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AWH Fluoroquinolone FDA Black Box Warning Guidance for Adult Patients

BACKGROUND

The FDA has issued a recent Black Box Warning against the use of fluoroquinolones (e.g., ciprofloxacin, levofloxacin, and moxifloxacin) as first-line treatment for acute sinusitis, acute exacerbation of chronic bronchitis (AECB), and uncomplicated urinary tract infections (uUTI) because the risks for serious side effects including tendinitis, irreversible peripheral neuropathy, and CNS effects do not outweigh the benefits of treatment in these cases.[1] New labeling will be implemented to recommend reserving fluoroquinolone use for those patients with no other treatment options, such as severe Type I IgE-mediated reactions to β-lactams. Therefore, the AWH Antimicrobial Stewardship Program provides the following alternative treatment options listed in **Table 1** below.

RECOMMENDATIONS

Acute Sinusitis[2]

In adults, the majority of acute sinusitis is caused by viral pathogens such as Rhinovirus. When caused by bacteria, *Streptococcus pneumoniae* and *Haemophilus influenzae* are the most likely, followed by *Moraxella catarrhalis*. Antibiotics should be reserved for signs or symptoms lasting for ≥ 10 days without improvement, severe symptoms (fever ≥ 102°F, purulent nasal discharge or facial pain for 3-4 consecutive days) or "double sickening" with improvement after initial onset then fever, headache or increased nasal discharge. Amoxicillin-clavulanate is recommended as first-line therapy due to increasing β-lactamase production by strains of *H. influenzae* and *M. catarrhalis*. Resistance to doxycycline is on the rise in S. pneumoniae, therefore doxycycline should be reserved for use in patients with a severe Type I IgE-mediated hypersensitivity reaction to a β-lactam.

Acute Exacerbation of Chronic Bronchitis (AECB)[3]

At least half of acute exacerbation of chronic bronchitis are caused by bacterial infection. The most likely bacterial pathogens include *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*. Antibiotic use should be reserved for those with severe acute exacerbations with increased cough, sputum volume and sputum purulence. In patients with severe structural lung disease who chronically use cortico-steroids and are frequently exposed to antibiotics, *Pseudomonas aeruginosa* can be a cause of AECB and antipseudomonal agents such as cefepime or piperacillin-tazobactam can be considered as treatment options in place of antipseudomonal fluoroquinolones.

Uncompliated Urinary Tract Infection (uUTI)[4]

The majority of acute uncomplicated cystitis is caused by Escherichia coli, but other Enterobacteriaceae, *Staphylococcus saprophyticus*, and *Enterococcus* can be responsible as well. Antibiotics should be reserved for the treatment of symptomatic uUTI. Treatment of asymptomatic bacteriuria is only recommended for patients who are pregnant or about to undergo urological procedures. Nitrofurantoin and trimethoprim/sulfamethoxazole are considered equivalent for the first-line treatment of uUTI. β-lactams are considered as second-line alternative due to increased relapse rates.

Table 1. Alternatives to Fluoroquinolones for Bacterial Treatment[5]

Agent	Usual Adult Dosage	Cost[a]
Acute Sinusitis		
Amoxicillin/clavulanate	875/125 mg PO bid x 5-7 days	$$
Doxycycline (Severe Type I β-lactam allergy)	100 mg PO bid x 5-7 days	$$
Ampicillin/sulbactam (Severe infection)	1.5-3 g IV every 6 hours x 5-7 days[b]	$$$
AECB		
Doxycycline	100 mg PO bid x 5-7 days	$$
Amoxicillin/clavulanate	875/125 mg PO bid x 5-7 days	$$
Acute Uncomplicated Cystitis		
Trimethoprim/sulfamethoxazole	160/800 mg PO bid x 3 days	$
Nitrofurantoin monohydrate/macrocrystals	100 mg PO bid x 5 days	$$

[a]Approximate wholesaler acquisition cost (WAC) for generic product for 7 day course for acute sinusitis and AECB. For UTI cost is for recommended course. Costs approximated based on the following scale. $ = less than $20; $$ = $20-$100; $$$ = more than $100.
[b]When able, transition to PO amoxicillin/clavulanate to complete course.

REFERENCES

1. FDA Drug Safety Communication. http://www.fda.gov/Drugs/DrugSafety/ucm500143.htm. Accessed Nov 8, 2016.
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4. Gupta K, et al; Infectious Diseases Society of America; European Society for Microbiology and Infectious Diseases.. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011;52(5):e103-20.
5. Alternatives to Fluoroquinolones. *JAMA*. 2016;316(13):1404-140.

November 2016

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