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A new **PedJobs** has arrived

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## NEWS AND FEATURES

# Pediatric study compares ciprofloxacin, cephalosporin for UTI

from the AAP Priority Drugs and Pediatric Labeling Education Project Advisory Committee

*This is another in a series of AAP News articles that highlights new pediatric labeling based on the results of pharmaceutical clinical trials.*

The Food and Drug Administration (FDA) has approved new labeling for Cipro (ciprofloxacin) based on the results of pediatric safety studies.

Ciprofloxacin was approved for treatment of complicated urinary tract infections (cUTI) and pyelonephritis in pediatric patients ages 1 to 17 years, though not as a first-line agent. This second-line status is based on the higher rate of any adverse events (including joint-related adverse events) compared to the control.

To address concerns about the potential for arthropathy in pediatric patients, Bayer Pharmaceuticals (the manufacturer of Cipro) performed a randomized, controlled safety study in pediatric patients ages 1 through 16 years with cUTI or pyelonephritis. The study compared the use of IV/oral ciprofloxacin to IV ceftazidime/oral cefixime. The study compared the rates of arthropathy occurring by six weeks from the start of treatment in the ciprofloxacin and control patients. An independent pediatric safety committee (IPSC) reviewed the records of patients with musculoskeletal adverse events and decided whether the case represented possible arthropathy.

The study was designed to determine whether the rates of arthropathy were the same for ciprofloxacin and cephalosporin treatment. Equivalence was defined as having an upper bound of the confidence interval for the difference in the rate of arthropathy no greater than 6%. In other words, ciprofloxacin would be considered the same as the cephalosporin treatment if the study showed that the difference in arthropathy rates between the two arms could not be more than 6%.

Arthropathy as judged by the IPSC was reported in 31 of 335 (9.3%) ciprofloxacin patients and 21 of 349 (6%) cephalosporin patients. The difference in rates was 3.3% (95% CI, -0.8%, 7.2%). The rate of arthropathy with ciprofloxacin treatment was not equivalent to that seen with cephalosporin treatment. However, most cases of arthropathy

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were mild or moderate in severity and had resolved by the one-year followup visit.



The IPSC definition of a possible event was fairly broad, accounting for higher than expected rates of arthropathy in both treatment arms. The rate of all adverse events was 41% in ciprofloxacin patients and 31% in cephalosporin patients. The most frequent events for ciprofloxacin-treated patients were gastrointestinal (diarrhea, vomiting and abdominal pain).

Clinical response rates were similar (95.7% vs. 92.6%) for both treatment groups. The dose of IV ciprofloxacin was 6-10 mg/kg (maximum 400 mg/dose) every eight hours. The dose of oral ciprofloxacin was 10-20 mg/kg (maximum 750 mg/dose) every 12 hours. Patients in the trial were treated for 10 to 21 days.

Overall, these results show that the clinical response was similar whether ciprofloxacin or the cephalosporin was used, but the rate of adverse events was higher for ciprofloxacin patients. These results suggest that initial treatment of cUTI with ceftazidime and/or cefixime would be as effective as ciprofloxacin, but specific circumstances may warrant treatment with ciprofloxacin.

The study did not include patients younger than 1 year of age, so the risk of arthropathy for infants still is unclear.

Additional information also is needed about whether athletes or other groups may be at higher risk for joint problems. The label does include a note about an adolescent female who stopped ciprofloxacin for wrist pain and was shown to have an ulnar cartilage tear. She was diagnosed with overuse syndrome secondary to sports injury, but a contribution from ciprofloxacin could not be excluded. She recovered without surgical intervention.

Practitioners who identify joint problems in pediatric patients treated with ciprofloxacin, other fluoroquinolones or any other therapeutic agent are encouraged to report these adverse events to MedWatch ([www.fda.gov/medwatch/index.html](http://www.fda.gov/medwatch/index.html)).

More information about the pediatric study of ciprofloxacin is available at [www.fda.gov/cder/pediatric/Summaryreview.htm](http://www.fda.gov/cder/pediatric/Summaryreview.htm). This site provides summaries of medical and clinical pharmacology reviews for ciprofloxacin and other drugs granted exclusivity.

*Disseminating information about new drug labeling is an objective of the AAP/FDA contract, Priority Drugs and Pediatric Labeling Education Project. The AAP Committee on Drugs (COD) is the Project Advisory Committee (PAC) for this initiative. For more information about this project, contact Sheryl Nelson at [ssnelson@aap.org](mailto:ssnelson@aap.org) or (800) 433-9016, ext. 7103.*

## Web sites highlight label changes

The drug described in this article, ciprofloxacin, is one of many with new labeling based on pediatric studies. Recent legislation has allowed the Food and Drug Administration (FDA) to offer incentives (exclusivity) to companies that perform pediatric studies. The cumulative list of drugs granted exclusivity with labeling changes that resulted from pediatric exclusivity studies is available on the FDA Web site at [www.fda.gov/cder/pediatric/labelchange.htm](http://www.fda.gov/cder/pediatric/labelchange.htm). This site highlights the changes made to the labels only from exclusivity.

The label may have been updated recently for other reasons. The Drugs@FDA Web site at [www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm](http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm) gives electronic access to the most recent label changes.

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