ADULT
ANTIBIOTIC GUIDELINE
FOR SEVERE SEPSIS AND SEPTIC SHOCK

Updated September 2016

Version 3





SEPSIS KILLS®

RECOGNISE · RESUSCITATE · REFER

CLINICAL EXCELLENCE COMMISSION

National Library of Australia Cataloguing-in-Publication entry
Title: Adult Antibiotic Guideline for Severe Sepsis & Septic Shock
SHPN: (CEC) 160035

Suggested citation
Clinical Excellence Commission, 2016, Adult Antibiotic Guideline for Severe Sepsis & Septic Shock
Sydney: Clinical Excellence Commission

Clinical Excellence Commission
Board Chair: Associate Professor Brian McCaughan, AM
Chief Executive: Ms. Carrie Marr

Any enquiries about or comments on this publication should be directed to:
Clinical Excellence Commission
Locked Bag 8
Haymarket NSW 1240
Phone: (02) 9269 5500
Email: cec-sepsis@health.nsw.gov.au

CONTENTS

DOCUMENT PURPOSE

The Clinical Excellence Commission (CEC) Adult Antibiotic Guideline for Severe Sepsis & Septic Shock aims to guide the prescription and timely administration of antibiotics for **adult patients (16 years and over) that have a diagnosis of severe sepsis or septic shock,** where the source is suspected or unknown.

Definitions of sepsis[1]

SEPSIS	Infection, either suspected or confirmed, with systemic features such as fever, tachycardia, tachypnoea or elevated white cell count
SEVERE SEPSIS	Sepsis + organ dysfunction or hypoperfusion
SEPTIC SHOCK	Sepsis + hypotension despite adequate volume resuscitation

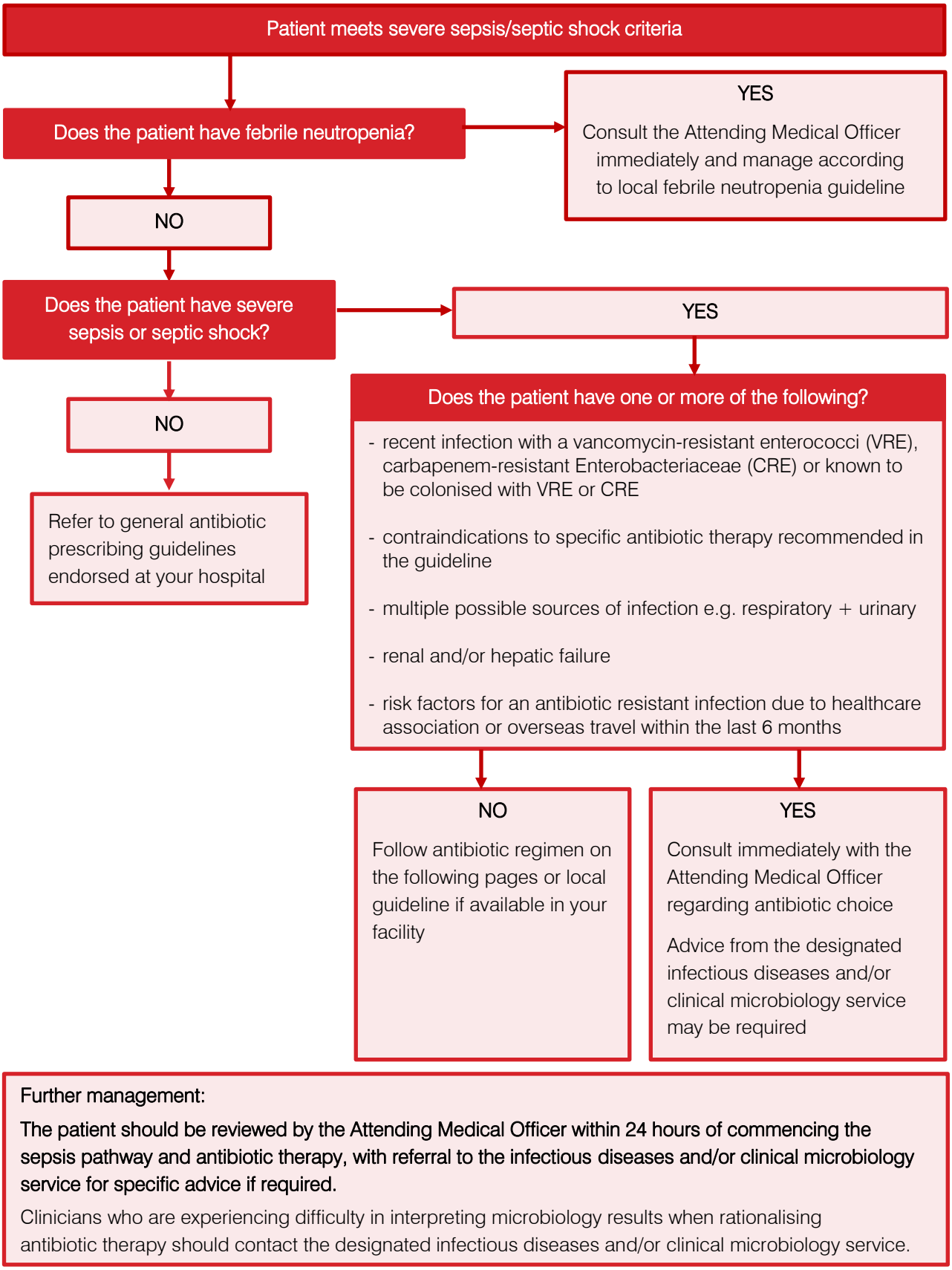
This guideline is not intended for:

- Paediatric and Neonatal patients → use antibiotic prescribing guidelines endorsed at your hospital e.g. *Therapeutic Guidelines: Antibiotic*
- Patients with febrile neutropenia → use local febrile neutropenia guideline
- Patients with immunological conditions → consult with the patient's usual health service provider. If a delay is anticipated, commence antibiotics according to this guideline with subsequent modification as appropriate
- Patients who do not have severe sepsis or septic shock as defined above, but have sepsis or infection, either suspected or confirmed → use antibiotic prescribing guidelines endorsed at your hospital e.g. *Therapeutic Guidelines: Antibiotic*
- Complex sources of sepsis such as necrotising fasciitis or sepsis from a suspected cardiac source, e.g. infective endocarditis → seek expert advice to determine therapy
- Patients who have been discharged from hospital in the last 7 days → seek expert advice to determine therapy.

IMPORTANT POINTS TO CONSIDER WHEN USING THIS GUIDELINE:

- The selection of appropriate antibiotic therapy is complex - this guideline is not intended to cover all possible scenarios
- Prompt administration of antibiotics and resuscitation fluids is vital in the management of the patient with sepsis. In patients diagnosed with severe sepsis or septic shock the goal is to commence antibiotic therapy within the first hour
- Obtain at least two sets of blood cultures and other clinical specimens (e.g. urine, cerebrospinal fluid, wound swabs) as appropriate PRIOR TO antibiotic commencement. Do not delay antibiotic administration to wait for results of investigations.
- If agents listed are not available in your hospital, consult the Attending Medical Officer and seek expert advice
- Patients must be weighed to ensure correct dosage of medications
- Clinicians must document the indication, drug name, dose, route of administration and review date for antibiotics in the patient's health record
- Antibiotic therapy should be reviewed by the treating team 24 hours and 48 hours after commencement
- Antibiotics should be reviewed once microbiology results are available, and continued, changed or ceased as required

ADULT ANTIBIOTIC GUIDELINE FOR SEVERE SEPSIS & SEPTIC SHOCK DECISION TREE



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 service for specific advice if required.

Clinicians who are experiencing difficulty in interpreting microbiology results when rationalising antibiotic therapy should contact the designated infectious diseases and/or clinical microbiology service.

INDICATION: SEVERE SEPSIS SECONDARY TO COMMUNITY-ACQUIRED PNEUMONIA [Note 1]

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	ceftriaxone **[Note 2]** 1 g, 12-hourly **PLUS** azithromycin 500 mg, daily **OR** benzylpenicillin 1.2 g, 4-hourly **PLUS** gentamicin **[Note 3]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** azithromycin 500 mg, daily	ceftriaxone **[Note 2]** 1 g, 12-hourly **PLUS** azithromycin 500 mg, daily	moxifloxacin 400 mg, daily

Note 1: Patients with severe CAP (see assessment of pneumonia severity) are more likely to require intensive respiratory or vasopressor support, usually in an intensive care unit. Empirical antibiotic therapy should treat a broad range of pathogens (*Streptococcus pneumoniae*, *Legionella pneumophila* and enteric Gram-negative bacilli). Importantly, also consider whether influenza or *Staphylococcus aureus* are potential causes of disease and treat accordingly.

Note 2: Many of the recommended regimens for CAP have broad anaerobic activity (e.g. amoxycillin+clavulanate, piperacillin+tazobactam, moxifloxacin, meropenem) and thus do not require the addition of metronidazole. Other regimens (e.g. cefepime, ceftriaxone) only have limited anaerobic activity; **ADD metronidazole 500 mg IV, 12-hourly for patients who have severe aspiration pneumonia, severe periodontal disease, history of chronic hazardous alcohol consumption or necrotising pneumonia.**

Note 3: Aminoglycosides (AGs) are rapidly bactericidal and effective for most Gram negative bacteria, including many ESBLs and *Pseudomonas spp*. However AGs are CONTRAINDICATED in myasthenia gravis, prior aminoglycoside allergy and vestibulocochlear disease. In severe sepsis 7mg/kg ideal body weight (IBW) is recommended (Link to IBW table). Precautions must be taken with creatinine clearance <60 ml/min or >80 years of age, and a dose of 4-5mg/kg (IBW) is recommended: see *Therapeutic Guidelines: Antibiotic* or seek expert advice. Monitoring the aminoglycoside plasma concentration is mandatory from the first dose of directed therapy or if therapy is planned for longer than 48 hours. Use the Cockcroft-Gault formula to estimate creatinine clearance.

INDICATION: SEVERE SEPSIS SECONDARY TO HOSPITAL-ACQUIRED PNEUMONIA , LOWER RISK OF MULTI-RESISTANT ORGANISMS [Note 1]

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	ceftriaxone **[Note 2]** 1 g, 12-hourly **OR** benzylpenicillin 1.2 g, 4-hourly **PLUS** gentamicin **[Note 3]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level	ceftriaxone **[Note 2]** 1 g, 12-hourly	moxifloxacin 400 mg, daily

Note 1: Patients hospitalised in a low-risk ward (for any duration) or in a high-risk area for less than 5 days should have therapy aimed at *Streptococcus pneumoniae* and non-MRO Gram negative bacilli as described above.

Note 2: Many of the recommended regimens for HAP have broad anaerobic activity (e.g. amoxycillin+clavulanate, piperacillin+tazobactam, moxifloxacin, meropenem) and thus do not require the addition of metronidazole. Other regimens (e.g. cefepime, ceftriaxone) only have limited anaerobic activity; **ADD metronidazole 500 mg IV, 12-hourly for patients who have severe aspiration pneumonia, severe periodontal disease, history of chronic hazardous alcohol consumption or necrotising pneumonia.**

Note 3: Aminoglycosides (AGs) are rapidly bactericidal and effective for most Gram negative bacteria, including many ESBLs and *Pseudomonas spp*. However AGs are CONTRAINDICATED in myasthenia gravis, prior aminoglycoside allergy and vestibulocochlear disease. In severe sepsis 7mg/kg ideal body weight (IBW) is recommended (Link to IBW table). Precautions must be taken with creatinine clearance <60 ml/min or >80 years of age, and a dose of 4-5mg/kg (IBW) is recommended: see *Therapeutic Guidelines: Antibiotic* or seek expert advice. Monitoring the aminoglycoside plasma concentration is mandatory from the first dose of directed therapy or if therapy is planned for longer than 48 hours. Use the Cockcroft-Gault formula to estimate creatinine clearance.

INDICATION: SEVERE SEPSIS SECONDARY TO HOSPITAL-ACQUIRED PNEUMONIA , HIGHER RISK OF MULTI-RESISTANT ORGANISMS [Note 1]

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	piperacillin+tazobactam 4+0.5 g, 6-hourly **PLUS** vancomycin **[Note 3]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	cefepime **[Note 2]** 2 g, 8-hourly **PLUS** vancomycin **[Note 3]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	seek expert advice

Note 1: Patients hospitalised for 5 days or longer in high-risk areas have infections which are more likely to be caused by multi-resistant organisms. As survival is improved by early appropriate therapy a broader-spectrum initial regimen is required.

Note 2: Many of the recommended regimens for HAP have broad anaerobic activity (e.g. amoxycillin+clavulanate, piperacillin+tazobactam, moxifloxacin, meropenem) and do not require the addition of metronidazole. Other regimens (e.g. cefepime, ceftriaxone) only have limited anaerobic activity; **ADD metronidazole 500 mg IV, 12-hourly for patients who have severe aspiration pneumonia, severe periodontal disease, history of chronic hazardous alcohol consumption or necrotising pneumonia.**

Note 3: In severe sepsis an IV loading dose is required: vancomycin 25-30 mg/kg actual body weight, with the second dose and interval to be determined according to creatinine clearance, calculated with the Cockcroft-Gault formula.

INDICATION: SEVERE SEPSIS SECONDARY TO URINARY TRACT SOURCE including recent urological procedures

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	gentamicin **[Note 1]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** amoxycillin/ampicillin 2 g, 6-hourly	gentamicin **[Note 1]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level	gentamicin **[Note 1]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level
	If ESBL-producing organisms are known or suspected [Note 2] **USE** amikacin **[Note 1]** 16 - 20 mg/kg daily	*If ESBL-producing organisms are known or suspected* [Note 2] **USE** amikacin **[Note 1]** 16 - 20 mg/kg daily	*If ESBL-producing organisms are known or suspected* [Note 2], **USE** amikacin **[Note 1]** 16 - 20 mg/kg daily
	OR	**OR**	
	meropenem 1 g IV, 8-hourly	meropenem 1 g IV, 8-hourly	

Note 1: Aminoglycosides (AGs) are rapidly bactericidal and effective for most Gram negative bacteria, including many ESBLs and *Pseudomonas spp*. However AGs are CONTRAINDICATED in myasthenia gravis, prior aminoglycoside allergy and vestibulocochlear disease. In severe sepsis 7mg/kg ideal body weight (IBW) is recommended (Link to IBW table). Precautions must be taken with creatinine clearance <60 ml/min or >80 years of age, and a dose of 4-5mg/kg (IBW) is recommended: see *Therapeutic Guidelines: Antibiotic* or seek expert advice. Monitoring the aminoglycoside plasma concentration is mandatory from the first dose of directed therapy or if therapy is planned for longer than 48 hours. Use the Cockcroft-Gault formula to estimate creatinine clearance.

Note 2: Risk factors for ESBL-producing organisms include travel to Asia or the Indian subcontinent in the previous 6 months, prolonged hospitalisation, residence in a long-term care facility, previous ESBL colonisation or infection, and broad spectrum cephalosporin or quinolone antibiotic use in the last month.

INDICATION: SEVERE SEPSIS SECONDARY TO BILIARY SOURCE e.g. ascending cholangitis

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	gentamicin **[Note 1]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** amoxycillin/ampicillin 2 g, 6-hourly	ceftriaxone 1 g, 12-hourly	gentamicin **[Note 1]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level
	In patients with chronic biliary obstruction **ADD** metronidazole 500 mg IV, 12-hourly	*In patients with chronic biliary obstruction* **ADD** metronidazole 500 mg IV, 12-hourly	*In patients with chronic biliary obstruction* Seek expert advice

Note 1: Aminoglycosides (AGs) are rapidly bactericidal and effective for most Gram negative bacteria, including many ESBLs and *Pseudomonas spp*. However AGs are CONTRAINDICATED in myasthenia gravis, prior aminoglycoside allergy and vestibulocochlear disease. In severe sepsis 7mg/kg ideal body weight (IBW) is recommended (Link to IBW table). Precautions must be taken with creatinine clearance <60 ml/min or >80 years of age, and a dose of 4-5mg/kg (IBW) is recommended: see *Therapeutic Guidelines: Antibiotic* or seek expert advice. Monitoring the aminoglycoside plasma concentration is mandatory from the first dose of directed therapy or if therapy is planned for longer than 48 hours. Use the Cockcroft-Gault formula to estimate creatinine clearance.

INDICATION: SEVERE SEPSIS SECONDARY TO GASTRO-INTESTINAL SOURCE e.g. acute peritonitis [Note 1]

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	gentamicin **[Note 2]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** amoxycillin/ampicillin 2 g, 6-hourly **PLUS** metronidazole 500 mg, 12-hourly	ceftriaxone 1 g, 12-hourly **PLUS** metronidazole 500 mg, 12-hourly	gentamicin **[Note 2]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** clindamycin 600 mg, 8-hourly

Note 1: If ESBL-producing organisms are known or suspected – seek expert advice. Risk factors for ESBL-producing organisms include travel to Asia or the Indian subcontinent in the previous 6 months, prolonged hospitalisation, residence in a long-term care facility, previous ESBL colonisation or infection, and broad spectrum cephalosporin or quinolone antibiotic use in the last month.

Note 2: Aminoglycosides (AGs) are rapidly bactericidal and effective for most Gram negative bacteria, including many ESBLs and *Pseudomonas spp*. However AGs are CONTRAINDICATED in myasthenia gravis, prior aminoglycoside allergy and vestibulocochlear disease. In severe sepsis 7mg/kg ideal body weight (IBW) is recommended (Link to IBW table). Precautions must be taken with creatinine clearance <60 ml/min or >80 years of age, and a dose of 4-5mg/kg (IBW) is recommended: see *Therapeutic Guidelines: Antibiotic* or seek expert advice. Monitoring the aminoglycoside plasma concentration is mandatory from the first dose of directed therapy or if therapy is planned for longer than 48 hours. Use the Cockcroft-Gault formula to estimate creatinine clearance.

INDICATION: SEVERE SEPSIS SECONDARY TO CELLULITIS INCLUDING SURGICAL WOUND INFECTION

consult with surgical team

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	flucloxacillin 2 g, 6-hourly *If there is a risk of MRSA* ADD vancomycin **[Note 1]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	cephazolin 2 g, 8-hourly *If there is a risk of MRSA* ADD vancomycin **[Note 1]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	vancomycin **[Note 1]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level
	If Gram-negative organisms are suspected e.g. post–gastrointestinal or genital-tract surgery ADD gentamicin **[Note 2]** 7 mg/kg, ideal body weight daily, second dose and interval to be determined according to creatinine level OR for water related infections: **[Note 3]** ADD ciprofloxacin 400mg, 12-hourly		

Note 1: In severe sepsis an IV loading dose is required: vancomycin 25-30 mg/kg actual body weight, with the second dose and interval to be determined according to creatinine clearance, calculated with the Cockcroft-Gault formula.

Note 2: Aminoglycosides (AGs) are rapidly bactericidal and effective for most Gram negative bacteria, including many ESBLs and *Pseudomonas spp*. However AGs are CONTRAINDICATED in myasthenia gravis, prior aminoglycoside allergy and vestibulocochlear disease. In severe sepsis 7mg/kg ideal body weight (IBW) is recommended (Link to IBW table). Precautions must be taken with creatinine clearance <60 ml/min or >80 years of age, and a dose of 4-5mg/kg (IBW) is recommended: see *Therapeutic Guidelines: Antibiotic* or seek expert advice. Monitoring the aminoglycoside plasma concentration is mandatory from the first dose of directed therapy or if therapy is planned for longer than 48 hours. Use the Cockcroft-Gault formula to estimate creatinine clearance.

Note 3: Severe sepsis following contact with water e.g. in fishermen, swimmers or aquarium owners, may involve *Aeromonas* spp. (source: fresh or brackish water, or mud); *Mycobacterium marinum* (most common source: fish tanks); *Shewanella putrefaciens*; and *Vibrio vulnificus*, *Vibrio alginolyticus* and other noncholera vibrios (source: salt or brackish water). Collect samples for Gram stain and cultures prior to commencing antibiotic therapy.

INDICATION: SEVERE SEPSIS SECONDARY TO DIABETIC FOOT INFECTION [Note 1]

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	piperacillin+tazobactam 4+0.5 g, 6-hourly	ciprofloxacin 400 mg, 12-hourly **PLUS** clindamycin 600 mg, 8-hourly	ciprofloxacin 400 mg, 12-hourly **PLUS** clindamycin 600 mg, 8-hourly

Note 1: Vancomycin may be required for severe limb or life threatening infection in addition to the above regimen, based on risk factors including previous colonization or infection, or prolonged admission on a high prevalence ward. The recommended dose of vancomycin in severe sepsis is vancomycin 25-30 mg/kg actual body weight, with the second dose and interval to be determined according to creatinine clearance, calculated with the Cockcroft-Gault formula.

INDICATION: SEVERE SEPSIS SECONDARY TO INTRAVASCULAR DEVICE SOURCE [Note 1]

Suspect IV device source when there is no other apparent focus for sepsis, even if there is no direct evidence of infection around the IV exit site. Early removal of the device is strongly recommended.

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	gentamicin **[Note 2]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** flucloxacillin 2 g, 6-hourly **PLUS** vancomycin **[Note 3]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	gentamicin **[Note 2]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** cephazolin 2 g, 8-hourly **PLUS** vancomycin **[Note 3]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	gentamicin **[Note 2]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** vancomycin **[Note 3]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level

Note 1: Intravascular devices may include venous access devices, permanent pacemakers or defibrillators, or endovascular prostheses such as stents.

Note 2: Aminoglycosides (AGs) are rapidly bactericidal and effective for most Gram negative bacteria, including many ESBLs and *Pseudomonas spp*. However AGs are CONTRAINDICATED in myasthenia gravis, prior aminoglycoside allergy and vestibulocochlear disease. In severe sepsis 7mg/kg ideal body weight (IBW) is recommended (Link to IBW table). Precautions must be taken with creatinine clearance <60 ml/min or >80 years of age, and a dose of 4-5mg/kg (IBW) is recommended: see *Therapeutic Guidelines: Antibiotic* or seek expert advice. Monitoring the aminoglycoside plasma concentration is mandatory from the first dose of directed therapy or if therapy is planned for longer than 48 hours. Use the Cockcroft-Gault formula to estimate creatinine clearance.

Note 3: In severe sepsis an IV loading dose is required: vancomycin 25-30 mg/kg actual body weight, with the second dose and interval to be determined according to creatinine clearance, calculated with the Cockcroft-Gault formula.

INDICATION: SEVERE SEPSIS SECONDARY TO TOXIC SHOCK SYNDROME

<table>
<tr><th rowspan="2">ROUTE OF ADMINISTRATION</th><th colspan="3">PENICILLIN ALLERGY STATUS</th></tr>
<tr><th>NO PENICILLIN ALLERGY</th><th>NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY</th><th>IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)</th></tr>
<tr><td rowspan="3">Intravenous (IV) or intraosseous</td><td>flucloxacillin 2 g, 4 hourly
PLUS
clindamycin
600 mg, 8-hourly</td><td>cephazolin 2 g, 6-hourly
PLUS
clindamycin
600 mg, 8-hourly</td><td rowspan="2">vancomycin [Note 1]
25-30 mg/kg actual body weight loading dose
second dose and interval to be determined according to creatinine level
PLUS
clindamycin
600 mg, 8-hourly</td></tr>
<tr><td colspan="2">If there is a risk of MRSA
ADD
vancomycin [Note 1]
25-30 mg/kg actual body weight loading dose,
second dose and interval to be determined according to creatinine level</td></tr>
<tr><td colspan="3">Consider the addition of IV immunoglobulin
normal immunoglobulin 1 to 2 g/kg IV for up to 2 doses during the first 72 hours</td></tr>
</table>

Note 1: In severe sepsis an IV loading dose is required: vancomycin 25-30 mg/kg actual body weight, with the second dose and interval to be determined according to creatinine clearance, calculated with the Cockcroft-Gault formula.

INDICATION: SEVERE SEPSIS SECONDARY TO NEUROLOGICAL SOURCE, ORGANISM OR SUSCEPTIBILITY UNKNOWN
including meningitis, EXCLUDING neurosurgical infections

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	dexamethasone **[Note 1]** 10 mg, starting before or with the first dose of antibiotic, then 6-hourly for 4 days **PLUS** ceftriaxone 4 g, daily or 2 g, 12-hourly review within 48 hours	dexamethasone **[Note 1]** 10 mg, starting before or with the first dose of antibiotic, then 6-hourly for 4 days **PLUS** vancomycin **[Note 2]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level **PLUS** ciprofloxacin 400 mg, 8-hourly	dexamethasone **[Note 1]** 10 mg, starting before or with the first dose of antibiotic, then 6-hourly for 4 days **PLUS** vancomycin **[Note 2]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level **PLUS** ciprofloxacin 400 mg, 8-hourly
		OR	**OR**
		dexamethasone 10 mg, starting before or with the first dose of antibiotic, then 6-hourly for 4 days **PLUS** moxifloxacin 400 mg, daily	dexamethasone 10 mg, starting before or with the first dose of antibiotic, then 6-hourly for 4 days **PLUS** moxifloxacin 400 mg, daily
	If there is a risk of listeria [Note 3] **ADD** benzylpenicillin 2.4 g, 4 hourly	*If there is a risk of listeria* [Note 3] **ADD** trimethoprim+sulfamethoxazole 160+800 mg, 6-hourly	*If there is a risk of listeria* [Note 3] **ADD** trimethoprim+sulfamethoxazole 160+800 mg, 6-hourly

Note 1: Do not give dexamethasone if serious concern of encephalitis.
Note 2: In severe sepsis an IV loading dose is required: vancomycin 25-30 mg/kg actual body weight, with the second dose and interval to be determined according to creatinine clearance, calculated with the Cockcroft-Gault formula.

Note 3: Patients at risk of listeria include:
- pregnant women, their unborn and newborn children
- older people (generally considered to be persons over 65-70 years)
- people of all ages whose immune systems have been weakened by disease or illness, for example cancer, leukaemia, AIDS, diabetes, liver or kidney disease, and anyone on medication that can suppress the immune system, for example, prednisone or cortisone, including transplant patients.

INDICATION: SEVERE SEPSIS SECONDARY TO NEUROSURGICAL PROCEDURE

including external ventricular drains, shunt procedures, and brain or spinal surgery

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	ceftazidime 2 g, 8-hourly **PLUS** vancomycin **[Note 1]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	ceftazidime 2 g, 8-hourly **PLUS** vancomycin **[Note 1]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	vancomycin **[Note 1]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level **PLUS** ciprofloxacin 400 mg IV, 8-hourly
	OR	**OR**	
	meropenem 2 g, 8-hourly **PLUS** vancomycin **[Note 1]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	meropenem 2 g, 8-hourly **PLUS** vancomycin **[Note 1]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	

Note 1: In severe sepsis an IV loading dose is required: vancomycin 25-30 mg/kg actual body weight, with the second dose and interval to be determined according to creatinine clearance, calculated with the Cockcroft-Gault formula.

INDICATION: SEVERE SEPSIS (COMMUNITY OR HEALTHCARE- ASSOCIATED) DUE TO UNKNOWN SOURCE

focus of infection not apparent

ROUTE OF ADMINISTRATION	PENICILLIN ALLERGY STATUS		
	NO PENICILLIN ALLERGY	NON-IMMEDIATE PENICILLIN HYPERSENSITIVITY	IMMEDIATE PENICILLIN HYPERSENSITIVITY (or severe prior reaction)
Intravenous (IV) or intraosseous	gentamicin **[Note 1]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** flucloxacillin 2 g, 4-hourly	gentamicin **[Note 1]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** cephazolin 2 g, 6-hourly	gentamicin **[Note 1]** 7 mg/kg, ideal body weight daily second dose and interval to be determined according to creatinine level **PLUS** vancomycin **[Note 2]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level
	If there is a risk of MRSA **ADD** vancomycin **[Note 2]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	*If there is a risk of MRSA* **ADD** vancomycin **[Note 2]** 25-30 mg/kg actual body weight loading dose second dose and interval to be determined according to creatinine level	

Note 1: Aminoglycosides (AGs) are rapidly bactericidal and effective for most Gram negative bacteria, including many ESBLs and *Pseudomonas spp*. However AGs are CONTRAINDICATED in myasthenia gravis, prior aminoglycoside allergy and vestibulocochlear disease. In severe sepsis 7mg/kg ideal body weight (IBW) is recommended (Link to IBW table). Precautions must be taken with creatinine clearance <60 ml/min or >80 years of age, and a dose of 4-5mg/kg (IBW) is recommended: see *Therapeutic Guidelines: Antibiotic* or seek expert advice. Monitoring the aminoglycoside plasma concentration is mandatory from the first dose of directed therapy or if therapy is planned for longer than 48 hours. Use the Cockcroft-Gault formula to estimate creatinine clearance.

Note 2: In severe sepsis an IV loading dose is required: vancomycin 25-30 mg/kg actual body weight, with the second dose and interval to be determined according to creatinine clearance, calculated with the Cockcroft-Gault formula.

NOTES FOR ANTIBIOTIC PRESCRIBING

Definitions of penicillin hypersensitivity	**Immediate hypersensitivity** involves the development of urticaria, angioedema, bronchospasm or anaphylaxis within one to two hours of drug administration. **Non-immediate hypersensitivity** is characterised by macular, papular or morbilliform rash, occurring several days after starting treatment. They are more common than immediate reactions, and may be caused by the infection or its treatment. **Severe prior reaction** involves a history of drug rash eosinophilia and systemic symptoms (DRESS) or Stevens-Johnson Syndrome, following administration of a penicillin or cephalosporin. All penicillin and cephalosporin class antibiotics are contraindicated in patients with history of DRESS, Stevens-Johnson Syndrome or IgE-mediated immediate penicillin or cephalosporin allergy. Refer to *Therapeutic Guidelines: Antibiotic* for more information on antimicrobial hypersensitivity.
Definitions of lower risk and higher risk of MRO	Refer to *Therapeutic Guidelines: Antibiotic* for more information: Hospital-acquired pneumonia: lower risk of multidrug-resistant organisms Hospital-acquired pneumonia: higher risk of multidrug-resistant organisms
Vancomycin dosing and frequency	Refer to *Therapeutic Guidelines: Antibiotic* for more information on Vancomycin dosing and frequency.
Gentamicin dosing and frequency	**Contraindications**: • Previous vestibular or auditory toxicity due to an aminoglycoside • Serious hypersensitivity reaction to an aminoglycoside • Myasthenia gravis **Precautions:** • Pre-existing significant hearing problems • Pre-existing vestibular problems • Family history (first-degree relative) of auditory toxicity caused by an aminoglycoside • Chronic renal impairment (creatinine clearance less than 40 mL/min) or rapidly deteriorating renal function – consult AMO • Advanced age (e.g. 80 years or older), depending on calculated renal function. Refer to *Therapeutic Guidelines: Antibiotic* for more information on Gentamicin dosing and frequency. Dose should be based on ideal body weight. **Precautions must be taken with creatinine clearance <60 ml/min or age >80 years of age and a dose of 4-5mg/kg (IBW) is recommended: refer to *Therapeutic Guidelines: Antibiotic* or seek expert advice.** Lower doses are recommended for patients that are not critically ill. Refer to the antibiotic prescribing guidelines endorsed in your facility. One dose of gentamicin is recommended; for subsequent doses, assess renal function and adjust frequency accordingly. 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. Directed therapy (beyond 48 hours, based on microbiology results) should be used on the advice of infectious diseases physician or clinical microbiologist only.
Criteria for toxic shock	Refer to *Therapeutic Guidelines: Antibiotic* for more information: Severe sepsis and septic shock: Streptococcal and Staphylococcal toxic shock syndrome

MEDICATION ADMINISTRATION TABLE *Adapted with permission from The Australian Injectable Drugs Handbook, 6th Edition*

- From a microbiological perspective, injectable medication **must be prepared immediately prior to administration,** using aseptic technique.
- Reconstitute antibiotics with sterile water for injection (WFI) unless stated otherwise in the table below.
- Displacement volume is the volume that the powder component of a drug takes up upon reconstitution. It needs to be added to the diluent volume to ensure accuracy in calculating doses that are less than a full vial. Thus the diluent volume recommended in the Product Information (PI) may sometimes differ from the volume recommended in this guideline. The displacement volume provided is an estimate and this may vary between brands. Please check in the Product Information or with the manufacturer.

Volume of diluent to reconstitute a vial + displacement volume of drug powder = Final volume of vial

- 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.

Medication	Presentation (adult)	Reconstitution fluid/volume	Administration	Notes
amikacin	Vial 500 mg/2 mL	Reconstitution not required	**IV Injection:** For doses less than 500 mg inject over 3 to 5 minutes **Intermittent IV Infusion**: Dilute dose in a convenient volume of sodium chloride 0.9% and infuse over 15 to 30 minutes	Therapeutic drug monitoring may be required. Refer to *Therapeutic Guidelines: Antibiotic* for recommendations Watch for neuromuscular blockade/paralysis[4] Potential for ototoxicity and nephrotoxicity, adjust in renal failure[4]
amoxycillin	Vial 500 mg, 1 g	500mg vial: 10 mL water for injection 1 g vial: 20 mL water for injection	**IV Injection:** Inject slowly over at least 3 to 4 minutes (preferably over 10 to 15 minutes)	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics Rapid IV administration may cause seizures

Medication	Presentation (adult)	Reconstitution fluid/volume	Administration	Notes
ampicillin	Vial 500 mg, 1 g	Reconstitute the vial with 10 - 20 mL of water for injection	**IV Injection:** Inject over 3 to 5 minutes	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics Rapid IV administration may cause seizures
azithromycin	Vial 500 mg	Add 5 mL water for injection	**Intermittent IV Infusion**: Dilute 5 mL of the reconstituted solution in 250 mL sodium chloride 0.9% and infuse over 60 minutes	Severe allergic reactions may occur Local infusion-site reactions may occur
benzylpenicillin	Vial 600 mg, 1.2 g	600 mg vial: Add 10 mL water for injection 1.2 g vial: Add 20 mL water for injection	**IV Injection:** Inject slowly over 5 to 10 minutes. Do not inject faster than 300 mg/minute	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics Rapid IV administration may cause seizures
cefepime	Vial 1 g, 2 g	Reconstitute the vial with 5-10 mL sodium chloride 0.9%	**IV Injection:** Inject slowly over 3 to 5 minutes	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics
ceftazidime	Vial 1 g, 2 g	Reconstitute the vial with 10 mL water for injection	**IV Injection:** Inject slowly over 3 to 5 minutes to avoid vein irritation	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics

Medication	Presentation (adult)	Reconstitution fluid/volume	Administration	Notes
ceftriaxone	Vial 500 mg, 1 g, 2 g	500 mg vial: Add 5 mL water for injection 1 g vial: Add 10 mL water for injection 2 g vial: Add 40 mL water for injection	**IV Injection:** Inject doses up to 1 g over 2 to 4 minutes **Intermittent IV Infusion**: Dilute dose in 40 mL of sodium chloride 0.9% and infuse over at least 30 minutes	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics
cephazolin	Vial 500 mg, 1 g, 2 g	Reconstitute the vial with 10 mL of water for injection	**IV Injection:** Inject slowly over 3 to 5 minutes	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics
ciprofloxacin	Vial/infusion bag: 100 mg/50 mL 200 mg/100 mL 400 mg/200 mL	Reconstitution not required	**Intermittent IV Infusion:** Infuse over at least 60 minutes	Contraindicated in patients with known hypersensitivity reactions to ciprofloxacin and other quinolones
clindamycin	Ampoule 300mg/2 mL, 600 mg/4 mL	Reconstitution not required	**Intermittent IV Infusion:** Dilute doses up to 600 mg in 50 mL sodium chloride 0.9% and infuse over at least 20 minutes. Dilute doses up to 1200 mg in 100 mL sodium chloride 0.9% and infuse over at least 30 to 40 minutes. Maximum rate is 30 mg/minute. Do not infuse more than 1200 mg in 60 minutes	

Medication	Presentation (adult)	Reconstitution fluid/volume	Administration	Notes
dexamethasone	Vial 4 mg/1 mL, 8 mg/2 mL	Reconstitution not required	**IV Injection:** Inject slowly over at least 3 minutes	
flucloxacillin	Vial 500 mg, 1 g	500 mg vial: Add 10 mL water for injection 1 g vial: Add 15-20 mL water for injection	**IV Injection:** Inject slowly over 3 to 4 minutes	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics
gentamicin	Ampoule 10mg/mL 40mg/mL 60mg/1.5mL 80 mg/2 mL	Reconstitution not required	**IV Injection:** Inject undiluted over 3 to 5 minutes	Dose by IDEAL BODY WEIGHT [2] (not by actual body weight) Therapeutic drug monitoring may be required for use beyond 48 hours Refer to gentamicin notes on page 20. For further information refer to Therapeutic Guidelines: Antibiotic.
immunoglobulin	Review product information and refer to local policy and guidelines for administration			
meropenem	Vial 500 mg, 1 g	500 mg vial: Add 10 mL water for injection 1 g vial: Add 20 mL water for injection	**IV Injection:** Inject over 5 minutes	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics
metronidazole	Infusion bag 500 mg/100 mL	Reconstitution not required	**Intermittent IV Infusion:** Infuse 500 mg undiluted over 20 minutes at a rate of 25 mg/minute	
moxifloxacin	Infusion bag 400 mg/250 mL	Reconstitution not required	**Intermittent IV Infusion**: Infuse undiluted over 60 minutes	

Medication	Presentation (adult)	Reconstitution fluid/volume	Administration	Notes
piperacillin +tazobactam	Vial 4.5 g	Reconstitute the 4.5 g vial with 20 mL of sodium chloride 0.9% or water for injection	**Intermittent IV Infusion**: Dilute the dose with 50 mL sodium chloride 0.9%. Infuse over 20 to 30 minutes	Contraindicated in patients with immediate hypersensitivity to penicillins, carbapenems and cephalosporin antibiotics
trimethoprim + sulfamethoazole	Ampoule 80 mg+400 mg	Dilute 2 ampoules using sodium chloride 0.9% to 250 mL	**Intermittent IV Infusion**: Infuse over 60 to 90 minutes	
vancomycin	Vial 500 mg, 1 g	500 mg vial: Add 10 mL water for injection 1 g vial: Add 20 mL water for injection	**Intermittent IV Infusion**: Dilute the 500 mg dose with 100 mL and the 1 g dose with 200 mL sodium chloride 0.9%. **Maximum rate of 10 mg/minute**	Infusion related effects are common. If these occur, decrease infusion rate and monitor closely A maximum rate of infusion of 10 mg/minute is recommended to minimise the risk of red man syndrome. Red man syndrome presents as tingling, flushing or rash of the face, neck and upper body, muscle spasm of the chest and back, and rarely hypotension and shock-like symptoms. If symptoms of red man syndrome occur, slow the rate of the infusion

References

1. Surviving Sepsis Campaign. International Guidelines for management of Severe Sepsis and Septic Shock: 2012 [internet] 2016. [Cited 2016, January 18] Available from: http://www.sccm.org/Documents/SSC-Guidelines.pdf
2. *Therapeutic Guidelines: Antibiotic*. Version 15, 2014 *Therapeutic guidelines: antibiotic*. Version 15. Melbourne: Therapeutic Guidelines Limited; 2014. Accessed through *eTG complete* (via CIAP)
3. Australian Injectable Drugs Handbook, 6th Edition Accessed via CIAP
4. Australian Medicines Handbook Pty Ltd Accessed via CIAP

Clinical Excellence Commission
Locked Bag 8
Haymarket NSW 1240
Phone: (02) 9269 5500
Email: CEC-info@health.nsw.gov.au
Web: www.cec.health.nsw.gov.au

CLINICAL
EXCELLENCE
COMMISSION