### 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

<table>
<thead>
<tr>
<th>Corrected Gestational Age/Postmenstrual Age</th>
<th>Dose (mg of piperacillin/kg)</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30th weeks</td>
<td>100 mg/kg/dose</td>
<td>8 hourly</td>
</tr>
<tr>
<td>30th–35th weeks</td>
<td>80 mg/kg/dose</td>
<td>6 hourly</td>
</tr>
<tr>
<td>≥ 36th weeks*</td>
<td>80 mg/kg/dose</td>
<td>6 hourly</td>
</tr>
</tbody>
</table>

*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.
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, glycopyronium 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.\(^5\) 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.\(^6\)

**References**