg/kg/day div- ided doses every 6 to 8 hours; maximum dose: 1,500 mg/day; use in combination with metronidazole (IDSA [Solo- mkin 2010])
Lyme disease, cardiac or CNS manifestations of recur- rent arthritis: Infants, Children, and Adolescents: IV: 150 to 200 mg/kg/day in divided doses every 6 to 8 hours for 14 to 28 days; maximum daily dose: 6 g/day (AAP [HaIperin 2013])
Meningitis: Infants, Children, and Adolescents: IV: 225 to 300 mg/kg/day divided every 6 to 8 hours; maximum dose: 2,000 mg/day; use in combination with vanco- mycin for empiric coverage (IDSA [Tunkel 2004]; IDSA [Tunkel 2017]); some experts recommend 300 mg/kg/day divided every 4 to 6 hours with a maximum daily dose of 12 g/day (Red Book [AAP 2018])
Peritonitis (Peritoneal dialysis): (ISPD [Warady 2012]): Infants, Children, and Adolescents: Intraperitoneal: Intermittent: 30 mg/kg/dose every 24 hours in the long dwell
CEFOTAXIME

Continuous: Loading dose: 500 mg per liter of dialysis or maintenance dose: 250 mg per liter; Note: 125 mg/liter has also been recommended as a maintenance dose (Aronoff 2007)

Pneumonia:
Bacterial pneumonia (HV-exposed/positive): Infants, Children, and Adolescents: IV: 150 to 200 mg/kg/day divided every 6 to 8 hours; maximum dose: 2,000 mg/kg; dose (HHS [OI adult 2018]; HHS [OI pediatric 2016]) Community-acquired pneumonia (CAP): Infants >3 months, Children, and Adolescents: IV: 50 mg/kg dose every 8 hours; maximum dose: 2,000 mg; Note: May consider addition of vancomycin or clindamycin to therapy if community-acquired MRSA is suspected. In children ≥5 years, a macrolide antibiotic should be added if atypical pneumonia cannot be ruled out (IDSA 2011).
Salmonellosis (HV-exposed/positive): Adolescents: IV: 1,000 mg every 8 hours (HHS [OI adult 2018])
Skin and soft tissue infections, necrotizing:
Infants, Children, and Adolescents: IV: 50 mg/kg/dose every 6 hours in combination with metronidazole or clindamycin; maximum dose: 2,000 mg/dose. Continue until further debridement is not necessary, patient has clinically improved, and patient is afebrile for 48 to 72 hours (IDSA [Stevens 2014]).

Surgical prophylaxis: Children and Adolescents: IV: 50 mg/kg within 60 minutes prior to the procedure; may repeat in 3 hours if procedure is lengthy or if there is excessive blood loss; maximum dose: 1,000 mg; a larger maximum dose (2,000 mg) is recommended for obese patients (ASHPI/DOSA [Bratzler 2013]).
Urinary tract infection: Infants and Children 2 to 24 months: IM, IV, 150 mg/kg/day divided every 6 to 8 hours (AAP 2011).

Renal Impairment: Pediatric
Infants, Children, and Adolescents: The following adjustments have been recommended (Aronoff 2007). Note: Renally adjusted dose recommendations are based on doses of 100 to 200 mg/kg/day divided every 8 hours.
GFR 30 to 50 mL/min/1.73 m2: 35 to 70 mg/kg/dose every 8 to 12 hours
GFR 10 to 29 mL/min/1.73 m2: 35 to 70 mg/kg/dose every 12 hours
GFR < 10 mL/min/1.73 m2: 35 to 70 mg/kg/dose every 24 hours
Intermittent hemodialysis: 35 to 70 mg/kg/dose every 24 hours
Peritoneal dialysis (PD): 35 to 70 mg/kg/dose every 24 hours

Continuous renal replacement therapy (CRRT): 35 to 70 mg/kg/dose every 12 hours

Hepatic Impairment: Pediatric There are no dosage recommendations provided in the manufacturer’s labeling.

Preparation for Administration: Pediatric Parenteral: IM: Reconstitute powder for injection with SWFI to a final concentration between 230 to 330 mg/mL (see manufacturer’s labeling for specific details). Shake to dissolve. IV:
IV Push: Reconstitute vials with at least 10 mL SWFI to a concentration between 230 to 330 mg/mL (see manufacturer’s labeling for specific details). Dilute dose to a final concentration of 10 to 40 mg/mL with NS, D5W, D10W, D5½NS, D5½NS, or LR; some centers have used concentrations up to 60 mg/mL.

Administration: Pediatric Parenteral: IM: Administer directly to injection into a large muscle mass such as the upper outer quadrant of the gluteus maximus. Doses of 2,000 mg should be divided and administered at two different sites.
IV: Push: May be administered over 3 to 5 minutes; avoid rapid injection (<1 minute) due to association with arrhythmias.
Intermittent infusion: Infuse over 15 to 30 minutes.

Dietary Considerations Some products may contain sodium.

Monitoring Parameters
Observe for signs and symptoms of anaphylaxis during first dose; monitor infusion site for extravasation; with prolonged therapy, monitor renal, hepatic, and hematologic function periodically; number and type of leukocytes, platelets; use with caution with patients who have received cefotetan within 2 to 3 weeks (either as treatment or prophylaxis). Discontinue drug, if applicable, and institute supportive measures as clinically indicated. Use with caution in patients with a history of penicillin allergy. May rarely cause hemolytic anemia (including fatalities); associated with a higher risk of hemolytic anemia relative to other cephalosporins (approximately threefold); monitor carefully during use and consider cefotetan-associated immune anemia in patients who have received cefotetan within 2 to 3 weeks (either as treatment or prophylaxis). Discontinue drug, if applicable, and institute supportive measures as clinically indicated. Use with caution in patients with a history of gastrointestinal disease, particularly colitis. Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. May be associated with increased INR and subsequent bleeding, especially in nutritionally deficient patients, prolonged treatment, or patients with cancer, hepatic or renal disease. Monitor coagulation parameters and manage as clinically indicated (eg, administration of phytonadione). Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy.

Adverse Reactions
Gastrointestinal: Diarrhea
Hepatic: Increased serum transaminases
Hypersensitivity: Hypersensitivity reaction

Doseage Forms: US Exciptent information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product
Solution, Intravenous:
Clarifan in D5W: 1 g/50 mL (50 mL [DSC]); 2 g/50 mL (50 mL [DSC])

Solution Reconstituted, Injection:
Clarifan: 500 mg (1 ea [DSC]); 1 g (1 ea [DSC]); 2 g (1 g [DSC]); 10 g (10 g [DSC])
Generic: 500 mg (1 ea); 1 g (1 ea [DSC]); 2 g (1 g [DSC]); 10 g (10 g [DSC])

Solution Reconstituted, Injection [preservative free]:
Generic: 1 g (1 ea)

Solution Reconstituted, Intravenous:
Clarifan: 1 g (1 ea [DSC]); 2 g (1 g [DSC])

Dosage Forms: Canada Exciptent information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product Solution, Intravenous:

Solution Reconstituted, Injection:
Clarifan: 1 g (1 ea [DSC]); 2 g (1 g [DSC])

Generic: 500 mg (1 ea [DSC]); 1 g (1 ea); 2 g (2 g [DSC]); 10 g (10 g [DSC])

Cefotaxime Sodium see Cefotaxime on page 414
CefoTETan (SEF oh tee tan)

Medication Safety Issues
Sound-alike/look-alike issues:
CefoTETan may be confused with ceFAzolin, ceFOXitin, ceFATTidine, CefTin, ceFTRIAxone

Brand Names: US Cefotan
Therapeutic Category: Antimicrobial, Cephalosporin (Secon-ond Generation)

Generic Availability (US) Yes

Use Treatment of susceptible lower respiratory tract, skin and skin structure, bone and joint, urinal tract, gynecologic, and intra-abdominal infections (FDA approved in adults); surgical prophylaxis (FDA approved in adults); has also been used in the prophylaxis of peritonitis in patients with peritoneal catheters undergoing gastrointestinal or percutaneous procedures

Pregnancy Risk Factor B

Pregnancy Considerations Adverse events have not been observed in animal reproduction studies. Cefotetan crosses the placenta and produces therapeutic concentrations in the amniotic fluid and cord serum. Cefotetan is one of the antibiotics recommended for use with cesarean delivery.

Breastfeeding Considerations Very small amounts of cefotetan are excreted in human milk. The manufacturer recommends caution when giving cefotetan to a breastfeeding mother.

Contraindications Hypersensitivity to cefotetan, any component of the formulation, or other cephalosporins; previous cephalosporin-associated hemolytic anemia

Warnings/Precautions Hypersensitivity reactions, including anaphylaxis, may occur. If an allergic reaction occurs, discontinue treatment and institute appropriate supportive measures.

Use with caution in patients with a history of penicillin allergy. May rarely cause hemolytic anemia (including fatalities); associated with a higher risk of hemolytic anemia relative to other cephalosporins (approximately threefold); monitor carefully during use and consider cefotetan-associated immune anemia in patients who have received cefotetan within 2 to 3 weeks (either as treatment or prophylaxis). Discontinue drug, if applicable, and institute supportive measures as clinically indicated. Use with caution in patients with a history of gastrointestinal disease, particularly colitis. Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment. May be associated with increased INR and subsequent bleeding, especially in nutritionally deficient patients, prolonged treatment, or patients with cancer, hepatic or renal disease. Monitor coagulation parameters and manage as clinically indicated (eg, administration of phytonadione). Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy.