

Alert	The Antimicrobial Stewardship Team has listed this drug under the following categories: Restricted.		
Indication	Piperacillin is an extended- spectrum, semisynthetic beta-lactam penicillin. Tazobactam is a β lactamase inhibitor. It is active against many Gram positive and Gram negative bacteria including anaerobes and many Enterobacteriaceae. Susceptibility of coagulase-negative staphylococci (CONS) to this agent is can be variable and piperacillin-tazobactam should not be used as first-line for suspected CONS sepsis. [11].		
Action	Piperacillin is an extended- spectrum, semisynthetic beta-lactam penicillin. Tazobactam is a beta lactamase inhibitor		
Drug Type	Antibiotic – penicillin and beta-lactamase inhibitor.		
Trade Name	Tazocin EF, PiperTaz, Piptaz, DBL Piperacillin and Tazobactam, Tazopip		
Presentation	4.5 g vial (4 g piperacillin and 0.5 g tazobactam).		
Dosage / Interval			
	Corrected Gestational Age/Postmenstrual Age	Dose (mg of piperacillin/kg)	Interval
	< 30 ⁺⁰ weeks	100 mg/kg/dose	8 hourly
	30 ⁺⁰ –35 ⁺⁶ weeks	80 mg /kg/dose	6 hourly
	\geq 36 ⁺⁰ weeks*	80 mg/kg/dose	6 hourly
*Consider 4 hourly dosing if culture-proven sepsis in this group.			
Route	IV		
Preparation/Dilution	Add 17 mL WFI to the 4.5 g piperacillin + tazobactam powder for reconstitution to make a concentration of 200 mg/mL of piperacillin equivalent. Draw up 1 mL (200 mg of piperacillin equivalent) and add 9 mL of sodium chloride 0.9% to make a final volume of 10 mL with a concentration of 20 mg/mL of piperacillin equivalent.		
Administration	IV infusion over 30 minutes.		
Monitoring	Monitor complete blood count, renal and hepatic function during prolonged treatment (> 10 days).		
Contraindications	Hypersensitivity to any of the penicillins and/or cephalosporins or beta-lactamase inhibitors.		
Precautions	Prolonged therapy makes leucopenia, neutropenia and thrombocytopenia more likely.		
Drug Interactions	Piperacillin may enhance the nephrotoxic effect of vancomycin. Piperacillin + tazobactam along with high doses of heparin and oral anticoagulants may affect the blood coagulation system. Piperacillin may increase the serum concentration of flucloxacillin. Piperacillin may increase the prolongation of the neuromuscular blockade of vecuronium.		
Adverse Reactions	Generally well tolerated. Hypersensitivity reactions can occur. Rash (maculopapular), phlebitis, thrombophlebitis. Diarrhoea, nausea, vomiting, stomatitis and pseudomembranous colitis (<i>Clostridium difficile</i>). Black tongue, fever, anaphylactic shock, angioedema, bronchospasm. Leucopenia, thrombocytopenia, anaemia. Elevated transaminases. Renal impairment. Hypokalaemia, hypernatraemia, metabolic alkalosis. Candidiasis.		

Compatibility	<p>Tazocin EF contains citric acid monohydrate and disodium edetate (EDTA). PiperTaz, Piptaz, DBL Piperacillin and Tazobactam, Tazopip are EDTA-free.</p> <p>Fluids: Sodium chloride 0.9%, glucose 5%, glucose 10%</p> <p>Y-site: EDTA-free brands only (NOT Tazocin EF): Amino acid solutions, aminophylline, anidulafungin, aztreonam, bivalirudin, buprenorphine, calcium folinate, calcium gluconate monohydrate, clindamycin, dexamethasone, dexmedetomidine, dopamine, fluconazole, furosemide (frusemide), granisetron, heparin sodium, hydrocortisone sodium succinate, hydromorphone, linezolid, magnesium sulfate heptahydrate, methylprednisolone sodium succinate, metoclopramide, metronidazole, morphine sulfate pentahydrate, pethidine, potassium chloride, ranitidine, remifentanyl, tigecycline, trimethoprim + sulfamethoxazole, zidovudine.</p> <p>Y-site: Tazocin EF only: No information available.</p>
Incompatibility	<p>Fluids: Albumin, blood products and alkaline solutions.</p> <p>Y site: Aminoglycosides, aciclovir, albumin, amiodarone, azithromycin, caspofungin, chlorpromazine, ciprofloxacin, dobutamine, droperidol, ganciclovir, glycopyrronium bromide (glycopyrrolate), haloperidol lactate, hydralazine, insulin (short-acting), labetalol, midazolam, mycophenolate mofetil, pentamidine isetionate, promethazine, rocuronium, sodium bicarbonate, thiopentone, tobramycin, tranexamic acid, vecuronium, verapamil.</p>
Stability	Reconstituted solution is stable for 24 hours below 25°C or at 2–8°C. Immediate use is recommended.
Storage	Store vial below 25°C
Special comments	Doses are expressed as the piperacillin component.
Evidence summary	<p>Piperacillin + tazobactam is used for treatment of non-CNS systemic infections, necrotising enterocolitis and intra-abdominal infections.¹ However, pharmacokinetic data for premature infants are very limited. It is primarily excreted via kidneys by glomerular filtration and tubular secretion. Therefore, renal impairment may affect drug elimination.²</p> <p>Several dosing regimens have been suggested for neonates in the literature. However, PMA (Post-Menstrual Age)-based dosing regimen as adopted by the Neomed group is more practical and has been shown to achieve therapeutic targets in > 90% of infants regardless of the organism MIC in Monte Carlo simulation test.³ There are other regimens⁴ using a combination of birth weight, postnatal age and PMA but they are challenging to implement clinically and do not carry great advantage over PMA-alone based regimen. There are no clear advantages of prolonged (2–4 hour) infusion over short (over 30 minutes) infusion.³ While the PMA-based regimen recommends 4 hourly dosing for 35–49 weeks gestation, prolonging the interval to 6 hours in this group is reasonable particularly for culture negative sepsis as 6-hour regime still attains the target rate in 80% of this group.³</p>
References	<ol style="list-style-type: none"> Berger A, Kretzer V, Apfalter P, et al. Safety evaluation of piperacillin/tazobactam in very low birth weight infants. J Chemother 2004;16:166–71. Sorgel F, Kinzig M. The chemistry, pharmacokinetics and tissue distribution of piperacillin/tazobactam. J. Antimicrob. Chemother. 31(Suppl A):39–60. Cohen-Wolkowicz M, Watt KM, Chenguang Z, et al. Developmental pharmacokinetics of Piperacillin and Tazobactam using plasma and dried blood spots from infants. Antimicrobial Agents and chemotherapy 2014;58(5):2856–2865.. Li Z, Chen Y, Li Q, Cao D, Shi W, Cao Y, Wu D, Zhu Y, Wang Y, Chen C. Population pharmacokinetics of piperacillin/tazobactam in neonates and young infants. Eur. J. Clin. Pharmacol. 69:1223–1233. Perez-Vazquez A, Pastor JM, and Riancho JA. "Immune Thrombocytopenia Caused by Piperacillin/Tazobactam," Clin Infect Dis, 1998, 27(3):650–1. Reichardt P, Handrick W, Linke A, et al. "Leukocytopenia, Thrombocytopenia and Fever Related to Piperacillin/Tazobactam Treatment - a Retrospective Analysis in 38 Children With Cystic Fibrosis," Infection, 1999, 27(6):355–6. Zaki SA and Lad V. "Piperacillin-Tazobactam-Induced Hypokalemia and Metabolic Alkalosis,"

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