Typhoid fever (Salmonella typhi): Limited data available; efficacy results variable: Infants, Children and Adolescents: Oral: 7.5 to 10 mg/kg/dose every 12 hours for 7 to 14 days [Cao 1999; Girgis 1995; Stephens 2002]

Urinary tract infection; acute: Oral: Manufacturer’s labeling: Infants ≥6 months, Children, and Adolescents: 8 mg/kg/day in divided doses every 12 to 24 hours; maximum daily dose: 400 mg/day

Alternate dosing: Infants ≤2 months and Children ≤2 years: Initial: 8 mg/kg/day every 24 hours for 7 to 14 days (infants ≤2 months, shorter course of 5 to 7 days) have been shown to be inferior to longer durations of therapy (AAP 2011)

Renal Impairment: Pediatric
Infants ≤6 months, Children, and Adolescents: Very limited data available; some clinicians have suggested the following (Dascsher 2005; Dhib 1991): Mild to moderate impairment: No adjustment recommended
Severe impairment (eg, GFR ≤10 to 20 mL/minute/1.73 m²): Reduce dose by 50%
Acute: Reduce dose by 50%
Hemodialysis, peritoneal dialysis: Not significantly removed

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

Preparation for Administration Oral: Powder for suspension: Reconstitute powder for oral suspension with appropriate amount of water as specified on the bottle. Shake vigorously until suspended.
Administration Oral: May be administered with or without food; administer with food to decrease GI distress; chewable tablets must be crushed or chewed before swallowing.

Monitoring Parameters With prolonged therapy, monitor renal and hepatic function periodically; number and type of stools/day for diarrhea. Observe for signs and symptoms of anaphylaxis during first dose. When used as part of alternative treatment for gonococcal infection, test-of-cure 7 days after dose (CDC 2012).

Tetracyclines Positively interacts with Coombs’, false-positive urinary glucose test using cupric sulfate (Benedict’s solution, Clinitest®, Fehling’s solution), may cause false- positive urine ketones using tests with nitroprusside (but not those using nitroferricyanide).

Dosage Forms Excerpt information presented when available (limited, particularly for generics); consult specific product labeling.
Capsule, Oral: Suprax: 200 mg
Suspension Reconstituted, Oral:
Tablet Chewable, Oral:
Cefixime Trihydrate see Cefixime on page 386
Cefotan see CefotEthen on page 390

Cefotaxime (sdf oh TAKS eem)

Medication Safety Issues Sound-alike-look-alike issues: Cefotaxime may be confused with cefOXitin, cefoxuroxine

International issues: Spectrocef [Italy] may be confused with Spectracef brand name for cefotaxime [US, Great Britain, Mexico, Portugal, Spain]
Brand Names: US Claronor in DSW [DSC]; Claronor [DSC]
Brand Names: Canada Cefotaxime Sodium For Injection; Claronor
Therapeutic Category Antibiotic, Cephalosporin (Third Generation)
Generic Availability (US) May be product dependent
Use Treatment of susceptible lower respiratory tract, skin and skin structure, bone and joint, intra-abdominal, genitourinary tract, and gynecologic infections, bacteremia/sepsis, endocarditis, documented or suspected central nervous system infections (eg, meningitis, ventriculitis) (FDA approved in all ages); prevention of postoperative surgical site infection in contaminated or potentially contaminated surgical procedures [eg, gastrointestinal and genitourinary tract surgeries and hysterectomy (intra-abdominal) and caesarian section (FDA approved in all ages)]; has also been used for the treatment of peritonitis in patients with peritoneal catheters

Precautionary Factors

Pregnancy Considerations Adverse events have not been observed in animal reproduction studies. Cefotaxime crosses the human placenta and can be found in fetal tissues. Use in women in midgestation is not recommended; it was not found following first trimester exposure to cephalosporins. During pregnancy, peak cefotaxime serum concentrations are decreased and the serum half-life is shorter. Cefotaxime is excreted in breast milk. The manufacturer recommends that caution be exercised when administering cefotaxime to nursing women. Nondose-related effects could include modification of bowel flora. The pregnancy-related changes in cefotaxime pharmacokinetics continue into the early postpartum period.

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

Warnings/Precautions A potentially life-threatening anaphylaxis has been reported in patients who received a rapid (<1 minute) bolus injection via central venous catheter. Granulocytopenia and more rarely agranulocytosis may occur, particularly during prolonged treatment (>10 days). Minimize tissue inflammation by changing infusion sites when needed. Use with caution in patients with a history of peptic ulcer disease; esophageal, ileocecal 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 or frequency adjustment, additional monitoring, and/or selection of alternative therapy.

Adverse Reactions Dermatologic: Pruritus, skin rash Gastrointestinal: Colitis, diarrhea, nausea, vomiting Hematologic & oncologic: Eosinophilia Local: Infection at injection site (IM), inflammation at injection site (IV), pain at injection site (IM), tenderness at injection site (IM) Miscellaneous: Fever Rare but important or life-threatening: Acute generalized exanematous pustulosis, acute renal failure, agranulocytosis, anaphylaxis, bone marrow failure, brain disease, candidiasis, cardiac arrhythmia (after rapid IV injection via a catheter), cholestasis, Clostridium difficile-associated diarrhea, erythema multiforme, granulocytopenia, hemolytic anemia, hepatitis, increased blood urea nitrogen, increased gamma-glutamyl transferase, increased alkaline phosphatase, increased bilirubin, increased serum creatinine, increased serum lactate dehydrogenase, 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:
- BCG (Intravesical); Cholera 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: BCG (Intravesical); BCG Vaccine (Immunization); Vitamin K Antagonists

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 13 weeks when frozen. IV injection in NS or DSW, solution is stable for 24 hours at room temperature. May be refrigerated for 13 weeks. Thawed solutions of frozen premixed bags are stable for 24 hours at room temperature or 10 days when refrigerated.
Cefotaxime

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. Cefotaxime has activity in the presence of some beta-lactamases, both penicillinases and cephalosporinases, 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 strains are resistant to cefotaxime.

Pharmacodynamics/Kinetics (Adult data unless noted)
Distribution: Widely to body tissues and fluids including aqueous humor, ascitic fluid, pleural fluid, peritoneal fluid, bile, penicillin G, and murein hydrolases. Protein binding: 31% to 50%. Half-life elimination: Desacetylcefotaxime: 1.3 to 1.9 hours; prolonged with renal and/or hepatic impairment. Dose of 12/4 g/day divided every 4 to 6 hours with a maximum daily dose: 2,000 mg/day; use in combination with vancomycin for an empirical coverage (IDSA [Tunkel 2011]; IDSA [Workowski 2015]).

Dosing

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

Gestational Age Postnatal Age Dose
<3 weeks <14 days 50 mg/kg/dose every 12 hours
14 to 28 days 50 mg/kg/dose every 8 hours
≥32 weeks ≤7 days 50 mg/kg/dose every 12 hours
8 to 28 days 50 mg/kg/dose every 8 hours

Weight-directed dosing (Bradley 2018):

Body Weight Postnatal Age Dose
<1 kg ≤14 days 50 mg/kg/dose every 12 hours
15 to 28 days 50 mg/kg/dose every 8 hours
29 to 60 days 50 mg/kg/dose every 6 hours
≥7 days 50 mg/kg/dose every 12 hours
8 to 28 days 50 mg/kg/dose every 8 hours
≥2 kg ≤7 days 50 mg/kg/dose every 12 hours
8 to 28 days 50 mg/kg/dose every 6 hours
29 to 60 days 50 mg/kg/dose every 6 hours

Gonococcal infections, disseminated (including sepsis, arthritis, and meningitis); scalp abscess: IM; IV; ≥250 mg/kg/dose every 12 hours for 7 days; therapy should be extended to 10 to 14 days if meningitis is documented (CDC [Warkowksi 2015]).

Meningitis (IDSA [Tunkel 2004]): IV; Note: Treat for a minimum of 21 days, use smaller doses and longer intervals 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 6 to 8 hours

Pediatric

General dosing, susceptible infection: Infants, Children, and Adolescents: IM, IV; 150 to 180 mg/kg/day in divided doses every 6 hours; maximum daily dose: 8 g/day; higher doses necessary for treatment of meningitis (Bradley 2018; AAP 2018).

Acute bacterial rhinosinusitis, severe infection requiring hospitalization: Children and Adolescents: IV: 100 to 200 mg/kg/day divided every 6 hours to 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 daily dose: 12 g/day; beat for at least 4 to 5 weeks; longer durations may be necessary; may use in combination with gentamicin for some organisms (AHA [Baltimore 2015]).

Enteric bacterial infections, empiric treatment (HIV-exposed/positive): Infants: IV; 1,000 mg every 8 hours (HHS [OI adult 2018]).

Gonorrhea, disseminated infections (including arthritis and dermatitis-spermatic syndrome) (as an alternative to ceftriaxone) (CDC [Workowski 2015]): Adolescents: IV: 1,000 mg every 8 hours in combination with azithromycin for a total duration of at least 7 days.

Intrafamilial meningitis, complicated: Infants, Children, and Adolescents: IV: 150 to 200 mg/kg/day divided every 6 to 8 hours; maximum dose: 2,000 mg; use in combination with metronidazole (IDSA [Solo- mkin 2010]).

Lyme disease, cardiac or CNS manifestations or recurrent arthritis: Infants, Children, and Adolescents: IV: 200 mg/kg/day in divided doses every 6 to 8 hours for 14 to 28 days; maximum daily dose: 6 g/day (AAN [Halperin 2007]; IDSA [Wormser 2006]).

Meningitis: Infants, Children, and Adolescents: IV: 225 to 300 mg/kg/day divided every 6 to 8 hours; maximum dose: 2,000 mg/kg/day divided every 4 to 6 hours with a maximum daily dose of 12 g/day (Red Book [AAP 2018]).


Intermittent: 30 mg/kg/dose every 24 hours in the long dwell
Continuous: Loading dose: 500 mg per liter of dialy- sate; maintenance dose: 15 mg/kg per liter per day. Ni- lRT: 125 mg/liter has also been recommended as a main- tenance dose (Aronoff 2007).

Pneumonia:
Bacterial pneumonia (HIV-exposed/positive): Infants, Children, and Adolescents: IV: 150 to 200 mg/kg/day divided every 6 to 8 hours; maximum dose: 2,000 mg/day (HHS [OI adult 2018]); HHS [OI pediatric 2016].

Community-acquired pneumonia (CAP): Infants >3 months, Children, and Adolescents: IV: 50 mg/kg/day divided every 8 hours; maximum dose: 2,000 mg.

Note: May be added to a previous course of an oral antibiotic or considered to empirically cover an additional empirical spectrum, particularly if the acryste-negative organism is expected to empirically cover community-acquired MRSA sur- pect. In children ≥5 years, a macrolide antibiotic should be added in cases of atypical pneumonia cannot be ruled out (IDSA/PIDS [Bradley 2011]).

Salmonellosis (HIV-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/day divided every 6 hours in combination with metronidazole or clindamy- cin; maximum dose: 2,000 mg/day. Continue until further improvement is seen or直到 necessary, patient has clinically improved, and patient is afebrile for 48 to 72 hours (IDSA [Stevens 2014]).

Prophylaxis:
Children and Adolescents: IV: 50 mg/kg/day 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 (Aronoff 2007; 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).

Refrainal 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.

GRF 30 to 50 mL/min/1.73 m²: 35 to 70 mg/kg/day divided every 8 to 12 hours
GRF 10 to 29 mL/min/1.73 m²: 35 to 70 mg/kg/day divided every 12 hours
GRF <10 mL/min/1.73 m²: 35 to 70 mg/kg/day divided every 24 hours

Intermittent hemodialysis: 35 to 70 mg/kg/dose every 24 hours

Parenteral 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 adjustments provided in the manufacturer’s labeling.

Preparation for Administration Parenteral:
IM: Reconstitute powder for injection with SWFI to a final concentration between 330 to 330 mg/mL (see manu- facturer’s labeling for specific details). Shake to dissolve.
IV: Reconstitute with viable at least 10 mL SWFI to a maximum concentration of 200 mg/mL.