

Antimicrobial Stewardship Backgrounder

Avoid Fluoroquinolones as First-line Therapy

BOTTOM LINE: Due to increasing rates of resistance, risk of rare but serious disabling adverse effects, and significant association with *Clostridioides difficile* infection, fluoroquinolone (FQ) use should be limited or avoided as a first-line antimicrobial choice for common bacterial infections. FQ use should be focused towards culture and susceptibility confirmed infections where the benefit of a FQ outweighs these risks.

Background:

FQs - ciprofloxacin, levofloxacin, moxifloxacin - are broad-spectrum antibacterial drugs commonly used to treat urinary tract, respiratory, and intra-abdominal infections.

Health Canada, the US Food and Drug Administration (FDA), and the European Medicines Agency (EMA) have each issued safety warnings about rare but potentially disabling and persistent adverse effects caused by FQs, including the following¹⁻⁵:

- Cardiovascular: QTc prolongation (moxifloxacin > levofloxacin > ciprofloxacin)⁶, aortic aneurysm/dissection, aortic regurgitation, arrhythmias
- Metabolic: hypoglycemia, hyperglycemia
- Musculoskeletal: tendonitis, Achilles tendon rupture
- Neurological: neuropsychiatric disturbances, anxiety, depression, seizures, delirium, peripheral neuropathy
- Other: retinal detachment

Avoid use of FQs in patients with, or at high risk of, these conditions.

FQs are also associated with an increased risk of altering the microbiome, and resultant *Clostridioides difficile* infection (CDI)^{7,8}: moxifloxacin (3.39) >ciprofloxacin (1.90) >levofloxacin (1.55) >norfloxacin (1.09, NS) (adjusted relative risk compared to no antibiotic)⁷

Susceptibility data from Alberta 2020 antibiograms⁹:

- On average, 30% of *Escherichia coli* isolates are resistant to ciprofloxacin in Alberta (ranges from 20-41% resistant depending on specimen type, hospital, setting).
- Although *Streptococcus pneumoniae* susceptibility to levofloxacin remains high at ~95-100%, amoxicillin and ceftriaxone have similar susceptibility rates with fewer potential risks.

Antibiotic utilization data from the Tracked Prescription Program (TPP) Alberta Antibiotic Prescription Atlas 2016-2020¹¹:

- Despite not being recommended as first-line empiric therapy, ciprofloxacin and levofloxacin remain among the most commonly prescribed antibiotic agents in the community setting in Alberta.
- In 2020, ciprofloxacin was the 6th most prescribed antibiotic.

Optimizing Use of FQs:

- Due to increasing resistance of common bacterial isolates, the potential for rare but disabling adverse effects, and increased risk of CDI, FQs should be avoided as first-line therapy. FQs should be reserved for use only in patients who have no other effective and safer treatment options.
- The table below summarizes preferred empiric first-line and alternative treatment options for several common infections in adult patients. Therapy may need to be adjusted based on culture & susceptibility results.

- Microbiology labs in the province will soon be changing the susceptibility reporting for urinary isolates of *Escherichia coli*, *Proteus mirabilis*, and *Klebsiella spp.* (excluding *K. aerogenes*):
 - If other agents also test as susceptible, the following comment will be added, and ciprofloxacin will not be reported: *Ciprofloxacin is not routinely reported, given the potential for significant adverse events and increasing antimicrobial resistance.*
 - If the urinary isolate is resistant to ciprofloxacin, this result will be reported.

- If a FQ is being considered for use, the risks and benefits should be weighed, discussed with the patient, and the consent discussion documented in the patient's medical record¹².

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Empiric Therapy of Urinary Tract, Respiratory, and Intra-abdominal Infections in Adults – Avoiding FQs¹⁰

See www.bugsanddrugs.org for more details.

		First-line	Second-line/Alternative	
Urinary	Uncomplicated cystitis (no systemic features or functional/structural GU abnormalities)	Nitrofurantoin (if CrCl >40mL/min)	Cephalexin OR Cefixime OR TMP-SMX Fosfomycin – reserve for ESBL-producing isolates	
	Complicated*** lower UTI	Cefixime OR Amoxicillin-clavulanate*	TMP-SMX OR Ciprofloxacin	
	Complicated*** upper UTI OR Uncomplicated pyelonephritis	Initial IV: Ceftriaxone OR Gentamicin x 1-3 dose(s) then switch to oral therapy as per susceptibility results; choose an agent other than a FQ whenever possible		
Respiratory	Acute bacterial sinusitis	Amoxicillin*	Cefuroxime axetil OR Doxycycline	
	Acute otitis media	Amoxicillin*	Cefuroxime axetil OR Doxycycline	
	Acute exacerbation of chronic bronchitis (AECB). Antibiotic therapy is recommended if 2 or more of the following are present: ↑ sputum volume, ↑ sputum purulence, ↑ dyspnea			
	< 4 exacerbations per year	Amoxicillin* OR Doxycycline OR TMP-SMX	Amoxicillin-clavulanate* OR Cefuroxime axetil	
	≥ 4 exacerbations per year	Amoxicillin-clavulanate* OR Cefuroxime axetil	Azithromycin OR Clarithromycin	
	Community-acquired pneumonia (CAP), Outpatient - Severity based on CRB-65 score**			
	CRB-65=0** (mild)	Amoxicillin*	Doxycycline OR Azithromycin OR Clarithromycin	
	CRB-65=1 or 2** (moderate)	Amoxicillin* OR Amoxicillin-clavulanate*	Cefuroxime axetil	
	Community-acquired pneumonia (CAP), Hospitalized			
	Nonsevere	Ceftriaxone	If CRB-65=1 and significant comorbidity OR CRB-65=2, ADD: Doxycycline OR Azithromycin OR Clarithromycin	
Severe (CRB-65=3 or 4**)	Ceftriaxone AND Azithromycin			
Intra-abdominal	Diverticulitis	(TMP-SMX AND Metronidazole) OR Amoxicillin-clavulanate		
	Appendicitis, complicated (gangrene, perforation, abscess, peritonitis)	Ceftriaxone AND Metronidazole Note: In uncomplicated appendicitis, antibiotics are recommended for surgical prophylaxis, but NOT for empiric therapy.		
	Cholecystitis Note: Antibiotics are not needed for mild cases.	Ceftriaxone +/- Metronidazole	Amoxicillin-clavulanate* IV/PO	
	Acute cholangitis	Piperacillin-tazobactam*	Imipenem	

*Avoid penicillins in patients with severe penicillin allergy. Consider second line/alternative therapy; see [cross-reactivity table](#) in Bugs & Drugs for agents safe to give.

**CRB-65 Pneumonia Severity of Illness Score: 1 point for each of: confusion, RR>30 breaths/min, systolic BP<90mmHg or diastolic BP<60 mmHg, age≥65 years

***Complicated = systemic features or functional/structural GU abnormalities

Abbreviations: BP = blood pressure, CrCl = creatinine clearance, ESBL = extended-spectrum β-lactamase, GU = genitourinary, IV = intravenous, PO = oral, RR = respiratory rate, TMP-SMX = trimethoprim-sulfamethoxazole, UTI = urinary tract infection

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