

**NHS Grampian Staff Protocol For The Administration Of Intravenous Piperacillin/Tazobactam In Adults Via Extended Infusion**

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**Version 4**

**Executive Sign-Off**

This document has been endorsed by the Director of Pharmacy and Medicines Management

Signature: 

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<b>Policy, Protocol, Procedure or Process Document:</b>	Protocol
<b>Document application:</b>	Applicable to the whole of the acute sector
<b>Purpose/description:</b>	To provide guidance for medical, nursing and pharmacy staff about how to dose, monitor and administer extended infusions of piperacillin/tazobactam safely and effectively in adults.
<b>Responsibility:</b>	Responsibility for the effective management of the Acute Sector's policy, protocol, procedure and process documentation ultimately lies with the General Manager for the Acute Sector. Delegation for formulating, disseminating and controlling these documents falls to either a named individual or a working group.
<b>Policy statement:</b>	It is the responsibility of supervisory staff at all levels to ensure that their staff are working to the most up to date and relevant policies, protocols procedures. By doing so, the quality of the services offered will be maintained, and the chances of staff making erroneous decisions which may affect patient, staff or visitor safety and comfort will be reduced.

**Responsibilities for ensuring registration of this document on the NHS Grampian Information/ Document Silo:**

Lead Author/Co-ordinator: Specialist Antibiotic Pharmacists

**Physical location of the original of this document:** Pharmacy and Medicines Directorate, Westholme

**Job title of creator of this document:** Specialist Antibiotic Pharmacists

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Lead Author/Co-ordinator: Specialist Antibiotic Pharmacists

**Responsibilities for implementation:**

Organisational: Acute Sector Operational Management Team and Acute Sector General Manager

Hospital/Interface services: Deputy General Managers and Clinical Leads

Operational Management Unit: Unit Operational Managers

Departmental: Clinical Leads  
Area: Line Managers

**Review:** This protocol will be reviewed at least every three years or sooner if current recommendations change.

**Responsibilities for review of this document:**

Lead Author/Co-ordinator: Specialist Antibiotic Pharmacists

**Review date:** This policy will be reviewed in three years or sooner if current treatment recommendations change

**Revision History:**

Revision Date	Previous Revision Date	Summary of Changes (Descriptive summary of the changes made)	Changes Marked* (Identify page numbers and section heading )
July 2015	May 2015	Added advice to give loading dose and supporting reference.	p1, 2
May 2019	July 2015	Added sentence to first paragraph with supporting evidence for protocol.	p1

		<p>Changed wording from treatment for pseudomonas infections and coliforms with high MICs to treatment for resistant gram-negative infections.</p> <p>Added instructions on how to prescribe.</p> <p>Simplified infusion time for loading dose to 30 minutes.</p> <p>Added dosing recommendations for patients on CVVH or CVVHD/HDF as a recent study showed that in patients receiving CRRT, the use of piperacillin continuous infusion ensured optimal exposure for less susceptible pathogens. Added recommendation to exclude patients on haemodialysis, HDF/high flux or APD/CAPD</p>	
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\* Changes marked should detail the section(s) of the document that have been amended, i.e. page number and section heading.

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## NHS Grampian Staff Protocol For The Administration Of Intravenous Piperacillin/Tazobactam In Adults Via Extended Infusion

Piperacillin/tazobactam contains a beta-lactam penicillin, piperacillin, that exhibits time dependent bacterial killing. Free beta lactam levels do not have to remain above the minimum inhibitory concentration (MIC) for the entire dosing interval; near maximal bactericidal effect is typically observed when the concentration exceeds the MIC for 50% of the dosing interval.<sup>1</sup> It has been suggested that administering piperacillin/tazobactam as an infusion for longer than the conventional 30 minute infusion time produces a drug concentration in excess of the MIC for a longer period which may achieve improved outcomes in critically ill patients.<sup>1,2</sup> A recent systematic review and meta-analysis concluded that prolonged infusion of antipseudomonal  $\beta$ -lactams for the treatment of patients with sepsis was associated with significantly lower mortality than short-term infusion.<sup>3</sup>

Additionally, administration of a loading dose immediately prior to commencing the first extended infusion allows rapid attainment of therapeutic levels.<sup>4</sup>

For these reasons the NHS Grampian Antimicrobial Management Team have agreed that **Infection Specialists or Medical Microbiologists can recommend** the use of extended infusions of piperacillin/tazobactam for patients (usually in critical care settings, i.e. ICU, Surgical HDU or Medical HDU) for treatment of resistant gram-negative infections. This is an off-label method of administration for piperacillin/tazobactam. It is appreciated that this method of infusion may not be possible in certain patients depending on venous access and infusion compatibilities.

Piperacillin/tazobactam should be prescribed on the main Prescription and Administration Record (PAR) (PECOS code ZOP105). The loading dose should be prescribed in the once-only section on the front page. The maintenance dose should be prescribed in the regular medication section, annotated 'as per extended infusion protocol' in the additional comments box. Maintenance infusions will also need prescribed on a Syringe/Volumetric Pump Prescription Sheet (PECOS code ZOP107).

The following patients should be **excluded** from this protocol for the administration of piperacillin/tazobactam by extended infusion: patients on haemodialysis, HDF/High flux or APD/CAPD.

The guidance below details how these infusions should be administered.

<b>Administration Of Extended (off-label) Infusion</b>	
All patients should receive a <b>loading dose<sup>4</sup></b> over 30 minutes immediately followed by the first 4 hour <b>extended infusion</b> then subsequent infusions at 6, 8 or 12 hourly intervals according to renal function (as noted below).	
<b>Loading dose<sup>4</sup>:</b>	4.5g infusion over 30 minutes.
<b>Usual Adult Daily Maintenance Dose:</b>	4.5g every 6 - 8 hours in normal renal function. Each dose via 4 hour extended infusion.
<b>Renal Impairment:</b> <a href="#">5.6.7</a>	
Not on dialysis but creatinine clearance (CrCl) 20 - 40mL/minute	Maximum dosage suggested in SPC is 4.5g every 8 hours.
Not on dialysis but CrCl <20mL/minute	Maximum dosage suggested in SPC is 4.5g every 12 hours.
CVVH or CVVHD/HDF	Dose as CrCl 20 – 40mL/minute above or calculate individual clearance rate (see <a href="#">Renal Drug Database</a> for information on calculation)
<b>Hepatic Impairment:</b>	
Patients with hepatic impairment can receive a loading dose and 4 hour extended infusions at usual adult dosage.	

<b>Reconstitution Directions:</b> <a href="#">1.5.6.8</a>	
•	Each vial of 4.5g should be reconstituted with 20mL of water for injections or 0.9% sodium chloride.
•	The contents of the vial should then be further diluted to the desired volume (50 to 100mL) with sodium chloride 0.9% or glucose 5%.
•	For loading dose – administer 50 - 100mL over 30 minutes.
•	For extended infusion - administer 50 - 100mL over 4 hours via a rate-controlled infusion device.
•	Start infusion immediately after preparation to reduce risk of microbial contamination.
•	Flush before and after administration with <a href="#">sodium chloride 0.9%</a> .

## Glossary

HDF	intermittent haemodiafiltration
APD/CAPD	ambulatory peritoneal dialysis/continuous ambulatory peritoneal dialysis
CVVH	continuous arteriovenous/venovenous haemofiltration
CVVHD/HDF	continuous venovenous haemodialysis/haemodiafiltration

## References:

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5. Summary of Product Characteristics for Tazocin 2.25g and 4.5g Powder for Solution for Infusion Pfizer Ltd Last updated on [www.medicines.org.uk](http://www.medicines.org.uk) on 7/9/17
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With thanks to NHS Tayside Antimicrobial Management Group for allowing us to use their Piperacillin/Tazobactam Extended Infusion Guidelines for writing version 1.

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This policy has been reviewed and agreed by;

- NHS Grampian Antimicrobial Management Team – May 2019