Piperacillin + tazobactam | 2015

Alert	The Antimicrobial Stewardship Team has listed this drug under the following categories: Restricted.
Indication	Therapy of non-CNS infections caused by susceptible Gram positive and Gram negative bacteria including anaerobes and many Enterobacteriaceae. Susceptibility of coagulase-negative staphylococci (CONS) to this agent 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
≥ 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 (*Clostridium difficile*). Black tongue, fever, anaphylactic shock, angioedema, bronchospasm. Leucopenia, thrombocytopenia, anaemia. Elevated transaminases. Renal impairment. Hypokalaemia, hypernatraemia, metabolic alkalosis. Candidiasis.
Compatibility	Tazocin EF contains citric acid monohydrate and disodium edetate (EDTA). PiperTaz, Piptaz, DBL Piperacillin and Tazobactam, Tazopip are EDTA-free.

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	Fluids: Sodium chloride 0.9%, glucose 5%, glucose 10%
	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, remifentanil, tigecycline, trimethoprim + sulfamethoxazole, zidovudine.
	Y-site: Tazocin EF only: No information available.
Incompatibility	Fluids: Albumin, blood products and alkaline solutions.
	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.
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	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] 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 regimens [4] 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]
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