FDA Panel Rejects Gemifloxacin for Sinusitis

BY ELIZABETH MECHCATIE
Senior Writer

GAITHERSBURG, MD. — A Food and Drug Administration advisory panel has recommended against approving the fluoroquinolone gemifloxacin for treating acute bacterial sinusitis, because of the noninferiority design of the studies submitted for approval and concerns about the increased rate of rashes associated with the drug in clinical trials and since approval.

At a meeting in September, the FDA's Anti-Infective Drugs Advisory Committee voted 11 to 2 that the safety and effectiveness data presented did not demonstrate an acceptable risk-benefit profile of a 5-day course of gemifloxacin for treating acute bacterial sinusitis (ABS). Panelists recommended that effectiveness should be shown in a placebo-controlled superiority trial; several panelists thought the drug had potential as a second-line treatment for ABS and also recommended studying gemifloxacin for ABS treatment failures. The FDA usually follows the advice of its advisory panels.

Two panelists said that based on the previous standard of noninferiority studies, they believed the drug had been shown to be effective, but they voted no because placebo-controlled trials are now considered the standard for approval. Among the panel's concerns about rashes were that the appearance of a rash would lead to testing and treatment, and that patients would be labeled as "quinolone sensitive" and would no longer be considered for quinolone treatment.

Gemifloxacin, an oral broad-spectrum fluoroquinolone marketed as Factive by Oscient Pharmaceuticals, was approved in 2003 for treating mild to moderate community-acquired pneumonia (CAP) due to *Streptococcus pneumoniae* (including multidrug-resistant strains), *Hemophilus influenzae*, *Moraxella catarrhalis*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Klebsiella pneumoniae* and for treating acute bacterial exacerbations of chronic bronchitis (ABECB) due to *S. pneumoniae*, *H. influenzae*, *Hemophilus parainfluenzae*, and *M. catarrhalis*. A 7-day dosing regimen is approved for CAP; a 5-day regimen is approved for the bronchitis indication.

At that time, the FDA did not approve gemifloxacin for ABS, concluding that the benefits did not outweigh the risk of adverse events because of concerns that included the higher rate of cutaneous reactions and because there was no unmet need for treating ABS. Since then, the drug has been prescribed off-label for ABS.

Patients who develop rashes on gemifloxacin could be labeled allergic to all quinolones and would have no access to a quinolone when they needed it.

In another attempt to get gemifloxacin approved for ABS, Oscient provided the four clinical studies of more than 6,500 patients submitted to the FDA previously, new studies of more than 1,000 patients, and postmarketing safety data collected since the drug was approved. The indication under FDA review was for treating ABS due to *S. pneumoniae, H. influenzae, M. catarrhalis, Staphylococcus aureus (*methicillin-susceptible strains only*), K. pneumoniae,* and *Escherichia coli* at a dose of 320 mg once a day for 5 days.

During the advisory panel vote, Dr. Donald M. Poretz, who is in private practice in Annandale, Va., pointed out that antibiotics are overused, sinusitis is overdiagnosed, and plenty of drugs are available to treat bacterial sinusitis. "I'm not sure this would add anything to our armamentarium other than a greater rate of rash," he said, noting that some people who develop rashes on gemifloxacin would be labeled as allergic to all quinolones and would have no access to a quinolone when they needed it.

Dr. Richard Frothingham of the infectious diseases department at Duke University, voted in favor of approval and said he believed that gemifloxacin had been shown to be effective for ABS. He backed approval with the condition that the package insert include more information about the associated rashes. Even if the drug is not approved for ABS, this label—and company detailing to physicians—should clearly indicate that rashes are far more common with gemifloxacin than with comparators, he added, noting that rash is not even listed in the current label. ■

Pages 30a—30b