

Polymyxin B IV for infections outside of the urinary tract



Areas where Protocol/Guideline applicable	Inpatient ward areas including intensive care
Authorised Prescribers:	Infectious Diseases specialist or Microbiologist
Indication for use	<p>Antibacterial for the treatment of proven infections due to susceptible gram negative bacilli including <i>E.coli</i>, <i>Klebsiella sp</i>, <i>Pseudomonas sp</i>, <i>Acinetobacter sp</i> resistant to all of cefepime or ceftazidime, imipenem or meropenem, piperacillin-tazobactam, and ciprofloxacin.</p> <p>Some gram-negative organisms are intrinsically resistant to polymyxin B i.e. <i>Serratia spp.</i>, <i>Proteus spp.</i>, <i>Morganella spp.</i>, <i>Burkholderia Cepacia</i>, and <i>Providencia spp.</i></p> <p>Note: POLYMYXIN B IV is a highly restricted drug that requires specific approval from the Infectious Diseases or Microbiology service and the TGA Special Access Scheme (SAS) prior to use.</p>
Clinical condition Patient selection: Inclusion criteria	<p>Diagnosis of infection from susceptible gram negative organism with no susceptibility to all of cefepime, ceftazidime, imipenem or meropenem, piperacillin-tazobactam, ciprofloxacin.</p> <p>Do not use for infections arising from the urinary tract (polymyxin E/colistin is the preferred polymyxin for UTI)</p>
Proposed Place in Therapy	<p>Used for multi-drug resistant gram-negative infections only when susceptibility of the organism or drug availability mean there are no more suitable treatment options.</p> <p>Polymyxin B has a “detergent effect” on the cell membrane that allows restoration of antibacterial activity of drugs considered resistant as monotherapy.</p>
Adjunctive Therapy If part of combination therapy, list other drugs	Usually used in combination in moderate to severe infections with other antibiotics such as meropenem, although supportive data are limited. Please seek ID advice.
Contra-indications	<p>Known hypersensitivity to polymyxin B, or its excipients.</p> <p>Not recommended for inhalation therapy due to potential for damage to lung epithelial cells</p>

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<p>Precautions</p>	<p>Dosing is expressed in many forms:</p> <div style="border: 3px double black; padding: 5px; text-align: center; margin: 10px auto; width: fit-content;"> <p>1mg = 10,000 units</p> </div> <p>Nephrotoxic: Acute tubular necrosis (reversible)</p> <p>Neurotoxic: circumoral and peripheral paresthesia, vertigo, dizziness, blurred vision, ataxia, slurred speech, irritability, extremity numbness</p> <p>Neuromuscular blockade (can manifest as respiratory arrest)</p> <p>May exacerbate or unmask myasthenia gravis</p>
<p>Pregnancy Category</p>	<p>C</p>
<p>Important Drug Interactions</p>	<p>Nephrotoxic drugs (e.g. amphotericin, aminoglycosides, cidofovir, foscarnet, vancomycin): may increase risk of nephrotoxicity. Rifampicin co-administration may also increase nephrotoxicity. Where co-administration cannot be avoided, exercise caution when co-administering polymyxin B and other nephrotoxins, and monitor renal function closely.</p> <p>Non-depolarizing muscle relaxants (atracurium, vecuronium, pancuronium, tubocurarine): neuromuscular blockade may be enhanced with IM or IV use.</p>
<p>Dosage (for age 2 years and above)</p>	<p>For pathogens with MIC of 2mcg/ml or less:</p> <p>Loading dose (based on total body weight (TBW)*): 2.5mg/kg (25,000 units/kg) IV over 2 hours</p> <p>Maintenance dose (based on TBW*): (<i>12 hours post loading dose</i>) 1.5 mg/kg (15,000 units/kg) over 1 hour IV 12-hourly</p> <p>No dose adjustment required for patients with renal insufficiency.</p> <p>*Obesity: If obese (BMI≥30), suggest loading dose and maintenance dose based on adjusted body weight (ABW). There is limited experience with doses of >200mg (and >400mg in 24 hours) and increased risk of adverse effects with higher doses (including thoracic pain, paraesthesias, dizziness, dyspnoea and hypoxemia). Please consult with antimicrobial stewardship (AMS) pharmacist in morbid obesity.</p>
<p>Duration of therapy</p>	<p>Duration should be based on bacterial cultures and the patient's clinical response as guided by the Infectious Diseases Team.</p>
<p>Prescribing Instructions</p>	<p>Polymyxin B must be prescribed on the eMR or eRIC. In the absence of eMM systems, the appropriate paper medication chart may be used. Please obtain SAS A approval via the TGA online portal prior to prescribing.</p>

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<p>Administration Instructions</p>	<p>Reconstitute the 500, 000 unit vial with 2-10mL of WFI. Dilute the dose in 300-500 mL of glucose 5% and infuse over 60 to 120 minutes. The reconstituted solution should be used as soon as possible but is stable for 72 hours at 2-8°C. <i>Do not freeze.</i></p> <p>In fluid restricted patients: Doses of 0.5-1.5mg/kg have been diluted in 50 mL (Glucose 5% or Sodium chloride 0.9%) and infused over 60 minutes every 12-48 hours.</p>
<p>Monitoring requirements</p>	<p>Check renal function prior to therapy initiation. Daily electrolytes and urea, full blood count. Daily blood cultures until negative if bacteraemic. Regular monitoring of non-invasive blood pressure, pulse, temperature measurements.</p> <p>Monitor for signs and symptoms:</p> <p>Neuromuscular blockage: depressed respiration, muscle weakness, apnoea.</p> <p>Neurologic: peri-oral paresthesias, numbness of extremities, blurred vision, ataxia, drowsiness, irritability, dizziness.</p> <p>Nephrotoxicity: dose dependent reversible tubular necrosis. Increased risk nephrotoxicity with high daily dose, cumulative dose, and length of therapy. Also concomitant nephrotoxins (see “Important drug interactions”), obesity, age, diabetes mellitus, and hypertension.</p> <p>Skin hyperpigmentation reported (skin darkness of face, ears, neck and upper chest and head during therapy).</p> <p>Effectiveness is determined by clinical response and bacterial cultures</p> <p>Polymyxin B therapeutic drug monitoring (TDM) is not routinely done however may be available and helpful, especially for dosing uncertainty/obesity. Please contact AMS Pharmacist for assistance.</p>
<p>Management of Complications</p>	<p>Consideration of discontinuation of therapy and management of the specific complication, if severe.</p>

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<p>Basis of Protocol/Guideline: (including sources of evidence, references)</p>	<p>The Sanford Guide to Antimicrobial Therapy Web Edition. Available at: webedition.sanfordguide.com. Accessed January 10, 2025.</p> <p>UptoDate. Available at: https://www.uptodate.com.acs.hcn.com.au/contents/polymyxins-an-overview. Accessed January 10, 2025.</p> <p>Pharmacotherapy 2019; 39(1): 10-39.</p> <p>International Journal of Infectious Diseases. 2015; 30: 125-132.</p> <p>Antimicrobial Agents and Chemotherapy. 2018; 62(3): e01475-17.</p> <p>Antimicrobial Agents and Chemotherapy 2017; 61:e20690-16.</p> <p>Polymyxin B. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: www.micromedexsolutions.com. Accessed January 10, 2025.</p> <p>Australian Injectable Drug Handbook. 9th Ed.</p> <p>Johns Hopkins ABX Guide 2012. 3rd ed.</p> <p>Lancet ID 2015; 15: 225-34.</p> <p>CID 2008; 47: 1298.</p> <p>JAC 2010; 65: 2231.</p> <p>CID 2013; 57: 524</p> <p>CID 2014; 59(1): 88-94.</p> <p>CID doi:10.1093/cid/civ717</p>
<p>Groups consulted in development of this guideline</p>	<p>ID pharmacist, ID Department, Microbiology Department, Antimicrobial Stewardship Committee for Prince of Wales Hospital and St George Hospital, Clinical Applications Advisory Committee</p>

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