

PIPERACILLIN/TAZOBACTAM EXTENDED INFUSION GUIDELINES

Beta-lactam antibiotics effect their bactericidal action through duration of time in which the free concentration in serum is above the MIC of the organism (1). Changes in pharmacokinetic parameters in setting of sepsis and shock can result in sub-therapeutic concentrations. Extended infusion results in sustained beta-lactam concentrations and increased bacterial killing. This has been recommended by Surviving Sepsis Campaign in 2021 (2). Due to practicalities, it is recommended that this is implemented with priority in critically unwell patients (3). For these reasons the critical care infection group has produced this guideline.

The indication and dosing of piperacillin/tazobactam follows that described in local antimicrobial prescribing guidelines (antimicrobial companion); this protocol is designed to give details on how infusions are administered. It is appreciated that the method of infusion may not be possible in certain patients depending on venous access and compatibilities, in these cases standard intermittent boluses should be used.

Reconstitution

- Each vial of 4.5g should be reconstituted with 20ml of sterile water for injections or 0.9% sodium chloride.
- The contents of the vial should then be added to a 100ml infusion bag of 0.9% sodium chloride or 5% dextrose.
- Infuse intravenously over 30 minutes or 4 hours, as per below.
- Start intravenous infusion as soon as possible after preparation to reduce risk of microbial contamination.

Prescribing first antibiotic dose

- Prescribe as STAT dose.
- Infuse initial dose over 30 minutes.

Prescribing ongoing doses

- Following first dose, give all further doses as an extended infusion (over 4 hours) at time interval according to renal function and indication (as per below table).

Medicine (Approved Name)		For Use	Date/Time					
PIPERACILLIN/TAZOBACTAM			06					
Dose / Amount	Route	Quantity	10					
4.5g	IV							
Diluent/Undiluted + Volume		Date	12					
0.9% NaCl 100mL								
Rate/Duration	Start Date	Pharmacy	14					
over 4 hours	31.1.23							
Comments/Indication/Review Date			18					
An Indication								
Review date.			22					
Prescriber - sign + print			24					
KIRKPATRICK NMP 443								

Critical Care Guidelines: PIPERACILLIN TAZOBACTAM EXTENDED INFUSION GUIDELINE

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Document Version: 3.0

Authoriser: Lothian Critical Care Directorate QIT Editorial Board

Authorisation Date: 09/02/2023

Review Date: July 2023

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Creatinine Clearance (CrCl)	Indication	Dose
>40ml/min	Neutropenic sepsis, known <i>Pseudomonas spp.</i> infection or on advice of infection specialist	4.5g every 6 hours
>40ml/min	All other indications	4.5g every 8 hours
20-40ml/min	All indications	4.5g every 8 hours
<20 ml/min	All indications	4.5 g every 12 hours
Renal replacement – CVVHD/HDF	All indications	4.5g every 8 hours
Renal replacement – intermittent haemodialysis/peritoneal dialysis	Do not use extended infusions for these patients. No data demonstrating improved outcomes. Use standard 30-minute infusion at time interval indicated by renal drug handbook	

(4, 5,6)

Discharge from critical care

- Stop extended infusion and switch to intermittent 30-minute infusions. Dose and time interval same as for extended infusion dosing.

References

- (1) European Committee on Antimicrobial Susceptibility Testing. Clinical breakpoints and dosing of antibiotics v12.0. Available at: https://www.eucast.org/clinical_breakpoints
- (2) Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47(11):1181-1247. doi:10.1007/s00134-021-06506-y
- (3) Scottish Antimicrobial Prescribing Group. Changes to antibiotic susceptibility reporting from microbiology laboratories. Jan 2022. Available at: https://www.sapg.scot/media/6598/20220120-changes-to-antibiotic-susceptibility-reporting-from-microbiology-laboratories_fk-sq.pdf
- (4) De Waele JJ, Lipman J, Carlier M, Roberts JA. Subtleties in practical application of prolonged infusion of beta-lactam antibiotics. International journal of antimicrobial agents. 2015;45(5):461-463. Available at: <https://doi.org/10.1016/j.ijantimicag.2015.01.007>
- (5) Sanford Healthcare Centre. Extended-Infusion Piperacillin-Tazobactam Protocol. Aug 2016. Available at: <file:///C:/Users/katherine.hill/Downloads/SHC-Extended-Infusion-Piperacillin-Tazobactam.pdf>
- (6) The Renal Drug Database. <https://renaldrugdatabase.com>. Accessed 09/06/22

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