

Piperacillin Sodium–Tazobactam Sodium

Brand names	Zosyn, generics
Medication error potential	None reported
Contraindications and warnings	<p>Contraindications: In those with a history of allergic reactions to any of the beta-lactams, including penicillins and/or cephalosporins.⁽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 who are sensitive to multiple allergens and in those with a history of penicillin, cephalosporins, or other beta-lactam hypersensitivity.⁽²⁾</p> <p>Superinfection: Piperacillin–tazobactam use may cause superinfection and/or <i>Clostridium difficile</i>-associated diarrhea, which has been reported and may range in severity from mild diarrhea to fatal colitis.⁽²⁾ Antibiotic use that is not for treatment of <i>C. difficile</i> may need to be discontinued.⁽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⁾</p> <p>Nephrotoxicity: Piperacillin–tazobactam has been found to be an independent risk factor for renal failure in critically ill patients. The manufacturer recommends alternative antibiotics be considered in this population.⁽³⁵⁾ Combined use with vancomycin may increase the risk of acute kidney injury. This has been reported in both <i>adult</i> and pediatric patients.⁽³⁵⁻³⁷⁾</p>
Infusion-related cautions	Thrombophlebitis has been reported. ⁽²⁾
Dosage	<p>Piperacillin–tazobactam is available in a ratio of 8:1 (piperacillin:tazobactam).⁽²⁾ <i>Doses are based on piperacillin component.</i></p> <p>Neonates: Safety in patients <2 months of age has not been established.⁽²⁾ 200–300 mg/kg/day divided q 8–12 hr.^(3,6) Up to 400 mg/kg/day has been recommended for some neonatal populations.^(29,30)</p> <p>Infants and children: Inappropriate in mild-to-moderate infections.⁽⁶⁾ For severe infections in those 2–9 months of age, give 240 mg/kg/day divided q 8 hr up to 16 g/day.^(2,6) In those >9 months of age (up to 40 kg), give 300 mg/kg/day divided q 8 hr up to 16 g/day.^(2,6) Those weighing more than 40 kg should receive <i>adult</i> dose of 12 g/day divided q 6 hr.⁽²⁾ Based on a single-dose pharmacokinetic study, doses of 100 mg/kg q 8 hr for bacteria whose minimum inhibitory concentration (MIC) is 2 mg/L and q 6 hr if the MIC is between 4 and 8 mg/L should be effective.⁽⁷⁾</p> <p>Cystic fibrosis: Up to 600 mg/kg/day divided q 4 hr has been recommended.⁽³¹⁾</p>
Dosage adjustment in organ dysfunction	If CrCl is 30–50 mL/min, give 140–200 mg/kg/day divided q 6 hr; if CrCl is <29 mL/min, give 105–150 mg/kg/day divided q 8 hr. ⁽¹⁰⁾ No adjustment necessary in liver impairment. ⁽¹¹⁾
Maximum dosage	400 mg/kg/day ⁽⁷⁾ up to 16 g of piperacillin component daily ⁽¹¹⁾
Additives	2.84 mEq of sodium/g of piperacillin ⁽²⁾
Suitable diluents	NS, SW, bacteriostatic water, bacteriostatic NS, and D5W ^(2,12)
Maximum concentration	Reconstituted to 200 mg/mL (piperacillin component); should be further diluted in 50–150 mL. ⁽²⁾



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Preparation and delivery

Stability: Thaw frozen container at room temperature (20°C to 25°C) or under refrigeration (2°C to 8°C).⁽¹²⁾ Do not force thaw by immersion in water baths and do not microwave.⁽¹²⁾ Do not refreeze.⁽¹²⁾

Compatibility: See Appendix D for PN compatibility information.⁽¹⁸⁾ Zosyn brand contains EDTA and sodium citrate while generic brands do not, resulting in differing compatibilities among brands.⁽¹²⁾ Although amikacin and gentamicin are compatible in vitro for Y-site infusion, reformulated Zosyn contains EDTA, which is not compatible with tobramycin.⁽²⁾

IV push

Not administered by this method

Intermittent infusion

Infuse over at least 30 minutes.^(2,12)

Continuous infusion

Continuous infusions of 8–13.5 g piperacillin/24 hr have been studied in *adults*.⁽¹⁹⁻²¹⁾ Prolonged infusions over 4 hours have also been studied in *adults*.⁽²²⁾ In pediatric pharmacokinetic modeling studies, continuous or prolonged infusions showed benefit over standard 30-minute infusion times.^(23,32,33)

Other routes of administration

None

Comments

Rare adverse effects: Piperacillin may be more allergenic (e.g., fever, rash) in patients with cystic fibrosis.^(24,34) Serum-like sickness and coagulopathy associated with fever, rash, and abnormal liver function tests occurred in two patients with cystic fibrosis who received piperacillin.⁽²⁵⁾

Abnormal coagulation tests (e.g., clotting time, platelet aggregation, and prothrombin time) may occur,⁽²⁾ especially in patients with cystic fibrosis⁽²⁵⁾ or renal failure.⁽²⁾ Piperacillin should be discontinued if bleeding occurs.⁽²⁾

Tonic-clonic seizures have been reported in an 11-year-old child receiving IV piperacillin (3 g q 4 hr) over 30 minutes.⁽²⁶⁾

Monitoring: Coagulation parameters should be frequently monitored during coadministration with large doses of heparin, oral anticoagulants, or other drugs that may affect the blood coagulation system or the thrombocyte function.⁽²⁾

Drug interactions: Piperacillin may decrease the clearance of methotrexate.^(2,27) Perioperative use of piperacillin may prolong the neuromuscular blockade of vecuronium or other nondepolarizing muscle relaxants.⁽²⁾ Probenecid may decrease the clearance of piperacillin.⁽²⁾ Consult appropriate resources before combining any drug with piperacillin-tazobactam.

Laboratory interference: A false-positive urinary glucose results when cupric sulfate solution-based tests are used.⁽²⁾ It is recommended that glucose tests based on enzymatic glucose oxidase reactions be used.⁽²⁾ Piperacillin-tazobactam may cause a false-positive *Aspergillus* infection result when performed with the Bio-Rad Laboratories Platelia *Aspergillus* EIA test; hence, interpret reports cautiously and confirmed by other diagnostic measures.⁽²⁾

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