

# SEPSIS INTRAVENOUS ANTIBIOTIC GUIDELINE ADULT - INPATIENT

The Clinical Excellence Commission (CEC) Adult Inpatient Sepsis Intravenous Antibiotic Guideline aims to guide the prescription and timely administration of antibiotics for **adult inpatients** that have a diagnosis of sepsis, severe sepsis or septic shock and have been admitted to hospital for 48 hours or more.

The guideline is based on the recommendations in *Therapeutic Guidelines: Antibiotic* version 14, 2010<sup>1</sup>. It is intended to provide an accessible resource, which can be adapted to suit individual facility preferences in liaison with the antimicrobial stewardship team and local antimicrobial susceptibility patterns. Antimicrobial stewardship teams may wish to refer to their latest hospital cumulative antibiogram, if available, when modifying the guideline.

**Prompt administration of antibiotics and resuscitation fluids is vital in the management of the patient with sepsis. The goal is to commence antibiotic therapy within the first hour of the recognition and diagnosis of severe sepsis.**

The selection of appropriate antimicrobial therapy is complex and this guideline is not intended to cover all possible scenarios.

Clinicians must review antimicrobial therapy within 24 hours of commencement, and change or cease antibiotics as required once microbiology results are available.

This guideline is not intended for:

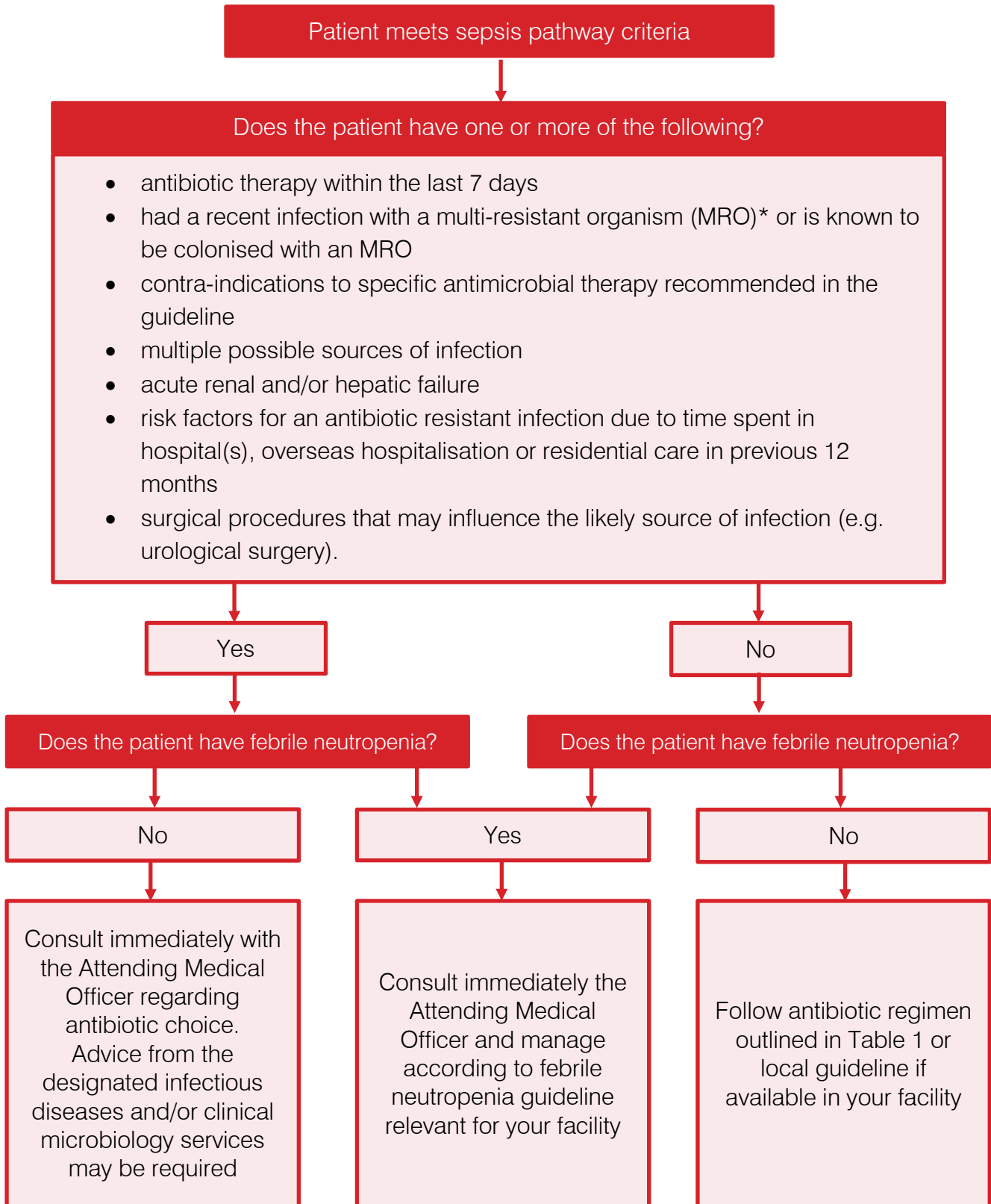
- patients with FEBRILE NEUTROPENIA who should be managed using local febrile neutropenia guidelines
- small hospitals and multi-purpose services where it would be more appropriate to use the Sepsis Adult FIRST DOSE Empirical Intravenous Antibiotic Guideline – Emergency Department
- patients who are deemed to have had incubating or unrecognised community acquired sepsis on admission. Use the Sepsis Adult FIRST DOSE Empirical Intravenous Antibiotic Guideline – Emergency Department

Obtain **at least two sets of blood cultures from separate venepuncture sites** before antibiotic administration.

Obtain other clinical specimens as appropriate **but do not delay administration of antibiotics** or wait for results of investigations.

The antimicrobial treatment indication and plan should be documented in the patient record.





\*Examples of MROs include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), extended-spectrum beta-lactamase (ESBL) producing organisms and carbapenem-resistant Gram negative organisms

**TABLE 1: ANTIBIOTIC PRESCRIBING (review after 24 hours)**

Apparent source of sepsis	Sepsis antibiotic regimen	Penicillin allergic <u>not immediate</u> hypersensitivity	Penicillin or cephalosporin allergic <u>Immediate</u> hypersensitivity or severe prior reaction
<p>Sepsis secondary to hospital acquired pneumonia, <i>low risk of MRO</i></p> <p><i>(generally patient who has been in hospital &lt; 5 days who does not have risk factors for MRO)</i></p>	ceftriaxone 1 g IV, daily	ceftriaxone 1 g IV, daily	moxifloxacin 400 mg IV, daily
	OR	OR	
	benzylpenicillin 1.2 g IV, 6-hourly PLUS gentamicin 4 to 6 mg/kg IV, for 1 dose (severe sepsis 7 mg/kg)	cefotaxime 1 g IV, 8-hourly	
	OR		
	cefotaxime 1 g IV, 8-hourly		
	OR		
	piperacillin+tazobactam 4+0.5 g IV, 8-hourly		
OR			
ticarcillin+clavulanate 3+0.1 g IV, 6-hourly			
<p>Sepsis secondary to hospital acquired pneumonia, <i>high risk of MRO</i></p>	piperacillin+tazobactam 4+0.5 g IV, 6-hourly	cefepime 2 g IV, 8-hourly	Seek expert advice
	OR	<i>If the patient is ventilated</i> ADD gentamicin 4 to 6 mg/kg IV, for 1 dose (severe sepsis: 7 mg/kg)	
	ticarcillin+clavulanate 3+0.1 g IV, 6-hourly		
	OR		
	cefepime 2 g IV, 8-hourly		
	<i>If the patient is ventilated</i> ADD gentamicin 4 to 6 mg/kg IV, for 1 dose (severe sepsis: 7 mg/kg)		
<i>If MRSA prevalent in your hospital</i> ADD vancomycin 1.5g IV, 12-hourly	<i>If MRSA prevalent in your hospital</i> ADD vancomycin 1.5g IV, 12-hourly		



**TABLE 1: ANTIBIOTIC PRESCRIBING (review after 24 hours)**

Apparent source of sepsis	Sepsis antibiotic regimen	Penicillin allergic <u>not immediate</u> hypersensitivity	Penicillin or cephalosporin allergic <u>Immediate</u> hypersensitivity or severe prior reaction
Severe sepsis with an apparent urinary tract source	gentamicin 4-7 mg/kg IV, for 1 dose PLUS ampicillin 2 g IV, 6-hourly	gentamicin 4-7 mg/kg IV, for 1 dose	gentamicin 4-7 mg/kg IV, for 1 dose
		OR	
		ceftriaxone 1 g IV, daily <i>if gentamicin is contraindicated</i>	
		OR	
		cefotaxime 1 g IV, 8-hourly <i>if gentamicin is contraindicated</i>	
Severe sepsis with an apparent biliary or gastrointestinal tract source	ampicillin 1 g IV, 6-hourly PLUS gentamicin 4 to 7 mg/kg IV, for 1 dose PLUS metronidazole 500 mg IV, 12-hourly	metronidazole 500 mg IV, 12-hourly PLUS ceftriaxone 1 g IV, daily	gentamicin 4 to 7 mg/kg IV, for 1 dose AND seek expert advice
		OR	
		metronidazole 500 mg IV, 12-hourly PLUS cefotaxime 1 g IV, 8-hourly	
Severe sepsis resulting from a skin infection (including cellulitis) or surgical site infection	flucloxacillin 2 g IV, 6-hourly	cephazolin 2 g IV, 8-hourly	clindamycin 450 mg IV, 8-hourly
	<i>If MRSA prevalent in your hospital</i> ADD vancomycin 1.5g IV, 12-hourly	<i>If MRSA prevalent in your hospital</i> ADD vancomycin 1.5g IV, 12-hourly	OR
			vancomycin 1.5 g IV, 12-hourly
Maternal sepsis (peri or post-partum) if source unclear	piperacillin+tazobactam 4+0.5 g IV, 8-hourly	ceftriaxone 1g IV, 24-hourly PLUS metronidazole 500mg IV 12-hourly	Seek expert advice
	<i>If patient meets criteria for toxic shock</i> ADD clindamycin 600mg IV, 8-hourly		
	<i>If likely to be MRSA colonized</i> ADD vancomycin 1.5g IV, 12-hourly	<i>If patient meets criteria for toxic shock</i> ceftriaxone 1g IV, 24-hourly PLUS clindamycin 600mg IV, 8-hourly <i>in place of above regimen</i>	



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Apparent source of sepsis	Sepsis antibiotic regimen	Penicillin allergic <u>not immediate</u> hypersensitivity	Penicillin or cephalosporin allergic <u>Immediate</u> hypersensitivity or severe prior reaction
Maternal sepsis likely to be due to Group A streptococcal infection	benzylpenicillin 2.4g IV, 4-hourly PLUS clindamycin 600mg iv 8-hourly	cephazolin 2 g IV, 6-hourly PLUS clindamycin 600mg iv 8-hourly	Seek expert advice
	OR	OR	
	benzylpenicillin 2.4g IV, 4-hourly PLUS lincomycin 600 mg IV 8-hourly	cephazolin 2 g IV, 6-hourly PLUS lincomycin 600 mg IV 8-hourly	
Severe sepsis, unknown source or focus, including possible IV line-associated sepsis <b>Removal of the infected IV device is usually required</b>	flucloxacillin 2 g IV, 6-hourly PLUS gentamicin 4-7 mg/kg IV, for 1 dose	cephazolin 2 g IV, 8-hourly PLUS gentamicin 4-7 mg/kg IV, for 1 dose	vancomycin 1.5 g IV, 12-hourly PLUS gentamicin 4-7 mg/kg IV, for 1 dose
	<i>If MRSA prevalent in your hospital</i> ADD vancomycin 1.5g 12-hourly	<i>If MRSA prevalent in your hospital</i> ADD vancomycin 1.5g 12-hourly	

**NOTES FOR TABLE 1**

Definitions of penicillin hypersensitivity	<p><b>Immediate hypersensitivity</b> involves the development of urticaria, angioedema, bronchospasm or anaphylaxis within one to two hours of drug administration.</p> <p><b>Severe prior reaction</b> involves a history of drug rash eosinophilia and systemic symptoms (DRESS) or Stevens-Johnson Syndrome following administration of a penicillin or cephalosporin.</p> <p>All penicillin and cephalosporin class antibiotics are contraindicated in patients with history of drug rash eosinophilia and systemic symptoms (DRESS), Stevens-Johnson Syndrome or IgE-mediated immediate penicillin or cephalosporin allergy.</p> <p>Refer to <i>Therapeutic Guidelines: Antibiotic</i> for more information  <a href="http://etg.hcn.com.au/desktop/tgc/abg/1315.htm">http://etg.hcn.com.au/desktop/tgc/abg/1315.htm</a></p>
Definitions of low risk and high risk of MRO	<p>Refer to <i>Therapeutic Guidelines: Antibiotic</i> for more information  <a href="http://etg.hcn.com.au/desktop/tgc/abg/5313.htm">http://etg.hcn.com.au/desktop/tgc/abg/5313.htm</a></p>
Doses for renal impairment (creatinine clearance ≤ 60mL/min)	<p><b>Consult AMO (who may request referral to ID/Microbiology) in conjunction with guidance provided in <i>Therapeutic Guidelines: Antibiotic</i></b>  <a href="http://etg.hcn.com.au/desktop/tgc/abg/8571.htm">http://etg.hcn.com.au/desktop/tgc/abg/8571.htm</a></p>

Gentamicin and vancomycin dosing and frequency	Refer to <i>Therapeutic Guidelines: Antibiotic</i> for more information <a href="http://etg.hcn.com.au/desktop/tgc/abg/7823.htm">http://etg.hcn.com.au/desktop/tgc/abg/7823.htm</a> <a href="http://etg.hcn.com.au/desktop/tgc/abg/7971.htm">http://etg.hcn.com.au/desktop/tgc/abg/7971.htm</a>
Criteria for toxic shock	Refer to <i>Therapeutic Guidelines: Antibiotic</i> for more information <a href="http://etg.hcn.com.au/desktop/tgc/abg/6225.htm">http://etg.hcn.com.au/desktop/tgc/abg/6225.htm</a>
Notes for gentamicin	<p>One dose of gentamicin is recommended; for subsequent doses, assess renal function and adjust frequency accordingly</p> <p>Use for a maximum of 48 hours as empirical therapy pending outcome of investigations; monitoring of plasma concentrations NOT required if gentamicin is not used beyond 48 hours</p> <p>Directed therapy (beyond 48 hours, based on microbiology results) should be used on the advice of infectious diseases physician or clinical microbiologist only</p> <p>Dose should be based on ideal body weight or actual body weight – <b>whichever of the two is lower</b></p> <p><b>The maximum dose of gentamicin in severe sepsis is 640 mg</b></p> <p>For other indications, the maximum dose is lower. Refer to Table 2.24 in <i>Therapeutic guidelines: Antibiotic</i>, version 14, 2010.</p> <p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>Previous vestibular or auditory toxicity due to an aminoglycoside</li> <li>Serious hypersensitivity reaction to an aminoglycoside</li> </ul> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>Pre-existing significant hearing problems</li> <li>Pre-existing vestibular problems</li> <li>Neuromuscular disorders, including myasthenia gravis</li> <li>Chronic liver disease or severe cholestasis (bilirubin above 90 micromol/L)</li> <li>Chronic renal failure or deteriorating renal function – consult AMO</li> </ul>



**TABLE 2: ANTIBIOTIC ADMINISTRATION <sup>2,3</sup>**

- Reconstitute antibiotics with sterile water for injection (WFI) unless stated otherwise.
- If further dilution is required for IV injection or infusion, use sterile sodium chloride 0.9% or sterile glucose 5% unless stated otherwise.
- Where possible use separate dedicated lines for resuscitation fluid and for medications. When injecting antibiotics directly into an IV injection port which has resuscitation fluid running:
  - clamp the infusion fluid line and flush with 20 mL sterile sodium chloride 0.9% solution
  - administer antibiotic over the required time
  - flush the line with 20 mL sterile sodium chloride 0.9% solution and recommence resuscitation fluid.

Antibiotic	Presentation (adult)	Reconstitution fluid/volume	Final volume	Minimum administration time	Notes
ampicillin	Vial 1 g	10 mL WFI	10 - 20 mL	3 – 5 minutes	Penicillin class antibiotic
benzylpenicillin	Vial 600 mg	2 mL WFI	10 mL	3 – 5 minutes	Penicillin class antibiotic  <b>Doses ≥ 1.2 g must be administered over 30 minutes</b>
	Vial 1.2 g	4 mL WFI			
cefepime	Vial 1 g	10 mL NS	10 mL	3 - 5 minutes	Cephalosporin class antibiotic  <b>Doses ≥ 2 g must be administered over 20 minutes</b>
ceftriaxone	Vial 1 g	10 mL WFI	10 mL	2 – 4 minutes	Cephalosporin class antibiotic incompatible with calcium containing solutions, flush thoroughly before and after with sodium chloride 0.9%
cefotaxime	Vial 1 g	10mL WFI	10 mL	3 – 5 minutes	Cephalosporin class antibiotic
cephazolin	Vial 1 g	10 mL WFI	10 mL	3 – 5 minutes	Cephalosporin class antibiotic
clindamycin	Ampoules 300 mg/2 mL 600 mg/4 mL	N/A	600 mg in 50 mL	20 minutes	Check product is clear of any crystals prior to administration
			900 mg in 100 mL	30 minutes	



Antibiotic	Presentation (adult)	Reconstitution fluid/volume	Final volume	Minimum administration time	Notes
flucloxacillin	Vial 1 g	5 mL WFI	10 mL	3 - 5 minutes (1 g)	Penicillin class antibiotic <b>Repeated doses of 2 g via a peripheral line should be further diluted and infused over 20 – 30 minutes</b>
			20 mL	10 minutes (2 g)	
gentamicin	Ampoule 80 mg/2 mL	N/A	10- 20 mL	(240mg or less) 3 – 5 minutes	Refer to notes for gentamicin
			50 mL or 100 mL	(more than 240mg) 30 minutes	
lincomycin	Vial 600mg/2mL	N/A	100mL	60 minutes	
metronidazole	Infusion bag 500 mg / 100 mL	N/A	See presentation column	20 minutes	
moxifloxacin	Infusion bag 400 mg / 250 mL	N/A	See presentation column	60 minutes	May prolong QT interval and lead to ventricular arrhythmias. May induce seizures in epileptics
piperacillin with tazobactam	Vial 4 g/0.5 g	20 mL WFI	50 mL	30 minutes	Penicillin class antibiotic
ticarcillin with clavulanic acid	Vial 3 g/0.1 g	13 mL WFI	50 mL	30 minutes	Penicillin class antibiotic
vancomycin	Vial 500 mg	10 mL WFI	Dilute to maximum concentration of 5mg/mL for peripheral line	Maximum of 10 mg/minute	Infusion related effects are common, decrease infusion rate and monitor closely if these occur
	Vial 1 g	20 mL WFI			



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## FURTHER MANAGEMENT

The patient should be reviewed by the Attending Medical Officer within 24 hours of commencing the sepsis pathway and antibiotic therapy, with referral to the infectious diseases and/or clinical microbiology services for specific advice.

Microbiology results are generally available within 48-72 hours, and should be used to guide further management of the patient. This may include de-escalating or ceasing antimicrobial therapy.

Clinicians that are experiencing difficulty in assessing positive or negative microbiology results when rationalising antibiotic therapy at 48-72 hours should contact the designated infectious diseases and/or clinical microbiology services.

*Check local instructions regarding referral*

### References

1. Antibiotic Expert Group. *Therapeutic Guidelines: Antibiotic. Version 14*. Melbourne: Therapeutic Guidelines Limited; 2010. Accessed through eTG complete (via CIAP).
2. Burridge N (ed). *Australian Injectable Drugs Handbook (4th ed)*. The Society of Hospital Pharmacists Australia; 2008.
3. Rossi S (ed). *Australian Medicines Handbook*. Chapter 5. Adelaide: Australian Medicines Handbook



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