**DESCRIPTION**

- Piperacillin is a penicillin antibiotic which interferes with cell wall peptidoglycan synthesis by binding to penicillin-binding proteins resulting in cell lysis.\(^{(1, 2)}\)
- Tazobactam is a beta-lactamase inhibitor with limited antibacterial activity. It extends the spectrum of activity of piperacillin to cover many beta-lactamase producing organisms.\(^{(1, 2)}\)

**INDICATIONS AND RESTRICTIONS**

Piperacillin with tazobactam is used in the treatment of mixed (aerobic and anaerobic) or nosocomial infections, especially if *P. aeruginosa* is involved.\(^{(1, 2)}\)

**IV: Monitored (orange) antibiotic**

- If the use is consistent with a standard approved indication, this must be communicated to ChAMP by documenting that indication on all prescriptions (inpatient and outpatient).
- The ChAMP team will review if ongoing therapy is required and/or if the order does not meet ChAMP Standard Indications.
- If use is not for a standard approved indication, phone approval must be obtained from ChAMP before prescribing.

**CONTRAINDICATIONS**

- Piperacillin with tazobactam is generally contraindicated in patients with a history of high risk allergy to penicillins.
- Piperacillin with tazobactam is contraindicated in patients with a history of jaundice or hepatotoxicity from piperacillin with tazobactam.\(^{(1)}\)

**PRECAUTIONS**

- Piperacillin with tazobactam may be prescribed in selected patients with high risk allergy to another Beta-lactam sub-class (e.g. some cephalosporins, carbapenems) in discussion with immunology.\(^{(1, 3-5)}\)
- In patients with a previous low risk reaction to Piperacillin with tazobactam or other another penicillin (delayed rash \[>1hr after initial exposure\]) without mucosal or systemic involvement) the risk of subsequent reaction to that agent is low. Re-challenge
may be acceptable in discussion with immunology.

- Patients with pre-existing coagulation disorders and/or currently taking anticoagulant agents have an increased risk of bleeding.\(^{(1)}\)
- Patients with Cystic Fibrosis have an increased risk of rash and drug fever.\(^{(1)}\)
- Each 1 gram of piperacillin with 125mg of tazobactam (Pipertaz®) contains 54mg (2.35mmol) of sodium. High doses and/or prolonged courses of piperacillin with tazobactam may result in electrolyte imbalance.\(^{(1, 5, 6)}\) Sodium content varies between brands.\(^{(6)}\)

### FORMULATIONS

Available at PCH:
- 4g piperacillin/500mg tazobactam powder for injection vial

Other formulations available:
- 2g piperacillin/250mg tazobactam powder for injection vial
- 4g piperacillin/500mg tazobactam powder for injection vial – multiple generic brands

### DOSAGE

- The doses listed below fall within the standard range.
- Higher doses may be prescribed for certain situations in consultation with an infectious diseases or clinical microbiology consultant.

**Doses are expressed as, and should be prescribed as the piperacillin component**

**Neonates:**
- Please refer to KEMH [Neonatal Medication Protocols](#)

**IV:**
- **Usual dose:** 100mg/kg/dose (maximum 4 grams of piperacillin component) 8 hourly.\(^{(1, 3, 7)}\)
- **Severe infections:** 100mg/kg/dose (maximum 4 grams of piperacillin component) 6 hourly.\(^{(1, 3)}\)

**Continuous infusions for HiTH:**
- **Usual dose:** 300mg/kg/DAY via continuous infusion
- **Severe infections:** 400mg/kg/DAY via continuous infusion.

Refer to [Hospital in the Home Antimicrobial Guidelines](#) for further information.

### DOSAGE ADJUSTMENT

**Dosage adjustment required in renal impairment:**
- Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 40mL/min).
- To calculate the estimated glomerular filtration rate (eGFR) use the following formula:
### Piperacillin tazobactam Monograph

**Children's Antimicrobial Management Program (ChAMP)**

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#### eGFR (mL/min/1.73m²) = \[
\frac{36.5 \times \text{height (in cm)}}{\text{Serum creatinine (micromol/L)}} \]

- CrCl > 40mL/minute/1.73m²: normal dosing
- CrCl 20 - 40mL/minute/1.73m²: 100% 8 hourly
- CrCl <20mL/minute/1.73m²: 100% 12 hourly

**Dosage adjustment required in hepatic impairment:**

No dosage requirements are required in hepatic impairment, however the half-life of piperacillin with tazobactam is extended in patients with hepatic cirrhosis.\(^4,7\)

### RECONSTITUTION

- Reconstitute each 4 gram vial of piperacillin tazobactam with 37mL sodium chloride 0.9% to give 100mg/mL of piperacillin solution.

### ADMINISTRATION

#### IV infusion:

- Dilute to a final concentration of between 15mg/mL and 100mg/mL and infuse over 20 to 30 minutes or longer.\(^6\)
- Avoid rapid infusion as this may result in seizures.\(^5-7\)

#### Continuous infusion:

- May be given over 24 hours by continuous infusion in Hospital in the Home patients.\(^6\) Contact Pharmacy for advice.

### MONITORING

- Renal, hepatic and haematological function should be monitored weekly with prolonged therapy (i.e. longer than 7 days).\(^1,4\)
- Serum potassium should be monitored in patients likely to develop hypokalaemia during treatment such as patients treated with high doses who are also prescribed cytotoxic medications or diuretics or those with concurrent hepatic disease.\(^1\)

### ADVERSE EFFECTS

**Common:** Diarrhoea, nausea, vomiting, headache, constipation, anaemia, insomnia, local reaction with intravenous infusion (pain, burning, erythema, infiltration, swelling and induration at the injection site and thrombophlebitis), *Clostridium difficile* associated disease and immunologic reactions (rash, erythema, urticaria, contact dermatitis, fever, angioedema, bronchospasm, interstitial nephritis, haemolytic anaemia, eosinophilia, serum sickness-like syndrome, exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis).\(^1,9\)

**Rare:** Cholestatic hepatitis and jaundice, transient increase in liver enzymes and bilirubin, bleeding abnormalities (prolonged bleeding time and/or altered platelet aggregation with high doses), hypokalaemia, black tongue, electrolyte disturbances, neurotoxicity (e.g. drowsiness, hallucinations, coma, seizure, generally with high doses), blood dyscrasias (e.g. neutropenia, related to dose and duration of treatment, thrombocytopenia, eosinophilia, pancytopenia), dyspepsia, stomatitis, hypotension, flushing,
myalgia, hypoglycaemia.\textsuperscript{(1, 9)}

| COMPATIBLE FLUIDS | • Glucose 5%  
|                  | • Sodium chloride 0.9\%\textsuperscript{(6)} |

| STORAGE | • Store vials below 25°C\textsuperscript{(5, 6)}  
|         | • Store syringes prepared by Pharmacy Compounding Service (PCS) between 2 and 8°C.\textsuperscript{(6)} |

| INTERACTIONS | Piperacillin with tazobactam has drug interactions; please consult PCH approved references (e.g. 
|               | Clinical Pharmacology), your ward pharmacist or Pharmacy on 63546 for more information |
|              | • IV aminoglycoside antibiotics are inactivated by IV penicillins and cephalosporins. Aminoglycoside antibiotics are rapidly bactericidal and should be administered first. The line should then be flushed well with a compatible fluid and the penicillin administered.\textsuperscript{(5)} |
|              | • Piperacillin with tazobactam inhibits methotrexate excretion and may result in increased methotrexate levels.\textsuperscript{(1, 4, 9)} |
|              | • Piperacillin with tazobactam used in conjunction with vecuronium, rocuronium or other non-depolarising neuromuscular blockers can prolong the neuromuscular blockade.\textsuperscript{(1, 4, 5, 9)} |
|              | • Piperacillin with tazobactam can inhibit platelet aggregation and may alter the anticoagulant effect of warfarin and other anticoagulant agents. INR and/or clotting must be monitored and dose adjustments made as appropriate.\textsuperscript{(4, 5, 9)} |
|              | • The use of vancomycin in conjunction with piperacillin and tazobactam may increase the risk of acute kidney injury. Renal function should be monitored closely.\textsuperscript{(4, 5)} |

| COMMENTS | |

| MANUFACTURER SAFETY DATA SHEET (SDS) | To access to the Manufacturer SDS for this product, use the following link to ChemAlert. |

**Please note: The information contained in this guideline is to assist with the preparation and administration of piperacillin tazobactam. Any variations to the doses recommended should be clarified with the prescriber prior to administration**
Related internal policies, procedures and guidelines

- **Antimicrobial Stewardship Policy**
- **ChAMP Empiric Guidelines**
- **KEMH Neonatal Medication Protocols**
- **Hospital in the Home Antimicrobial Guidelines**

References

7. Piperacillin and tazobactam: Pediatric drug information [Internet]. Lexicomp. 2020 [cited 20/05/2020].
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