

Imipenem–Cilastatin Sodium

Brand names	Primaxin IM, Primaxin IV
Medication error potential	None reported
Contraindications and warnings	<p>Contraindications: Patients with a known hypersensitivity to any component of this product.⁽²⁾</p> <p>Warnings</p> <p>Allergic reactions: Serious hypersensitivity and occasionally fatal anaphylactic reactions have been reported.⁽²⁾ These are more likely in patients with a history of penicillin, cephalosporin, or other beta-lactam hypersensitivity.^(2,3)</p> <p>Seizures: Neurotoxicity of the carbapenem antibiotics has been reported.⁽²⁾ Seizures occur most commonly in patients with renal impairment and/or underlying neurologic disorders. Not recommended in pediatric patients with CNS infections because of the risk of seizures.⁽²⁾ (See Rare Adverse Effects in the Comments section.)</p> <p>Superinfection: Imipenem use may cause superinfection and/or <i>Clostridium difficile</i>-associated diarrhea (CDAD), which has been reported and may range in severity from mild diarrhea to fatal colitis.⁽²⁾ If CDAD is suspected or confirmed, appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of <i>C. difficile</i>, and surgical evaluation should be instituted as clinically indicated.⁽²⁾ Antibiotic use that is not directed against <i>C. difficile</i> may need to be discontinued.⁽²⁾</p>
Infusion-related cautions	<p>IM suspensions should <i>not</i> be given intravenously.⁽²⁾</p> <p>Decrease administration rate in those who develop nausea during infusion.⁽²⁾</p> <p>May cause pain at the injection site, phlebitis/thrombophlebitis, and erythema.⁽²⁾</p>
Dosage	<p>Neonates (limited data are available)</p> <p>Postnatal age (PNA) <7 days: 40–50 mg/kg/day divided q 12 hr^(2,5,25)</p> <p>PNA ≥7 days: 50–90 mg/kg/day divided q 8 hr^(2,5,25)</p> <p>Infants and children</p> <p>4 weeks to 3 months: 100 mg/kg/day divided q 6 hr^(2,25)</p> <p>>3 months: 60–100 mg/kg/day divided q 6 hr^(2,5,7-10,25)</p> <p>Up to 2 g/day for fully susceptible organisms^(2,11) and 4 g/day^(2,25) for moderately-susceptible organisms</p>
Dosage adjustment in organ dysfunction	If CrCl is 30–50 mL/min, give 21–39 mg/kg/day divided q 8 hr ⁽¹⁴⁾ ; if CrCl is 10–29 mL/min, give 15–25 mg/kg/day divided q 12 hr. ⁽¹⁴⁾ One reference suggests if the CrCl is <10 mL/min, give 7.5–12.5 mg/kg q 24 hr ⁽¹⁴⁾ ; however, the manufacturer recommends the drug be withheld if CrCl is ≤5 mL/min unless the patient is undergoing daily hemodialysis. ⁽²⁾
Maximum dosage	Up to 100 mg/kg/day or 4 g/day is recommended. ⁽²⁾
Additives	The 250- and 500-mg IV vials contain 0.8 mEq (18.8 mg) and 1.6 mEq (37.5 mg) of sodium, respectively. ⁽¹⁶⁾ The 500- and 750-mg IM vials contain 1.4 mEq (32 mg) and 2.1 mEq (48 mg) of sodium, respectively. ⁽¹⁶⁾
Suitable diluents	D5W, D10W, NS, D5¼NS, D5½NS, D5NS ⁽²⁾



Imipenem–Cilastatin Sodium

Maximum concentration 5 mg/mL^(2,16)

Preparation and delivery **Compatibility:** See Appendix D for PN compatibility information.⁽¹⁷⁾

IV push Not recommended⁽²⁾

Intermittent infusion 2.5–5 mg/mL over 20–60 minutes^(2,16) The manufacturer recommends that smaller doses be infused over 15–30 minutes and that doses >500 mg be infused over 40–60 minutes.⁽²⁾ Doses ≤500 mg have been infused over 15 minutes in children.⁽¹⁸⁾

Infusion over at least 3 hours may be necessary to produce desirable concentrations for moderately susceptible infections in children.⁽¹⁹⁾

Continuous infusion No information

Other routes of administration Suspension for IM administration should be reconstituted with 1% lidocaine HCl without epinephrine.⁽¹⁶⁾ IM formulation should not be given IV. Dosing for pediatric patients by this route has not been established.

Comments **Rare adverse effects:** Neurotoxicity of the carbapenem antibiotics has been reported.^(20,21) Seizures as early as the first day of therapy have been reported in children with meningitis.⁽²²⁾ Seizures appear to be related to an underlying CNS disorder, impaired renal function, and/or large doses.⁽²¹⁾ Because of the risk of seizures, the drug should not be used in patients with CNS infections.⁽²⁾ Use cautiously in combination with drugs that lower the seizure threshold and in patients with renal dysfunction.⁽²³⁾

Drug interactions: Carbapenems may reduce serum valproic acid concentrations to subtherapeutic levels, resulting in loss of seizure control.^(2,24) Serum valproic acid concentrations should be monitored frequently after beginning or increasing the dose of a carbapenem. Alternative antibiotics should be considered in patients with seizures well controlled with valproic acid.⁽²⁾ Because imipenem is associated with numerous drug interactions, consult appropriate resources for dosing recommendations before combining any drug with imipenem.

Other: Although there is a theoretical allergic cross-reactivity of carbapenems with penicillins and cephalosporins, studies have found this to be very rare.^(26,27)

REFERENCES

2. Primaxin [prescribing information]. Whitehouse Station, NJ: Merck & Co Inc; December 2014.
3. Romano A, Gaeta F, Valluzzi RL, et al. IgE-mediated hypersensitivity to cephalosporins: cross-reactivity and tolerability of penicillins, monobactams, and carbapenems. *J Allergy Clin Immunol*. 2010;126(5):994-999.
5. Begue PC, Baron S, Challier P, et al. Pharmacokinetic and clinical evaluation of imipenem/cilastatin in children and neonates. *Scand J Infect Dis Suppl*. 1987;52:40-45.
6. Reed MD, Kliegman RM, Yamashita TS, et al. Clinical pharmacology of imipenem and cilastatin in premature infants during the first week of life. *Antimicrob Agents Chemother*. 1990;34(6):1172-1177.
7. Ahonkhai VI, Cyhan GM, Wilson SE, et al. Imipenem-cilastatin in pediatric patients: an overview of safety and efficacy in studies conducted in the United States. *Pediatr Infect Dis J*. 1989;8(11):740-744.
8. Nalin DR, Hart CB, Shih WJ, et al. Imipenem/cilastatin for pediatric infections in hospitalized patients. *Scand J Infect Dis Suppl*. 1987;52:56-64.
9. Freij BJ, Kusmiesz H, Shelton S, et al. Imipenem and cilastatin in acute osteomyelitis and suppurative arthritis. Therapy in infants and children. *Am J Dis Child*. 1987;141(3):335-342.
10. Alpert G, Dagan R, Connor E, et al. Imipenem/cilastatin for the treatment of infections in hospitalized children. *Am J Dis Child*. 1985;139(11):1153-1156.
11. Riikonen P. Imipenem compared with ceftazidime plus vancomycin as initial therapy for fever in neutropenic children with cancer. *Pediatr Infect Dis J*. 1991;10(12):918-923.
14. Drug Prescribing in Renal Failure [online database]. <https://kdpnet.kdp.louisville.edu/drugbook/pediatric/>. Accessed January 14, 2016.
16. ASHP's Interactive Handbook on Injectable Drugs [online database]. <http://www.interactivehandbook.com>. Accessed January 31, 2016.
17. Robinson CA, Sawyer JE. Y-site compatibility of medications with parenteral nutrition. *J Pediatr Pharmacol Ther*. 2009;14(1):48-56.
18. Jacobs RF, Kearns GL, Trang JM, et al. Single-dose pharmacokinetics of imipenem in children. *J Pediatr*. 1984;105(6):996-1001.

