MONOGRAPH

Piperacillin with tazobactam Monograph - Paediatric

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

- Penicillin antibiotic with beta-lactamase inhibitor.(1)

INDICATIONS AND RESTRICTIONS

Piperacillin with tazobactam is used in the treatment of mixed (aerobic and anaerobic) and/or nosocomial infections, especially if *Pseudomonas aeruginosa* is involved.(1)

Oral: 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

- Hypersensitivity to piperacillin, tazobactam or any component of the formulation or history of high-risk allergy to penicillins.[1-6]

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.[1-6]
- In patients with a previous low risk reaction to Piperacillin with tazobactam or other 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, 3-5]
- Patients with Cystic Fibrosis have an increased risk of rash and drug fever.[1, 3, 4]
- Each 1 gram of piperacillin with 125 mg of tazobactam (Pipertaz®) contains 54 mg (2.35 mmol) of sodium. High doses and/or prolonged courses of piperacillin with tazobactam may result in electrolyte imbalance. Sodium content varies between brands.[4-8]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- 4 g piperacillin/500 mg tazobactam powder for injection vial

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

All doses are expressed in and should be prescribed as the piperacillin component

IV:

- **Usual dose:** 100 mg/kg/dose (maximum 4 grams of piperacillin component) given 8 hourly.[1, 3, 6, 9]
- **Severe infections:** 100 mg/kg/dose (maximum 4 grams of piperacillin component) given 6 hourly.[1, 3, 5, 9]

Continuous infusions for HiTH via Baxter Infusor®:

- **Usual dose:** 300 mg/kg/DAY via continuous infusion (maximum of 12 grams/DAY)
- **Severe infections:** 400 mg/kg/DAY via continuous infusion (maximum of 16 grams/DAY).

Refer to Hospital in the Home Antimicrobial Guidelines for further information.

Renal impairment:

- eGFR calculator

- Dosage adjustment may be required in cases of impaired renal function (with creatinine clearance of less than 40 mL/min/1.73m^2).

eGFR	Adjustment based on usual dosing[6]	Adjustment based on severe infection dosing[6]
≥ 40 mL/minute/1.73m^2	Normal dosing	Normal dosing
≥ 20 to < 40 mL/minute/1.73m^2	70 mg/kg/dose 8 hourly	50 to 70 mg/kg/dose 6 hourly
< 20 mL/minute/1.73m^2	70 mg/kg/dose 12 hourly	50 to 70 mg/kg/dose 8 hourly

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.[3, 6]

RECONSTITUTION & ADMINISTRATION

- Reconstitute each 4 gram vial of piperacillin tazobactam with the volume of sodium chloride 0.9% in the table below, to give a concentration of 100 mg/mL.

Vial strength	Volume of sodium chloride 0.9% required	Resulting concentration	Powder volume[2]
4 gram (piperacillin component)	37 mL	100 mg/mL	3 mL (Kabi brand) *Sandoz, AFT brands = 3.15 mL however use the same reconstitution volume (37 mL, as the difference in final volume is not clinically significant)*

IV infusion:

- Give undiluted or further dilute to a final concentration of between 15 mg/mL and 100 mg/mL and infuse over 30 minutes or longer.[2, 8, 10]
- Avoid rapid infusion as this may result in seizures.[2, 5, 6]
- Piperacillin with tazobactam is also suitable for extended infusion. The required intermittent dose can be given over 3 to 4 hours.[2]
- Extended infusion times may be optimal for patients with critical infections due to *Enterobacterales* and *P. aeruginosa*. Discuss with Infectious Diseases.[11]

Continuous infusion:
The total daily dose may be given by continuous infusion over 24 hours via a Baxter Infusor® through Hospital in the Home (HiTH).[2, 10]

Volumes available	Maximum concentration	Minimum concentration	Minimum dose	Stability
120 mL and 240 mL	78.3 mg/mL Piperacillin component	17.5 mg/mL Piperacillin component	2100 mg/ day Piperacillin component	24 hours at 33°C

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

- Glucose 5%
- Sodium chloride 0.9%[2, 10]

Compatible at Y-site:

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

MONITORING

- Renal, hepatic and haematological function should be monitored weekly with prolonged therapy (i.e. longer than 7 days).[3, 4, 6, 10]
- 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, 3]

ADVERSE EFFECTS

Common: Diarrhoea, nausea, headache, constipation, anaemia, insomnia, local reaction with intravenous infusion (pain, burning, erythema, infiltration, swelling and induration at the injection site) 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, 8]

Infrequent: flushing, hypokalaemia, myalgia, thrombophlebitis, vomiting, *Clostridioides difficile* associated disease.[1, 8]

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),multi-organ hypersensitivity syndrome, epistaxis, stomatitis.[1, 8]

STORAGE

- Store vials below 25˚C and protect from light.[2, 5]
- Store syringes prepared by Pharmacy Compounding Service (PCS) between 2 and 8˚C.[2]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

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 CAHS internal policies, procedures and guidelines

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

References

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