Community Acquired Pneumonia (Adults) Clinical Guideline

Version No.: 2.0
Approval date: April 2021

Contents

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1. Introduction

This guideline has been developed by the SA expert Advisory Group on Antimicrobial Resistance (SAAGAR) to guide clinicians towards best practice in the management of community acquired pneumonia. It has been developed with reference to the Australian Therapeutic Guidelines: Antibiotic [1] and treatment recommendations are based on locally available bacterial susceptibility data.[2, 3]

This guideline does not apply to:

- patients who are significantly immunocompromised (e.g. patients actively receiving chemotherapy, and solid organ or bone marrow transplant recipients)
- patients who have chronic suppurative lung diseases (e.g. cystic fibrosis, bronchiectasis)
- patients with exacerbations of chronic obstructive pulmonary disease
- neonate or paediatric patients.
  - For advice on the management of Paediatric patients please refer to the South Australian Paediatric Clinical Practice Guideline for Community Acquired Pneumonia in Children, adapted from the Therapeutic Guidelines recommendations for empirical treatment of community-acquired pneumonia in children.

2. Background

Community acquired pneumonia (CAP) is a pneumonia occurring in individuals who are not in hospital or who have been in hospital for less than 48 hours. It is usually suspected in patients who present with acute respiratory symptoms (e.g. cough, dyspnoea, sputum production, pleuritic chest pain), fever and new infiltrates on chest X-ray.[4] In some patients, non-respiratory symptoms such as diarrhoea or headache may be prominent or, particularly in the elderly, clinical features may be nonspecific. [5]

Careful assessment of pneumonia severity is required in all patients to guide the need for inpatient management and the most appropriate empirical antibiotic therapy. This guideline describes the recommended management of adults with CAP, including residents of aged-care facilities who are being treated in hospital. It details assessment of pneumonia severity, clinical and microbiological investigations and empirical regimens for CAP in patients.

Management of patients with suspected COVID-19

If a person presents with **symptoms suggestive of COVID-19** (fever, shortness of breath, dry cough, muscle aches, tiredness, sore throat, headache, runny nose, loss of taste/smell, diarrhoea and nausea) they should be managed as a suspected case until this diagnosis can be excluded. Arrange for both a deep nasal swab and an oropharyngeal swab (plus sputum MC&S where this can be collected spontaneously and safely). Ensure patients are managed in accordance with infection control measures, including transmission-based precautions and appropriate personal protective equipment (PPE)(refer to SA Health Coronavirus Disease 2019 (COVID-19): Information for Health Professionals for further information).

Respiratory viruses can cause pneumonia as a sole pathogen, or as co-infection with bacterial pathogens. Despite frequent prescription of broad-spectrum empirical antimicrobials in patients with coronavirus associated respiratory infections, there is a paucity of data to support the association with respiratory bacterial/fungal co-infection.[6] The World Health Organization discourages the use of antibiotics for mild cases of COVID-19 while recommending antibiotic use for severe COVID-19 cases at increased risk of secondary bacterial infections and death.[7]

A national COVID-19 Clinical Evidence Taskforce has been established to undertake continuous evidence surveillance and synthesis to provide national, evidence-based guidelines for the clinical care of patients with COVID-19. These 'living' guidelines are continually updated weekly. Please note that antimicrobials included in these guidelines may not be on the SA hospital formulary - prescribers should check the formulary status before prescribing in SA public hospitals.

3. Definitions

In the context of this document:

BD	Twice daily
CAP	Community acquired pneumonia
CBE	Complete blood exam
CKD	Chronic kidney disease
COAD	Chronic obstructive airway disease
COPD	Chronic obstructive pulmonary disease
COVID-19	Coronavirus disease 2019
CrCl	Creatinine clearance
CRP	C-reactive protein
CXR	Chest X-ray
DRESS	Drug rash with eosinophilia and systemic systems
ID	Infectious Disease
IV	Intravenously
LDH	Lactate dehydrogenase
LFT	Liver function test
MIC	Minimum inhibitory concentration
Micro	Clinical microbiologist
ml / min	Millilitres per minute
PA	Posteroanterior
PAO2/FiO2	Arterial partial pressure of oxygen / Fraction of oxygen in inspired air
PCR	Polymerase chain reaction
PO	Per oral
PPE	Personal protective equipment
SBP	Systolic blood pressure
SJS/TEN	Stevens-Johnson syndrome / Toxic epidermal necrolysis
SpO_2	Saturation of peripheral oxygen - an estimation of the oxygen saturation level in the blood
TDS	Three times daily

4. Principles of the standards

The following National Safety and Quality Health Service Standards apply:[8]

Standard 1- Governance for Safety and Quality in Health Care
Create integrated governance systems that maintain and improve the reliability and quality of patient care, as well as improve patient outcomes.

Standard 3 – Preventing & Controlling Healthcare-Associated Infection
Improve infection prevention and control measures to help prevent infections, and the spread of antimicrobial resistance through the appropriate prescribing and use of antimicrobials

Standard 4- Medication Safety
Ensure competent clinicians safely prescribe, dispense and administer appropriate medicines to informed patients and carers.

5. General guidance

5.1 Aetiology of community acquired pneumonia

Even in rigorous clinical studies, the aetiology of CAP can be identified in only about 50% of cases.[9, 10] The importance of viral infections as a cause for CAP (around 15-30%) is increasingly recognised, probably due to increasing use of PCR-based techniques to identify respiratory viruses and widespread use of the pneumococcal conjugate vaccine.[11] Of the bacterial causes of CAP, *S. pneumoniae* is the most common (30-40%), followed by *Mycoplasma pneumoniae* (8-18%), *Haemophilus influenzae* (5%), *Legionella* sp. (3-7%) and *Chlamydophila* sp. (3-5%).[12, 13]

Determining the aetiology of CAP can assist in:

1. Identifying resistant pathogen(s) including *Legionella* which may have public health implications
2. Providing directed therapy
3. Adjusting therapy when patients fail initial empiric therapy
4. Monitoring the constantly changing epidemiology of CAP

5.2 Diagnostic tests

Diagnostic testing is an important tool in addition to clinical evaluation to support the clinician in confirming a differential diagnosis. While identifying the infecting organism may not alter empiric antibiotic choice, it is helpful in directing antibiotic therapy and informs duration of treatment. Obtaining a diagnosis for the aetiology of pneumonia can also provide useful prognostic information (i.e. bacteraemic *S. pneumoniae* pneumonia is associated with a high mortality).

The utility of various diagnostic tests, such as Gram stain, blood cultures, *Legionella* antigen, *Legionella* culture, and respiratory virus serology (low yield) have been reviewed.[14-18] PCR for respiratory viruses should be performed routinely on respiratory secretions of patients presenting with CAP. A sputum specimen has the highest sensitivity followed by a deep nasal swab. Serology for either atypical bacterial pathogens or respiratory viruses is no longer routinely recommended due to the low specificity of single measurements, delayed results and the need for paired titres for adequate interpretation.

5.3 Antibiotic susceptibility

Antibiotic susceptibility patterns of common respiratory pathogens are tracked by laboratory providers. The most common respiratory isolates from sputa from general practices in Adelaide include *H. influenzae*, *P. aeruginosa*, *S. pneumoniae*, *S. aureus* and *M. catarrhalis*.[3] These are not necessarily from patients with pneumonia but also include COAD exacerbations and bronchitis. Local data show that amoxicillin is effective therapy for the majority of circulating *S. pneumoniae* strains. *H. influenzae* causes only 5% of CAP and would be adequately covered by amoxicillin oral plus doxycycline, or benzylpenicillin IV plus azithromycin based on local data.[1, 3] For specific information on antibiotic susceptibility, clinicians are advised to refer to their local health network (LHN) antibiograms.

5.4 Risk stratification of patients presenting with CAP

One of the key features of managing community acquired pneumonia is to accurately assess a patient's risk of an adverse outcome and therefore choose the most appropriate location for treatment (home, general inpatient ward or intensive care) and the type of therapy (intravenous antibiotics versus oral, cover for atypical organisms or not). Several tools have been developed to attempt to predict patient outcome based on their presenting symptoms and underlying risk factors e.g. SMART-COP, Pneumonia Severity Index (PSI) and CURB-65.[1, 19, 20]

In the most recent Australian Therapeutic Guidelines: Antibiotic, "red flags" are now recommended over the previous severity scoring systems as they align with clinical decision-making pathways for identifying whether inpatient or outpatient management is preferred for optimal outcomes (Antibiotic Expert Group consensus). These red flags assist staff in determining whether a patient can be managed on a general inpatient ward or if ICU support may be required (where appropriate).[1]

In addition to red flags, the presence of patient co-morbidities and social circumstances should be considered when deciding whether to admit a patient to hospital. It is also essential that clinicians use their clinical judgement when assessing the need for hospital admission.[1]

Refer to Appendix 1 – Community acquired pneumonia pathway for more detail.

5.5 Treatment of CAP

Antibiotic recommendations for the empiric treatment of CAP are based on selecting agents effective against the major treatable bacterial causes and the local resistance patterns of microorganisms.[1, 3, 4] This guideline provides recommended empiric therapy only. Where results from sputum culture, Gram stain or PCR are available, the patient's therapy should be tailored to individual results.

Low-severity CAP

For low severity CAP, amoxicillin is the drug of choice for monotherapy because of increasing rates of *Streptococcus pneumoniae* resistance to tetracyclines and macrolides. Initial monotherapy with doxycycline can be used if atypical pathogens (e.g. *Mycoplasma pneumoniae, Chlamydophila [Chlamydia] pneumoniae*) are suspected based on epidemiology or the clinical presentation (e.g. a young adult who presents with non-productive cough for 5 or more days and bilateral lower zone infiltrates on chest X-ray). Note that the use of doxycycline should be avoided in pregnant patients [21] – azithromycin is the safe alternative.[1]

Clinical review of the patient within 48 hours is necessary in case modification of therapy is required. If the patient was treated with monotherapy initially but is not improving after 48 hours, consider escalating to combination therapy and reassess the need for hospital admission. If patient follow-up within 48 hours may not occur, consider using initial combination therapy instead.[1]

Moderate and high-severity CAP

Gentamicin is no longer routinely recommended for use in all moderate and high severity pneumonias in patients with risk factors for Gram negative pneumonias. The use of gentamicin may be warranted for empirical treatment of patients who have recently travelled or resided in tropical regions of Australia (see CAP in tropical regions below) or for directed treatment when Gram-negative bacilli are identified by culture (seek specialist ID/Micro advice).

Ceftriaxone is recommended to cover both Gram negative organisms and pneumococci in patients with significant renal impairment and in those with delayed penicillin allergy. However it is important to note that unlike gentamicin, ceftriaxone will not cover *Pseudomonas aeruginosa*. If there is particular concern about *P. aeruginosa* infection (e.g. in patients with a recent history of this organism in sputum culture) advice should be sought from the Infectious Diseases team in regards to the selection of an appropriate empiric antibiotic when gentamicin cannot be used.

For most cases of moderate to high-severity pneumonia oral azithromycin is adequate to empirically treat *Legionella pneumoniae* pneumonia (~5% of all pneumonias) due to its high and prolonged intracellular concentrations.[22] Where patients are unable to take oral therapy or for patients with high-severity pneumonia, IV therapy, at least for the first dose, is recommended.

CAP in tropical regions

The approach to management of CAP in patients who have recently travelled overseas or to Northern Australia (i.e. north of Mackay in Queensland, Tennant Creek in Northern Territory and Port Hedland in Western Australia) differs slightly due to the risk of Gram negative *Burkholderia pseudomallei* and *Acinetobacter baumannii* organisms [23, 24] – consult ID / Microbiology / Respiratory for specialist advice in these patients.

Atypical organism cover

The Therapeutic Guidelines recommends clarithromycin as the oral macrolide where atypical organisms are suspected, and azithromycin IV for the most severe pneumonias.[1] This guideline recommends oral azithromycin for CAP due to its single daily dosing, tolerability and its pharmacokinetic and pharmacodynamic properties which allow for a short course of therapy (i.e. 7 days for *Legionella sp.*). Doxycycline is an acceptable choice in place of azithromycin but requires a longer course of therapy.

5.6 Viral pneumonia

The microbial aetiology of CAP is changing, particularly with the widespread introduction of the pneumococcal conjugate vaccine, and there is increased recognition of the role of viral pathogens. Viral causes, including COVID-19 and influenza, should be part of the differential diagnosis for patients presenting with respiratory symptoms. Influenza is more likely to produce body aches, whilst COVID-19 is more likely to produce shortness of breath. Suspect COVID-19 where no other clinical focus of infection or alternate explanation of the patient's illness is evident.[25]

Consider empiric oseltamivir in patients with risk factors for poor outcomes from influenza such as those with established complications, or patients admitted to hospital with moderate to severe CAP.[16, 26] Treatment with oseltamivir is not recommended in otherwise healthy patients with a low risk of complications, as antiviral treatment offers little benefit in these patients.[27] Oseltamivir can be ceased once influenza has been excluded.

5.7 Considerations in pregnancy

- **Oseltamivir:** All pregnant patients who are hospitalised for CAP should be considered for oseltamivir therapy. Pregnant women are at higher risk of poor outcomes from influenza and the maternal benefit outweighs any risks of oseltamivir exposure to the foetus.[1] The limited published evidence describing the use of oseltamivir in pregnancy do not suggest any significant risk of developmental toxicity. [21]
- **Doxycycline:** Doxycycline is contraindicated in second and third trimester.[23] Use azithromycin 500mg orally daily for the recommended duration. Clinicians should provide reassurance for any inadvertent use of doxycycline for the first 16 weeks post conception. Contact SA Pharmacy Medicines Information on 81617555 Monday to Friday 09:00-17:00.

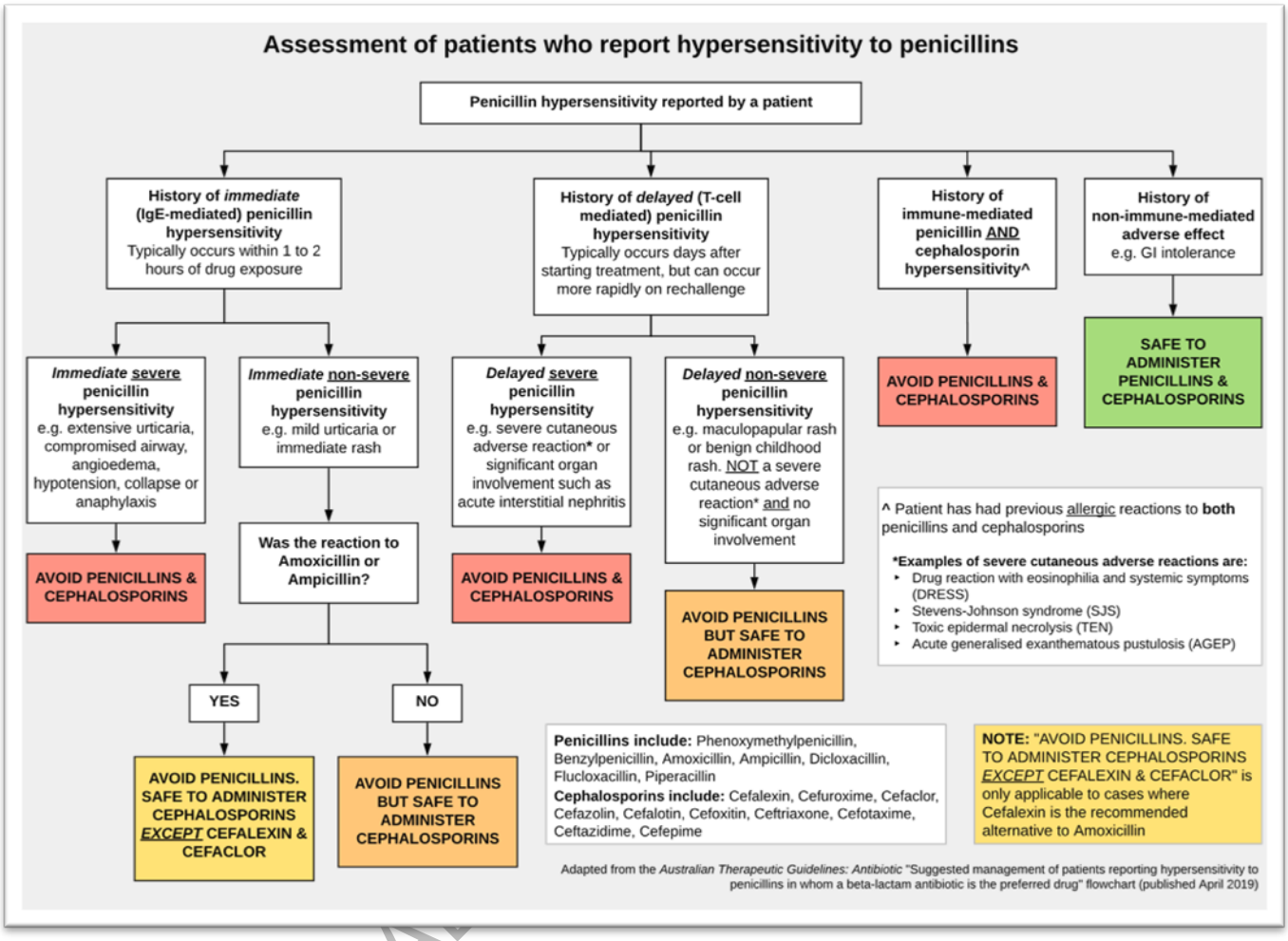
5.8 Considerations in breastfeeding

All antimicrobials mentioned in the CAP Pathway/Protocol are considered safe in breastfeeding. For more information, contact SA Pharmacy Medicines Information on 81617555 Monday to Friday 09:00-17:00.

5.9 Penicillin / cephalosporin hypersensitivity

Patients who are labelled as "penicillin allergic" are more likely to be treated with potentially less effective or broader-spectrum antibiotics, increasing the risk of adverse events, treatment failure and antibiotic resistance. They also have longer lengths of hospital stay and are at higher risk of multi-drug resistant organisms, readmission to hospital and treatment related adverse events.[28]

Appendix 1 provides guidance on the management of CAP for patients with documented penicillin allergy. The flowchart below, adapted from the Therapeutic Guidelines [1] can be used to assist in the assessment of penicillin allergy and selection of appropriate empiric treatment options. Where there is uncertainty about the most appropriate treatment in a patient with antibiotic allergies contact Infectious Diseases for further advice. For more information on the classification of penicillin / cephalosporin allergies, refer to the SA Health Antibiotic Allergies webpage.



5.10 Consulting Infectious Diseases / Microbiology / Respiratory

Input from ID / Microbiology / Respiratory speciality is recommended for:

- All patients with high severity CAP
- Failure to improve by day 3 of treatment
- All patients with complicated pneumonia (empyema, lung abscess, parapneumonic effusion, haemoptysis, concurrent bacteraemia, upper lobe pneumonia)
- Recent travel overseas or to Northern Australia (tropical areas carry a risk of Gram-negative pathogens including *Burkholderia pseudomallei* and *Acinetobacter baumannii*)
- Suspected tuberculosis infection
- Suspected staphylococcal or *Pseudomonas aeruginosa* pneumonia
- Suspected viral pneumonia or when there are high rates of community transmission
- Pregnant women

6. Safety, quality and risk management

National Safety and Quality Health Service Standards

 National Standard 1 Clinical Governance	 National Standard 2 Partnering with Consumers	 National Standard 3 Preventing & Controlling Healthcare-Associated Infection	 National Standard 4 Medication Safety	 National Standard 5 Comprehensive Care	 National Standard 6 Communicating for Safety	 National Standard 7 Blood Management	 National Standard 8 Recognising & Responding to Acute Deterioration
☒	☐	☒	☒	☐	☐	☐	☐

7. Appendices

Appendix 1 – Community acquired pneumonia (CAP) pathway (adults)

8. References

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9. Document Ownership & History

Document developed by: South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR)
File / Objective No.: 2017-01515 | eA987709
Next review due: 10/10/2022
Policy history: Is this a new policy (V1)? **N**
Does this policy amend or update and existing policy? Y
If so, which version? V1.1
Does this policy replace another policy with a different title? **N**
If so, which policy (title)?

ISBN No.: 978-1-76083-379-4

Approval Date	Version	Who approved New/Revised Version	Reason for Change
1/04/21	V2	Domain Custodian – Clinical Governance, Safety & Quality	Formally reviewed in line with scheduled timeline for review.
10/10/17	V1	Safety & Quality Strategic Governance Committee	Original approved version.

Appendix: Community Acquired Pneumonia (CAP) pathway (adults)

PRELIMINARY DIAGNOSIS OF CAP

Evidence of consolidation on CXR with <u>one</u> or more of the following:

- Temperature > 38°C **or** < 35°C
- Dyspnoea
- Cough (especially productive)
- Pleuritic chest pain

INITIAL INVESTIGATIONS

- Urgent chest x-ray (PA and lateral)
- Electrolytes, urea, creatinine, CRP, glucose, LFTs
- CBE & differential
- Oxygen saturation (on room air, if possible)
- Deep nasal and throat swab for respiratory pathogen PCR

Plus, for admitted patients:

- Blood cultures (2 sets) prior to antibiotics
- Urinary Legionella antigen assay
- Sputum Gram stain and culture (including Legionella)

If tappable pleural effusion or empyema on CXR:

- Consult a respiratory specialist if available
- Consider pleural aspiration
- Request pH, Gram stain and culture on fluid, protein, LDH, cell count

IS THERE A NEED FOR HOSPITAL ADMISSION?

Patients with any of the following parameters warrant inpatient management:

- Tachypnoea (respiratory rate ≥22 breaths/min)
- Tachycardia (heart rate >100 beats/min)
- Hypotension (SBP < 90 mmHg)
- Acute onset confusion
- Oxygen saturation < 92% on room air (or lower than baseline in patients with co-morbid lung disease)
- Multi-lobar involvement on CXR
- Blood lactate concentration >2 mmol/L

NO

ARE THERE OTHER REASONS TO ADMIT THE PATIENT?

Consider patient factors:

- Age
- Co-morbidities (e.g. diabetes, CKD)
- Inability to tolerate and absorb oral therapy
- Need for supportive oxygen therapy
- Functional status
- Goals of care
- Availability of home support
- History of substance/ ethanol abuse
- Social situation

NO → **Prescribe oral regimen as per <u>LOW</u> SEVERITY CAP and manage patient in the community (see Section 5.5)**

YES → **Consider inpatient admission if appropriate and prescribe oral regimen as per <u>LOW</u> SEVERITY CAP**

YES

IS THERE A NEED FOR INTENSIVE CARE SUPPORT?

- Respiratory rate ≥ 30 breaths/min
- Oxygen saturation < 90% on room air, PaO_2 <60mmHg or PaO_2/FiO_2 <250
- Multi-lobar or rapid progression of CXR infiltrates
- Hypotension (SBP < 90mmHg)
- Acute-onset confusion
- Poor peripheral perfusion or mottled skin
- Acute oliguria, elevated serum creatinine or uraemia (serum urea >7mmol/L or blood urea nitrogen ≥19mg/dL)
- Blood lactate concentration > 2 mmol/L
- Clinical deterioration despite appropriate initial therapy

NO → **Prescribe IV regimen for <u>MODERATE</u> SEVERITY CAP**

YES → **Prescribe IV regimen for <u>HIGH</u> SEVERITY CAP**

Consider seeking ICU consult

CONSULT ID / MICROBIOLOGY / RESPIRATORY FOR:

- All patients with high severity CAP
- Failure to improve by day 3 of treatment
- All patients with complicated pneumonia (empyema, lung abscess, parapneumonic effusion, haemoptysis, concurrent bacteraemia)
- Recent travel overseas or to Northern Australia (see section 5.5)
- Suspected tuberculosis infection
- Suspected staphylococcal or *Pseudomonas aeruginosa* pneumonia
- Suspected viral pneumonia or when there are high rates of community transmission
- Pregnant women

ANTIMICROBIAL RECOMMENDATIONS: TREATMENT OF CAP (ADULTS)

PENICILLIN HYPERSENSITIVITY

SAFE TO ADMINISTER PENICILLINS AND CEPHALOSPORINS	AVOID PENICILLINS BUT SAFE TO ADMINISTER CEPHALOSPORINS	AVOID PENICILLINS AND CEPHALOSPORINS

LOW SEVERITY CAP (Treatment duration 5 days)

Amoxicillin 1g orally 8 hourly for 5 days **AND/OR** **Doxycycline*#^**100mg orally 12 hourly for 5 days	**Cefuroxime** 500mg orally 12 hourly for 5 days **AND/OR** **Doxycycline*#^** 100mg orally 12 hourly for 5 days	**Doxycyline*#^** 100mg orally 12 hourly for 5 days

MODERATE SEVERITY CAP (Treatment duration 5–7 days)

Suitable for inpatient management on a general ward

Benzylpenicillin1.2g IV 6 hourly **AND** **Azithromycin** 500mg orally DAILY for 3 days #	**Ceftriaxone** 1g IV DAILY **AND Azithromycin** 500mg orally DAILY for 3 days #	**Moxifloxacin** 400mg† oral/IV DAILY (**Please note:** ID approval required)

HIGH SEVERITY CAP (Treatment duration 7 days)

Inpatient management – consider ICU consultation if consistent with patient's goals of care

Ceftriaxone 2g IV DAILY **AND** **Azithromycin** 500 mg IV/oral DAILY for 5 days #†	**Ceftriaxone** 2g IV DAILY **AND** **Azithromycin** 500mg IV/oral DAILY for 5 days #†	**Moxifloxacin** 400mg IV DAILY (**Please note:** ID approval required)

IV TO ORAL SWITCH

Consider after 48 hrs of therapy if there is clinical improvement and patient afebrile (if sputum culture results available switch to directed therapy)

Amoxicillin 1g orally 8 hourly **AND Azithromycin** 500mg orally daily	**Cefuroxime** 500mg orally 12 hourly **AND Azithromycin** 500mg orally daily	**Moxifloxacin** 400mg orally DAILY (**Please note:** ID approval required)

ADDITIONAL NOTES

For proven *Legionella*, continue **Azithromycin** for 7 days or **Doxycycline** for 14 days

* If intolerant/allergic to **Doxycycline** use **Roxithromycin** 300mg orally DAILY for 5 days

^ If pregnant, replace **Doxycycline** with **Azithromycin** 500mg orally DAILY for 3 days

†Oral therapy preferred but give IV if enteral route not available.

For all admitted patients with moderate or high severity CAP where influenza is suspected or when there are high rates of community influenza transmission, add oseltamivir 75mg PO 12-hourly (Refer to eTG or AMH for dose adjustment when CrCl < 60mL/min) and implement droplet precautions.
Empiric oseltamivir is recommended in all pregnant women pending testing (see sections 5.6 & 5.7).