

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>B 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 preferred for UTI)</p>
Contra-indications	Known hypersensitivity to polymyxin B, or its excipients.
Precautions	<p>Do not use as monotherapy (combine with carbapenem or tigecycline or rifampicin)</p> <p>Dosing is expressed in many forms: 1mg = 10 000 units</p> <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 myasthenia gravis</p>
Proposed Place in Therapy	Used in combination with either carbapenem, tigecycline, or rifampicin for multiresistant gram negative infections.
Dosage	<p>Loading dose: 2.5mg/kg (25 000 units/kg) IV over 2 hours</p> <p>Maintenance dose: (12 hours post loading dose) 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>

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Duration of therapy	Duration should be based on bacterial cultures and the patient's clinical response. In general, therapy should continue for at least 5 days after the last negative blood culture.
Important Drug Interactions	Nephrotoxic drugs (e.g. amphotericin, aminoglycosides, cidofovir, foscarnet): may increase risk of nephrotoxicity. Avoid co-administration Non-depolarizing muscle relaxants (atracurium, vecuronium, pancuronium, tubocurarine): neuromuscular blockade may be enhanced with IM or IV use
Administration Instructions	Dilute each 500,000 unit vial 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> In fluid restricted patients: Doses of 1.5mg/kg have been diluted in 50 mL and infused over 60 minutes.
Monitoring requirements	Daily electrolytes and urea, full blood count. Daily blood cultures until negative if bacteraemic. Signs and symptoms of neuromuscular blockage (i.e. depressed respiration, muscle weakness, apnoea). Non-invasive blood pressure, pulse, temperature measurements. Effectiveness is determined by clinical response and bacterial cultures
Management of Complications	Consideration of discontinuation of therapy and management of the specific complication, if severe.
Basis of Protocol/Guideline: (including sources of evidence, references)	The Sanford Guide to Antimicrobial Therapy 2019. 49 th ed. Polymyxin B. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: www.micromedexsolutions.com . Accessed August 23, 2017. Johns Hopkins ABX Guide 2012. 3 rd ed. Lancet ID 2015; 15: 225-34. CID 2008; 47: 1298. JAC 2010; 65: 2231. CID 2013; 57: 524 CID 2014; 59(1): 88-94.
Groups consulted in development of this guideline	ID pharmacist, ID Department, Microbiology Department, Antimicrobial Stewardship Committee for Prince of Wales Hospital and St George Hospital, Guidance Management Committee

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GOVERNANCE	
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