

GUIDANCE TO SUPPORT THE ADMINISTRATION OF PIPERACILLIN/TAZOBACTAM (TAZOCIN) 3-HOUR EXTENDED INFUSIONS IN ADULTS WHEN SUSCEPTIBLE, INCREASED EXPOSURE "I" IS REPORTED ON MICROBIOLOGY CULTURE AND SENSITIVITY RESULTS (RESERVED FOR USE IN CRITICAL CARE AREAS ONLY):

TARGET AUDIENCE	Clinical team prescribing and administering a 3-hour infusion of piperacillin/tazobactam (tazocin)
PATIENT GROUP	Patients admitted to critical care areas who need treatment for an infection with an "I" report to piperacillin/tazobactam (tazocin), based on culture and sensitivity results

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Clinical Guidelines Summary

The European Committee on Antimicrobial Susceptibility Testing (EUCAST) is a standing committee jointly organized by ESCMID (European Society of Clinical Microbiology and Infectious Diseases), ECDC (European Centre for Disease Prevention and Control) and is a network of established experts in the determination of antimicrobial breakpoints and in antimicrobial susceptibility testing. EUCAST recommends 3-hour infusions as standard. Due to practical constraints, and in line with other nations, this should be prioritised for patients within critical care areas only.

The revised EUCAST breakpoints have been reviewed locally. Please refer to the [Adult Guidance on Interpreting Antimicrobial Susceptibility Reporting](#).

Administration of β -lactam antibiotics as a 3-hour extended infusion is generally not included in the product licensing. However, these agents have been administered over 3 to 4-hours to achieve favourable kinetics/clinical benefits in some critical care units within the UK and is recognised practice endorsed by MEDUSA¹.

Dosing advice²:

Loading dose (STAT): 4.5g over 30 minutes followed immediately by first maintenance dose.

Maintenance dose: 4.5g (infused over 3 hours) every SIX to EIGHT hours.

No loading dose is required for patients who have a dose within the past SIX hours³. Refer to maintenance dosing advice for guidance with these patients.

Renal Dose Adjustments⁵:

Renal Function	Loading Dose	Renal Maintenance dose (extended infusion – over 3 hours)*
GFR > 40ml/min	4.5g STAT (Over 30 minutes)	4.5g every SIX to EIGHT hours <i>First maintenance dose should commence immediately after loading.</i>
GFR 20 – 40ml/min	4.5g STAT (Over 30 minutes)	4.5g every EIGHT hours <i>First maintenance dose should commence immediately after loading.</i>
GFR < 20ml/min	4.5g STAT (Over 30 minutes)	4.5g every TWELVE hours <i>First maintenance dose should commence immediately after loading.</i>

Dose Adjustments in Renal Replacement Therapy⁵:

Renal Replacement Therapy	Loading dose	Renal Maintenance dose (extended infusion – over 3 hours)*
CVVHD/HDF	4.5g STAT (Over 30 minutes)	4.5g every SIX to EIGHT hours <i>First maintenance dose should commence immediately after loading.</i>
HD	4.5g every TWELVE hours	
HDF/High flux	4.5g every TWELVE hours	

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Other Patient Considerations:

In obesity consider using 4.5g every SIX hours or a continuous infusion for isolates with higher minimum inhibitory concentration. Maximum dose of piperacillin (not piperacillin/tazobactam) is reported as 24 g/day. Consider dosing at upper end of recommended doses or use more frequent dosing⁴.

Administration¹:

- Each vial should be reconstituted with 20mls of water for injection, as per manufacturer's advice.
- Vial contents should then be made up to 100ml infusion bag or 50mls in a syringe, using sodium chloride 0.9% or Glucose 5%.
- Infuse the contents over 3-hours via a rate-controlled infusion device by peripheral or central line.
- Start the infusion as soon as possible after preparations to reduce the risk of microbial contamination.

AMOUNT OF DRUG	VOLUME	FINAL CONCENTRATION	DILUENT	SUITABLE FOR
4.5g	100mL	45mg/mL	Water for injection (reconstitution) then further dilute with Sodium Chloride 0.9% or Glucose 5%	Most patients
4.5g	50mL	90mg/mL		Fluid restricted patients

Compatibility:

For compatibility with other medications refer to Medicines Complete, MEDUSA or Thames Valley charts or discuss with clinical pharmacist¹¹.

Glossary:

HDF – intermittent haemodiafiltration

CVVH – continuous arteriovenous/venovenous haemofiltration

CVVHD/HDF – continuous venovenous haemodialysis/haemodiafiltration

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References/Evidence:

1. MEDUSA Monograph – Piperacillin with Tazobactam. Accessed 13/12/2024 - [Injectable Medicines Guide - Display - Piperacillin with tazobactam - Intravenous - Version 9 - IVGuideDisplayMain.asp](#)
2. Medicines complete – critical illness – piperacillin/tazobactam (Tazocin) monograph. Updated on the 01/09/2023. Accessed on the 03/06/2024 – <https://www.medicinescomplete.com/#/content/critical/69>
3. Administration of Beta-Lactam Antibiotics (Piperacillin/Tazobactam & Meropenem) by Extended Infusion in Adult Critical Care Patients – Accessed 25/07/2024 – <https://www.bedsformulary.nhs.uk/docs/Extended%20and%20Continuous%20Administration%20of%20Beta--%20Lactam%20Antibiotics%201.pdf>
4. Janson, B. & Thursky, K. (2012). Dosing of antibiotics in obesity. Current Opinion in Infectious Diseases, 25 (6), 634-649. Accessed 25/07/2024 - <https://pubmed.ncbi.nlm.nih.gov/23041773/>
5. Renal Drug Database - piperacillin/tazobactam (Tazocin) monograph. Updated on the 09/09/2019. Accessed on the 17/07/2024 – <https://www.renaldrugdatabase.com/s/article/TAZOCIN-PIPERACILLIN-TAZOBACTAM>
6. NHS Lanarkshire – Adult guidance on interpreting antimicrobial susceptibility reporting – Accessed 04/11/2024 – <https://rightdecisions.scot.nhs.uk/media/3tffgp43/eucast-adults-final.pdf>
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8. NHS Grampian Staff Protocol For The Administration Of Intravenous Piperacillin/Tazobactam In Adults Via Extended Infusion – Accessed 25/07/2024 – https://www.nhsgrampian.org//globalassets/foidocument/foi-public-documents1---all-documents/Protocol_PipTaz.pdf
9. Piperacillin/Tazobactam Extended Infusion Guidelines – Accessed the 25/07/2024 – <https://www.nhstaysideadtc.scot.nhs.uk/Antibiotic%20site/pdf%20docs/Tazocin%20Extended%20Infusion%20June%202011.pdf>
10. Continuous infusion of piperacillin/tazobactam and meropenem Cardiac Intensive Care Unit (CICU) and Cardiac step down ward – Accessed 25/07/2024 – <https://www.bsuh.nhs.uk/library/wp-content/uploads/sites/8/2021/11/Continuous-infusion-of-piperacillintazobactam-and-meropenem-2021.pdf>
11. Thames Valley Y-Site Intravenous Drugs Compatibility Chart (September 2015) – Accessed 04/11/2024 – https://www.southaccnetworks.nhs.uk/media/Thames_Valley_CCN/Our%20groups/Thames%20Valley%20YSite%20Intravenous%20Drugs%20Compatibility%20Chart.pdf
12. Extended-Infusion β -Lactam Therapy, Mortality, and Subsequent Antibiotic Resistance Among Hospitalized Adults with Gram-Negative Bloodstream Infections – Accessed 20/11/2024 – <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2820673>

Governance information for Guidance document

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CONSULTATION AND DISTRIBUTION RECORD	
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Distribution	Circulated to all acute sites for information, in particular critical care areas.

CHANGE RECORD			
Date	Lead Author	Change	Version
		<i>e.g. Review, revise and update of policy in line with contemporary professional structures and practice</i>	1

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2. You can include additional appendices with complimentary information that doesn't fit into the main text of your guideline, but is crucial and supports its understanding.

e.g. supporting documents for implementation of guideline, patient information, specific monitoring requirements for secondary and primary care clinicians, dosing regimen/considerations according to weight and/or creatinine clearance

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