# Antimicrobial Stewardship Matters

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# Avoid Fluoroquinolones as First-line Therapy

## At a Glance:

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 following[1-5]:

- **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 fluoroquinolones in patients with or at high risk of these conditions.***

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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 antibiograms[9]:

- 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.

## Optimizing use of fluoroquinolones

- 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.
- Table 1 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 and susceptibility results.
- 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 record[12].

**Microbiology labs in the province have changed 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.

## Table 1: Empiric Therapy of Urinary Tract, Respiratory, and Intra-abdominal Infections in Adults – Avoiding FQs[10]

| | | First-line | Second-line/Alternative |
|---|---|---|---|
| Urinary | **Uncomplicated cystitis** (no systemic features or functional/structural GU abnormalities) | Nitrofurantoin (if CrCl >30mL/min) | Cephalexin OR Cefixime OR TMP-SMX<br>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: increased sputum volume, increased sputum purulence, increased 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 |
| | | If CRB-65=1 and significant comorbidity OR CRB-65=2, ADD:<br>Doxycycline OR Azithromycin OR Clarithromycin | |
| | **Community-acquired pneumonia (CAP), Hospitalized** | | |
| | Nonsevere | Ceftriaxone | |
| | | If CRB-65=1 and significant comorbidity OR CRB-65=2, ADD:<br>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<br>Note: In uncomplicated appendicitis, antibiotics are recommended for surgical prophylaxis, but NOT for empiric therapy. | |
| | **Cholecystitis**<br>Note: Antibiotics are not needed for mild cases. | Ceftriaxone +/- Metronidazole | Amoxicillin-clavulanate* IV/PO |
| | **Acute cholangitis** | Piperacillin-tazobactam* | Meropenem |

*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

References are available upon request

See www.bugsanddrugs.org for more details.

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