

BC Provincial Antimicrobial Clinical Expert Group (PACE)

ALTERNATIVES TO FLUOROQUINOLONE ANTIBIOTIC THERAPY IN ADULTS

Fluoroquinolone (FQ) antibiotics have historically been prescribed to treat a wide range of infections. Health Canada, the US Food and Drug Administration and the European Medicines Agency have issued FQ safety warnings regarding serious adverse events that affect multiple organ systems including: musculoskeletal (tendon rupture); neurological (seizures, delirium, neuropsychiatric disturbances, peripheral neuropathy); cardiovascular (QTc prolongation, aortic dissection, aortic regurgitation, arrhythmias) and metabolic (hypoglycemia, hyperglycemia). FQs have a significant association with *Clostridioides difficile* infection. Therefore, FQs should be avoided as first-line treatment for common infections.

Table 1 summarizes the first-line antibiotic alternatives to FQ therapy. The options listed as second-line (or in penicillin allergy) can be used in place of FQs while maintaining equivalent clinical effectiveness. Refer to [Table 2: Safety of Beta-lactams in Penicillin-Allergic Patients](#) to determine the safety of using an alternative beta-lactam antibiotic in a patient with documented penicillin or cephalosporin allergy.

Note: This guideline is intended for adults since there are limited indications for the use of FQs in infants and children. These are guidelines for empiric therapy – therapy may need to be adjusted based on culture results.

Fluoroquinolones should be reserved for use only in patients who have no other treatment options

Table 1. Alternatives to Fluoroquinolone Therapy in Adults (*Denotes BCHA Pharmacy and Therapeutics Committee Restricted Antibiotic)

Syndrome	Key Points	First-Line Agent(s)	Second-Line Agent(s) or Penicillin Allergy Patients
Acute Sinusitis	Cases are viral and do not require antibiotic therapy Clinical presentation if bacterial infection: Symptoms > 10 days or worsening after 5-7 days	Amoxicillin	Cefuroxime or Doxycycline
Acute Otitis Media	Most cases are viral and do not require antibiotic therapy	Amoxicillin	Cefuroxime or Doxycycline
Acute Bronchitis	Acute bronchitis is almost exclusively viral in etiology and does not benefit from antibiotics	None	None
Acute Exacerbation of Chronic Obstructive	Only use antibiotics when at least 2 of the following 3 symptoms:	Amoxicillin	Doxycycline or

Syndrome	Key Points	First-Line Agent(s)	Second-Line Agent(s) or Penicillin Allergy Patients
Pulmonary Disease (AECOPD), less than 4 exacerbations/year	<ul style="list-style-type: none"> increased dyspnea increased sputum volume, or sputum purulence. 		TMP/SMX Azithromycin or Clarithromycin Note: these option have less activity against <i>S. pneumoniae</i> and <i>H.influenzae</i> than amoxicillin
AECOPD, 4 or more exacerbations/year		Amoxicillin-clavulanate or Cefuroxime	Cefuroxime
Community Acquired Pneumonia (CAP)	Calculate CRB-65 Score for Severity: One point for each of: <ul style="list-style-type: none"> Confusion (new disorientation) Respiratory rate ≥ 30 breaths/min Blood pressure (systolic <90 mmHg or diastolic ≤ 60 mmHg) Age ≥ 65 years 		
CAP Severity = Mild CRB65 = 0		Amoxicillin	Cefuroxime or Doxycycline <i>(refer to local antibiogram or BCCDC Antimicrobial Resistance Dashboard for doxycycline resistance rates)</i>
CAP Severity = Moderate CRB65 = 1 or 2	Include coverage for atypical pathogens (<i>Mycoplasma</i> , <i>Chlamydoiphila</i> or <i>Legionella</i>) if: <ul style="list-style-type: none"> CRB65 = 2 Significant co-morbidities 	Amoxicillin- clavulanate or Ceftriaxone PLUS Azithromycin or	Cefuroxime or Ceftriaxone PLUS Azithromycin or

Syndrome	Key Points	First-Line Agent(s)	Second-Line Agent(s) or Penicillin Allergy Patients
		Clarithromycin Or doxycycline	Clarithromycin Or doxycycline
CAP Severity = Severe CRB65 = 3 or 4	Include coverage for atypical pathogens (Mycoplasma, Chlamydoiphila or Legionella). Consider risk factors for MRSA and <i>Pseudomonas</i> – refer to local hospital treatment guidelines	Ceftriaxone PLUS Azithromycin	Ceftriaxone PLUS Azithromycin
Asymptomatic bacteriuria	Antibiotic therapy not indicated unless undergoing urologic procedure or pregnancy	None	None
Acute, uncomplicated cystitis		Nitrofurantoin or TMP-SMX or Cefixime or Fosfomycin*	Nitrofurantoin or TMP-SMX or Cefixime or Fosfomycin*
Pyelonephritis	begin with parenteral therapy then step-down to oral therapy within 1 to 3 days	IV therapy: Ceftriaxone or Gentamicin Oral therapy: TMP-SMX or Amoxicillin- clavulanate or Cefixime	IV therapy: Ceftriaxone or Gentamicin Oral therapy: TMP-SMX or Cefixime
Appendicitis, uncomplicated	Antibiotics can be discontinued if appendicitis without perforation, or small perforation fully managed by surgical source control	Pre-operative prophylaxis: Cefazolin PLUS Metronidazole	

Syndrome	Key Points	First-Line Agent(s)	Second-Line Agent(s) or Penicillin Allergy Patients
Appendicitis, complicated	Appendicitis with perforation	Ceftriaxone PLUS Metronidazole	Ceftriaxone PLUS Metronidazole
Cholecystitis, uncomplicated	Antibiotics can be discontinued after cholecystectomy if cholecystitis without perforation	Pre-operative-prophylaxis: Cefazolin If elderly ADD: Metronidazole	
Cholecystitis, complicated	Cholecystitis with perforation	Ceftriaxone PLUS Metronidazole	
Cholangitis		Mild-Moderate: Ceftriaxone Severe (or enterococcus suspected): Piperacillin-tazobactam	Mild-Moderate: Ceftriaxone Severe (or enterococcus suspected): Imipenem*
Diverticulitis	Oral therapy preferred unless mitigating circumstances	Amoxicillin- clavulanate IV therapy: Ceftriaxone PLUS Metronidazole	[Cefuroxime or Cefixime PLUS Metronidazole] or [TMP-SMX PLUS Metronidazole]

TABLE 2

Safety of Beta-Lactams in Penicillin Allergic Patients												
Beta-lactams	AMOXICILLIN*	AMPICILLIN	PENICILLIN	PIPERACILLIN*	CEFAZOLIN	CEPHALEXIN	CEFOXITIN	CEFPROZIL	CEFUROXIME	CEFIXIME	CEFOTAXIME	CEFTRIAXONE
AMOXICILLIN*	█	X	X	X	✓	X	✓	X	✓	✓	✓	✓
AMPICILLIN	X	█	X	X	✓	X	✓	X	✓	✓	✓	✓
PENICILLIN	X	X	█	X	✓	✓	X	✓	✓	✓	✓	✓
PIPERACILLIN*	X	X	X	█	✓	X	✓	X	✓	✓	✓	✓
CEFAZOLIN	✓	✓	✓	✓	█	✓	✓	✓	✓	✓	✓	✓
CEPHALEXIN	X	X	✓	X	✓	█	✓	X	✓	✓	✓	✓
CEFOXITIN	✓	✓	X	✓	✓	✓	█	✓	X	✓	✓	✓
CEFPROZIL	X	X	✓	X	✓	X	✓	█	✓	✓	✓	✓
CEFUROXIME	✓	✓	✓	✓	✓	✓	X	✓	█	X	X	X
CEFIXIME	✓	✓	✓	✓	✓	✓	✓	✓	X	█	X	X
CEFOTAXIME	✓	✓	✓	✓	✓	✓	✓	✓	X	X	█	X
CEFTRIAXONE	✓	✓	✓	✓	✓	✓	✓	✓	X	X	X	█

AVOID ALL beta-lactam antibiotics if:

- Delayed beta-lactam antibiotic allergy causing:
 - interstitial nephritis
 - hepatitis
 - hemolytic anemia
- Delayed severe skin allergic reactions:
 - Stevens-Johnson syndrome
 - toxic epidermal necrolysis
 - exfoliative dermatitis
 - acute generalized exanthematous pustulosis (AGEP)
 - drug reaction with eosinophilia and systemic symptoms (DRESS)

LEGEND:	
Penicillins	
1st Generation Cephalosporins	
2nd Generation Cephalosporins	
3rd Generation Cephalosporins	
✓	Different structure. CONSIDERED SAFE TO PRESCRIBE
X	Evidence of cross reaction. DO NOT PRESCRIBE

* Applies to beta-lactamase inhibitor combinations (amoxicillin-clavulanate and piperacillin-tazobactam)

References:

1. Bugs and Drugs. <http://bugsanddrugs.org/>
2. NICE Antimicrobial Prescribing Guidelines. <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/antimicrobial-prescribing-guidelines>
3. Chow AW et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. Clin Infect Dis. 2012;54:e72. <https://doi.org/10.1093/cid/cir1043>
4. Metlay JP et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019;200:e45. <https://doi.org/10.1164/rccm.201908-1581st>
5. Bratzler DW et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70:195. <https://doi.org/10.2146/ajhp120568>
6. Solomkin JS et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. Clin Infect Dis. 2010;50:133. <https://doi.org/10.1086/649554>