LANCASHIRE AND SOUTH CUMBRIA CRITICAL CARE NETWORK

CONTINUOUS AND EXTENDED ANTIMICROBIAL GUIDELINE

Contents

1. Indication

Meropenem, piperacillin/ tazobactam, and co-amoxiclav exhibit time dependent bactericidal properties.

Conventional dosing of antibiotics isn't appropriate for the majority of critically ill patients due to changes in volume of distribution, vascular tone and a phenomenon known as augmented renal clearance (ARC). ARC is identified by an elevated creatinine clearance above the reference range which results in an increase in the excretion of various drugs.

The incidence of those exhibiting ARC in Critical Care is between 10 – 65%, depending upon patient group. These patients, if septic have a higher-than-expected mortality and it is believed this is due to sub-therapeutic concentrations of antibiotics. Piperacillin/tazobactam, meropenem and co-amoxiclav at conventional dosing may not be effective in killing common pathogens seen in intra-abdominal infections due to their increased breakpoint. This is even more likely in critically ill patients who have ARC.

In October 2025, the Intensive Care Society and British Infection Association issued joint guidance and recommendations for meropenem and piperacillin/tazobactam administration in critically unwell adults. This guideline reflects new administration advice. Note patients on haemodialysis are excluded from dosing advice in this guideline.

Cockcroft and Gault equation for estimating creatinine clearance

$$\text{Creatinine clearance (mL/min)} = \frac{Y \times (140 - \text{age}) \times \text{weight}}{\text{Serum creatinine micromol/L}}$$

Where Y = 1.23 for males and 1.04 for females

Cockcroft and Gault does not apply to all patients. Exclusion criteria include: unstable serum creatinine, pregnancy, malnutrition, amputation and dialysis

Estimated glomerular filtration rate (eGFR)

Renal function is often reported using estimated Glomerular Filtration Rate (eGFR), reported in mL/minute/1.73m^2. This is not the same as creatinine clearance estimates, which is calculated in mL/minute. Since eGFR estimates have not yet been validated for drug dosing, dose adjustment in renal impairment should be based on estimates of creatinine clearance (e.g. calculated from the Cockcroft and Gault equation or from a 24-hour urine collection).

2. Dosing Information

2.1 Piperacillin/Tazobactam

All patients to receive 4.5g as an initial bolus over 30 min irrespective of weight.

If the patient has received Piperacillin/Tazobactam elsewhere > 4 hours previously, ensure a further bolus does is given.

Subsequent dosing based upon Creatinine Clearance

For the following indications; neutropenic sepsis, severe HAP or high dose recommended by a consultant microbiologist use 18g over 24 hours if creatinine clearance is greater than 40mL/min

Creatinine Clearance	Dose	Concentration	Rate
< 20mL/min	9g	9g in 250mL Sodium chloride 0.9% or Glucose 5%	10.4 mLs/hr
CVVHDF, no creatinine clearance available or >20 CrCl < 130 mL/min	13.5g	13.5g in 250mL Sodium chloride 0.9% or Glucose 5%	10.4 mLs/hr
≥ 130mL/min	18g	18g in 250mL Sodium chloride 0.9% or Glucose 5%	10.4 mLs/hr

(Example 70 Kg male with CrCl 160mL/min will receive a total of 22.5g in the initial 24 hours followed by 18g per 24 hours)

The dose for each 24 hours will need to be prescribed daily once the creatinine clearance is known.

If moving from 9g to 13.5g or 13.5g to 18g, prescribe an additional 4.5g Piperacillin/ Tazobactam as a bolus on the STAT section of the prescription chart.

2.2 Meropenem

All patients to receive 1g as an initial bolus over 30 min irrespective of weight.

If the patient has received Meropenem elsewhere > 4 hours previously, ensure a further bolus dose is given. Subsequent dosing based upon the latest Creatinine Clearance.

Creatinine Clearance	Dose	Concentration	Rate
< 25 mL/ min	1.5g	500mg diluted in 50mL Sodium chloride 0.9%	6.25mL/hour
No Creatinine Clearance available or CVVHDF	3g	1g diluted in 50mL Sodium chloride 0.9%	6.25mL/hour
< 150mL/ min	3g	1g diluted in 50mL Sodium chloride 0.9%	6.25mL/hour
≥ 150mL/min	4g	1g diluted in 50mL Sodium chloride 0.9%	8.3mL/hour
≥ 200mL/ min	5g	1g diluted in 50mL Sodium chloride 0.9%	10.4mL/hour

(Example 70 Kg male with CrCl 160mL/min will receive a total of 5g in the initial 24 hours followed by 4g per 24 hours)

The dose for each 24 hours will need to be prescribed daily once the creatinine clearance is known.

If increasing the total daily dose based upon Creatinine Clearance (i.e. from 1.5g to 3g or 3g to 4g) prescribe an additional bolus dose of meropenem on the STAT section of the prescription chart.

Neurological dose for those with presumed or confirmed CNS infection

The neurological dose for meropenem is 2g every 8 hours.

2.3 Co-Amoxiclav

An initial bolus dose is not required for co-amoxiclav

Creatinine Clearance	Dose	Concentration	Rate
< 20mL/min	1.2g every 12 hours	1.2g in 50mL	12.5mL/hour
CVVHDF, no clearance available or CrCl >20 mL/min	1.2g every 8 hours	1.2g in 50mL	12.5mL/hour

3. Preparation

Consult Adult Critical Care Drug Monographs for preparation of antimicrobials listed

4. Administration

Consult Adult Critical Care Drug Monographs for administration of antimicrobials listed

5. Monitoring

Discharging to ward

This guideline is for critical care patients only. For patients returning to the ward, switch to ward protocol

6. Additional Information

This prescribing guideline is for critical care patients only. For patients returning to the ward, consult Trust Antimicrobial Formulary guidelines.

7. References

Dulhunty JM, Brett SJ, De Waele JJ, et al. Continuous vs Intermittent β-Lactam Antibiotic Infusions in Critically Ill Patients With Sepsis: The BLING III Randomized Clinical Trial. JAMA. 2024;332(8):629–637. doi:10.1001/jama.2024.9779

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Intensive Care Society and British Infection Association. 2025. Position statement on the use of continuous infusion for piperacillin/tazobactam and meropenem within critical care settings within the UK https://ics.ac.uk/resource/experts-recommend-a-simple-change-to-antibiotic-administration-that-will-save-lives-in-sepsis.html [Accessed 28th October 2025].

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CONSULTATION		
	Committee/Group	**Date**
Consultation	Lancashire and South Cumbria Critical Care Network - Continuous Antimicrobial Infusions Project Antimicrobial Stewardship Committees [Local] Critical Care Clinical Effectiveness Group Meetings	September 2024 – October 2025
Approval Committee	Critical Care Clinical Effectiveness Group Meeting	November 2025
NEXT REVIEW DATE	November 2028	
AMENDMENTS	New clinical guideline	