

**Pharmacokinetics: Additional Considerations (Adult Data Unless Noted)**

Anti-infective considerations:

Parameters associated with efficacy: Time dependent, associated with time free drug concentration (fT) > minimum inhibitory concentration (MIC).

Organism specific:

*S. aureus* (methicillin-susceptible [MSSA]): Goal: ≥24% to 55% fT > MIC (bacteriostatic) (Turnidge 1998; Zelenitsky 2018); ≥55% to 100% fT > MIC (bacteriocidal) (Vogelman 1988; Zelenitsky 2018).

*E. coli*: Goal: ≥60% fT > MIC (bacteriostatic); ≥100% fT > MIC (2-log kill) (Vogelman 1988).

Population specific:

Critically ill patients in the ICU: Minimum goal: ≥50% fT > MIC; preferred goal: ≥100% fT > MIC (Roberts 2015); some experts favor ≥100% fT ≥4 times the MIC (Guilhaumou 2019).

Expected drug concentrations in patients with normal renal function:

Infants ≥9 months of age and children ≤10 years of age:

C<sub>max</sub> (peak), single dose: Mean dose: 22.7 mg/kg ± 4 mg/kg; 137 ± 87.9 mg/L (Nahata 1991).

Adults: C<sub>max</sub> (peak), steady state: 1 g every 8 hours: 94 ± 30.33 mg/L (Bhalodi 2013).

Postantibiotic effect: Generally little to no postantibiotic effect (<1 hour) for streptococci and gram-negative bacilli; for *S. aureus*: ~4 hours (Craig 1993; Craig 1998).

**Dosing**

**Neonatal**

General dosing: Limited data available:

Weight-directed dosing (Bradley 2022, De Cock 2014): Preterm and term neonates: IM, IV:

Body Weight	Postnatal Age	Dose
≤2 kg	≤7 days	50 mg/kg/day divided every 12 hours
	8 to 28 days	75 mg/kg/day divided every 8 hours
	29 to 60 days	100 to 150 mg/kg/day divided every 6 to 8 hours
>2 kg	≤7 days	100 mg/kg/day divided every 12 hours
	8 to 28 days	150 mg/kg/day divided every 8 hours
	29 to 60 days	100 to 150 mg/kg/day divided every 6 to 8 hours

Gestational age-directed dosing (Red Book [AAP 2021]):

Preterm and term neonates: IM, IV:

Gestational Age	Postnatal Age	Dose
<32 weeks	<7 days	25 mg/kg/dose every 12 hours
	7 to 28 days	25 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

Surgical prophylaxis: Limited data available:

Perioperative: Preterm and term neonates: IV: 30 mg/kg as a single dose; administer within 30 to 60 minutes prior to surgical incision; consider redosing in 4 hours if procedure lasts >4 hours (Bianchini 2022, IDSA/ASHP [Bratzler 2013], Murray 2014, Red Book [AAP 2021]).

Postoperative, cardiac surgery: **Note:** Continue for up to 48 hours after surgery; refer to institutional protocols (Murray 2014).

Term neonates:

PNA ≤7 days: IV: 30 mg/kg/dose every 12 hours.

PNA >7 days: IV: 30 mg/kg/dose every 8 hours.

**Pediatric**

General dosing, susceptible infection (Bradley 2019, Red Book [AAP 2018]): Infants, Children, and Adolescents: IM, IV:

Mild to moderate infections: 25 to 100 mg/kg/day divided every 8 hours; maximum daily dose: 6 g/day

Severe infections (eg, bone/joint infections): 100 to 150 mg/kg/day divided every 6 to 8 hours; maximum daily dose: 12 g/day

Endocarditis, prophylaxis before invasive dental procedures (alternative agent): Limited data available:

**Note:** Alternative agent for use in patients who are unable to take oral medication and who have penicillin or ampicillin allergy (excluding those with a history of anaphylaxis, angioedema, or urticaria) (AHA [Wilson 2021]). Recommended only in patients who are at highest risk for infective endocarditis (IE) or adverse outcomes (eg, history of IE, cardiac valve repair using

prosthetic valves or material, unrepaired cyanotic congenital heart disease [CHD], left ventricular assist device or implantable heart, repaired CHD with prosthetic material or device during first 6 months after procedure, pulmonary artery valve or conduit placement [eg, Melody valve, Contegra conduit], repaired CHD with residual defects at the site or adjacent to site of prosthetic patch or device, heart transplant recipients with cardiac valvulopathy) (AHA [Baltimore 2015], AHA [Wilson 2021], AHA/ACC [Nishimura 2017]).

Infants, Children, and Adolescents: IM, IV: 50 mg/kg as a single dose administered 30 to 60 minutes prior to dental procedure; maximum dose: 1,000 mg/dose (AHA [Wilson 2021]).

Endocarditis, treatment: Children and Adolescents: IV: 100 mg/kg/day in divided doses every 8 hours; usual adult dose: 2,000 mg/dose; maximum daily dose: 12 g/day; treat for at least 4 weeks; longer durations may be necessary; may use with or without gentamicin (AHA [Baltimore 2015]).

Peritonitis (peritoneal dialysis) (ISPD [Warady 2012]): Limited data available: Infants, Children, and Adolescents:

Prophylaxis:

Touch contamination of PD line: Intraperitoneal: 125 mg per liter

Invasive dental procedures: IV: 25 mg/kg administered 30 to 60 minutes before procedure; maximum dose: 1,000 mg/dose

Gastrointestinal or genitourinary procedures: IV: 25 mg/kg administered 60 minutes before procedure; maximum dose: 2,000 mg/dose

Treatment: Intraperitoneal:

Intermittent: 20 mg/kg every 24 hours in the long dwell

Continuous: Loading dose: 500 mg per liter of dialysate; maintenance: 125 mg per liter of dialysate

Pneumonia, community-acquired pneumonia (CAP), *S. aureus*, methicillin susceptible: Infants >3 months, Children, and Adolescents: IV: 50 mg/kg/dose every 8 hours (Bradley 2011); usual maximum dose for severe infections: 12 g/day (Red Book [AAP 2018])

Skin and soft tissue infection, *S. aureus*, methicillin susceptible (mild to moderate): (IDSA [Stevens 2014]): Infants, Children, and Adolescents:

*S. aureus*, methicillin susceptible skin and soft tissue infections including pyomyositis: IV: 50 mg/kg/day divided every 8 hours; maximum dose: 1,000 mg/dose; higher doses may be required in severe cases; duration of therapy at least 5 days, but longer may be necessary in some cases, eg, febrile and neutropenic patients: 7 to 14 days; pyomyositis: 14 to 21 days

*S. aureus*, methicillin susceptible necrotizing infection of skin, fascia, or muscle: IV: 100 mg/kg/day divided every 8 hours; maximum dose: 1,000 mg/dose; continue therapy until surgical debridement no longer necessary, clinical improvement and afebrile for 48 to 72 hours

Streptococcal, nonpurulent skin infection (cellulitis): IV: 100 mg/kg/day divided every 8 hours; maximum dose: 1,000 mg/dose; duration of therapy at least 5 days, but longer may be necessary in some cases

Surgical prophylaxis: Infants, Children, and Adolescents: IV: 30 mg/kg within 60 minutes prior to procedure, may repeat in 4 hours for prolonged procedure or excessive blood loss (eg, >1,500 mL in adults); maximum dose dependent upon patient weight: Weight <120 kg: 2,000 mg/dose; weight ≥120 kg: 3,000 mg/dose (ASHP/IDSA [Bratzler 2013], Red Book [AAP 2018])

Dosage adjustment for concomitant therapy: Significant drug interactions exist, requiring dose/frequency adjustment or avoidance. Consult drug interactions database for more information.

Altered Kidney Function: **Pediatric Note:** Dosing is based on pharmacokinetic parameters, limited pediatric studies, adult studies, and expert opinion (Aronoff 2007, Bilbao-Meseguer 2018, Heintz 2009, Hiner 1980, Nahata 1991, Salvador 2021, Trotman 2005, Udy 2010, Veltri 2004).

The following dose adjustments assume a usual recommended dose of 25 to 50 mg/kg/dose every 8 hours.

Altered kidney function:

Infants, Children, and Adolescents: IV, IM:

GFR ≥50 mL/minute/1.73 m<sup>2</sup>: No dosage adjustment necessary.

GFR 30 to <50 mL/minute/1.73 m<sup>2</sup>: 25 to 30 mg/kg/dose every 12 hours; doses up to 50 mg/kg/dose may be needed for severe infections; maximum dose: 2,000 mg/dose.