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AAP report details use of fluoroquinolones in children

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The Academy has released an updated clinical report regarding the use of fluoroquinolones in children that details new data available since the 2011 report was published and spotlights the indications, adverse event profile and practical prescribing information relevant to pediatricians.

The Use of Systemic and Topical Fluoroquinolones, from the AAP Committee on Infectious Diseases, is available at <http://bit.ly/2e9Pz9J> and will be published in the November issue of *Pediatrics*.

Fluoroquinolones represent a class of antibiotics that are used topically or systemically to treat a broad spectrum of bacterial infections. The most commonly prescribed fluoroquinolones approved by the Food and Drug Administration (FDA) include:



- ciprofloxacin, which provides broad gram-negative coverage;
- levofloxacin, which provides gram-positive, gram-negative, mycobacterial and atypical bacterial coverage; and
- moxifloxacin, which provides gram-positive, gram-negative, anaerobic and mycobacterial coverage.

Despite their broad spectrum of activity, fluoroquinolones are prescribed infrequently in children when compared to adults. Outlined here are the current FDA-approved indications for fluoroquinolones in children, updated information concerning safety and efficacy, and pediatric infections for which a fluoroquinolone may be considered for treatment.

Concerns for safety have limited fluoroquinolone use in children. They remain a drug of choice for specific indications and should not be used if an alternative agent is available.

The only FDA-approved indications for systemic use of ciprofloxacin in children are inhalation anthrax, plague, complicated urinary tract infections and pyelonephritis. Levofloxacin is FDA approved for inhalation anthrax and plague in children.

The restricted use in children is due to concerns of adverse effects, primarily based on the toxicity profile observed in animal studies involving canine puppies and quinolone exposure. Arthrototoxicity resulting in cartilage damage has been observed in young animals, prompting concern of similar toxicities in children. However, pediatric studies have not demonstrated an increase in long-term musculoskeletal adverse effects as compared



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to alternative antibiotics, though an increase in short-term arthropathy that resolves following cessation of the drug has been observed. Achilles tendon rupture, a rare complication associated with fluoroquinolone use in adults with chronic medical conditions, has not been reported in children.

Post-marketing reports of fluoroquinolone side effects involving the tendons, muscles, joints and central nervous system events resulted in the release of a revised *boxed warning* for systemic fluoroquinolones in July 2016 by the FDA (<http://bit.ly/2dFyskr>). The updated warning recommends restriction of fluoroquinolone antibiotics for routine use in certain uncomplicated infections, i.e., acute sinusitis, acute bronchitis (which should not be treated with antibiotics in general) or uncomplicated urinary tract infections, due to the risk of potential disabling side effects.

Fluoroquinolones also have been associated with the development of bacterial resistance and *Clostridium difficile*-associated diarrhea. The benefits of the fluoroquinolones (e.g., broad spectrum of activity and high oral bioavailability) and the risks of potential undesired side effects must be considered at the point of prescribing.

Clinical indications in which fluoroquinolones may be considered in children

Fluoroquinolones are not indicated as first-line systemic therapy in children. However, in cases where there are no reasonable alternatives due to multidrug-resistant pathogens or when an oral antibiotic is deemed optimal, fluoroquinolones may be considered.

The use of levofloxacin can be considered for the treatment of upper and lower respiratory infections when the history of a severe allergic reaction precludes the use of standard therapy such as amoxicillin or when a multidrug-resistant pathogen is implicated.

When an alternative antibiotic is unavailable based on bacterial resistance or formulation options, ciprofloxacin is a viable option in the setting of gastrointestinal infections due to *Salmonella* or *Shigella*. However, due to rising fluoroquinolone resistance among enteric pathogens, antimicrobial susceptibilities should be confirmed.

The use of a fluoroquinolone for the first-line treatment of complicated urinary tract infections or pyelonephritis caused by a multidrug-resistant gram-negative pathogen is indicated in children older than 1 year of age if a non-fluoroquinolone agent cannot be used based on susceptibility data or allergy history.

Several topical fluoroquinolones are approved for treatment of bacterial conjunctivitis and otitis externa. Overall, topical fluoroquinolones are safe and well-tolerated.

Practical prescribing of fluoroquinolones to children

When prescribing a fluoroquinolone to a child or adolescent, the clinician should review the risks and benefits of using this class of antibiotic with caregivers and patients, including instruction to contact their health care provider if they experience serious side effects, including rash, diarrhea, joint or tendon pain, confusion, or numbness or tingling of extremities while taking the antibiotic. Fluoroquinolones generally are well-tolerated and effective. They do have an important, albeit limited, role in treating children with infection.

Dr. Jackson is an ex officio member of the AAP Committee on Infectious Diseases and associate editor of the 2018 AAP Red Book. Dr. Goldman is assistant professor of pediatrics, Divisions of Pediatric Infectious Diseases and Clinical Pharmacology, Children's Mercy Hospitals and Clinics, Kansas City, Mo.