Piperacillin - Tazobactam

Newborn use only

2020

Alert	The Antimicrobial Stewardship Team has listed this drug under the following categories: Restricted.
Indication	Therapy of **non-CNS** systemic infections, necrotising enterocolitis and intra-abdominal infections caused by susceptible Gram positive and Gram negative bacteria including anaerobes and many Enterobacterales and *Pseudomonas* spp.(1) Susceptibility of coagulase-negative staphylococci (CONS) is generally not tested though oxacillin-resistant CONS should be considered resistant and piperacillin-tazobactam should not be used as first-line for suspected CONS sepsis.(2)
Action	β-lactam/β-lactamase inhibitor combination with a broad spectrum of antibacterial activity encompassing Gram-positive and Gram-negative aerobic bacteria and anaerobic bacteria, including many pathogens producing β-lactamases.(1) Piperacillin component is a semi synthetic penicillin that inhibits septum and cell wall synthesis of susceptible bacteria. Tazobactam is a beta lactamase inhibitor that enhances the antibiotic spectrum of piperacillin.
Drug type	Antibiotic – ureidopenicillin and beta-lactamase inhibitor.
Trade name	Piperacillin/Tazobactam Kabi, Tazocin EF, PiperTaz, Piptaz, PipTaz-AFT, Tazopip
Presentation	4.5 g vial (4 g piperacillin and 0.5 g tazobactam).
Dose	Dose based on piperacillin component (3, 4) **Corrected Gestational Age/Postmenstrual Age** / **Dose** / **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
Dose adjustment	**Therapeutic hypothermia** – Evidence is lacking to guide dose adjustment. **ECMO** – While standard dosing may be adequate for susceptible organisms, studies in adults have shown poor PK target attainment for the directed therapy of *Pseudomonas aeruginosa*. Seek infectious diseases consultant advice(5, 6) **Renal impairment** – Use with caution. Concurrent use with vancomycin has been suggested to be associated with an increased incidence of acute kidney injury in adults and children but unclear in neonates. (7-11) **Hepatic impairment** – No dose adjustment is required.
Maximum dose	
Total cumulative dose	
Route	IV
Preparation	Add 17 mL water for injection to the 4.5 g vial to make a concentration of 200 mg/mL of piperacillin equivalent solution. **FURTHER DILUTE** Draw up 2 mL (400 mg of piperacillin equivalent) and add 8 mL of sodium chloride 0.9% to make a final volume of 10 mL with a final concentration of 40 mg/mL of piperacillin equivalent.
Administration	IV infusion over 30 minutes. (3)
Monitoring	Complete blood count, electrolytes, 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 increases risk of leucopenia, neutropenia and thrombocytopenia. High doses may lead to hypernatraemia (owing to sodium content of preparations) (12)
Drug interactions	May potentially: • Enhance the nephrotoxic effect of vancomycin. • Affect the blood coagulation system when given with high doses of heparin and oral anticoagulants. • Increase the serum concentration of flucloxacillin. • 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. High doses may lead to hypernatraemia (owing to sodium content of preparations) Uncommon - Hypotension.
Compatibility	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, Hartmann's and alkaline solutions. (AIDH) Y site: Aciclovir, albumin, amikacin, amiodarone, azithromycin, caspofungin, chlorpromazine, ciprofloxacin, dobutamine, droperidol, ganciclovir, gentamicin, 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
Excipients	PiperTaz Sandoz, PipTaz AFT and Tazopip are EDTA-free. Contain 2.35 mmol of sodium for each 1 g of piperacillin. PipTaz AFT also contains sodium bicarbonate. Tazocin EF also contains citric acid monohydrate and disodium edetate (EDTA). Contains 2.84 mmol of sodium for each 1 g of piperacillin.
Special comments	Doses here are expressed as the piperacillin component.
Evidence	Refer to full version.
Practice points	Refer to full version.
References	Refer to full version.

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